PHARMACOLOGY-I

UNIT 5 NOTES

DRUGS ACTING ON CNS

- PARKINSON'S DISEASE
- ALZHEIMER'S DISEASE
- CNS STIMULANTS
- NOOTROPICS
- OPOID ANALGESIC
- OPOID ANTAGONIST
- DRUG ADDICTION
- DRUG ABUSE
- DRUG TOLERANCE
- DRUG DEPENDENCE

IMPERFECT PHARMACY

Antipsychotic Agents

Antipsychotic agents are drugs that diminish psychotic symptoms by altering neurotransmission in the brain, primarily through Dopamine (D_2) receptor antagonism or modulation.

Psychosis

- Psychosis is a severe mental disorder in which a person loses contact with reality, leading to distorted thinking, perception, emotions and behaviour.
- It is characterized by symptoms such as delusions, hallucinations and disorganized speech or behaviour.
- Schizoprenia is the most common type of psychotic disorder.

Key Features Of Psychosis

① Delusions - False, fixed beliefs not based in reality (e.g., bilieving someone is plotting against them).

② Hallucinations - Perceiving things that are not present (most commonly auditory, such as hearing voices).

③ Disorganized Thinking / Speech - Incoherent or illogical thought process and communication.

SCHIZOPHRENIA

- Schizophrenia is defined as Splitting of Mind.
- It is a serious psychotic disorder characterised by loss of contact with reality.
- It is a serious mental illness that has an effect on how a person feels, behaves & thinks
- Hallucination & Delusion are major characteristics of Schizophrenia.
- It is more common in men than women.

CAUSES

The exact causes of schizophrenia are not fully understood, but it is believed that many genetic, environmental & biological factors plays a key role in its development:

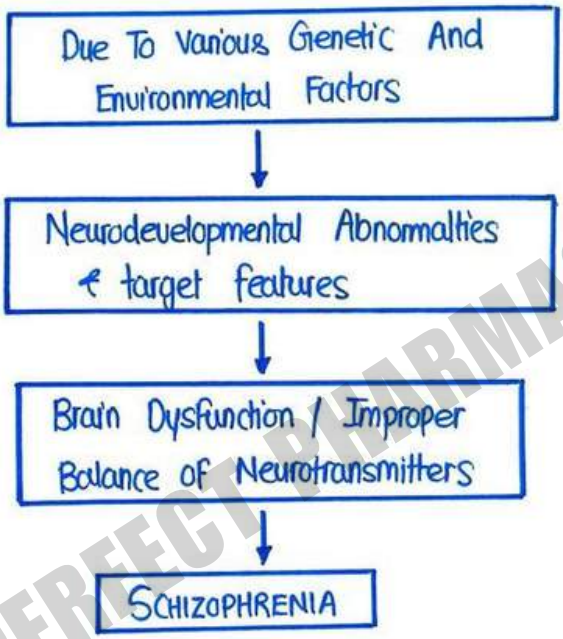
- Prenatal Factors
- Family History
- Social Factors
- Neurotransmitters Imbalance

SYMPTOMS

- Positive Symptoms
  - Hallucinations
  - Delusions
  - Disorganized Speech Behaviour
- Negative Symptoms
  - Emotional Unstableness, Loss of Interest / Motivation

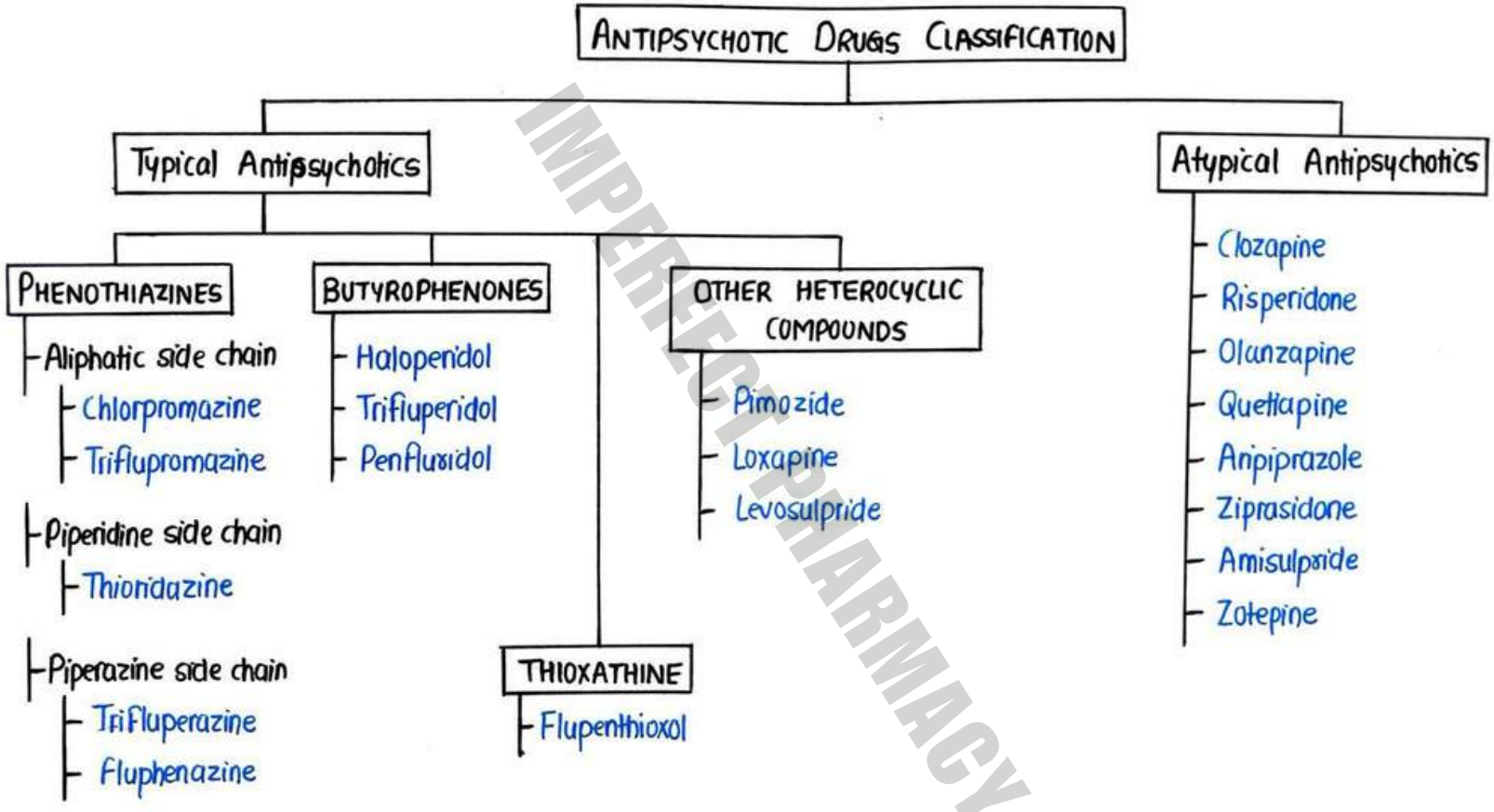
PATHOGENESIS

- The pathogenesis of schezophrenia is not fully understood.
- It involves combination of genetic, neurobiological & environmental factors:
- The Dopamine Hypothesis is one of the most well known theories for the pathogenesis of schizophrenia.
- According to schizophrenia is associated with Hyperactivity of Dopamine in certain pathway due to increased D_2 receptor sensitivity.



TREATMENT

- Pschychotherapy
- Antipsychotic Drugs
- Antidepressants
- Lifestyle Changes.



TYPICAL ANTIPSYCHOTIC AGENTS

- Typical antipsychotic agents are first-generation drugs used to treat psychotic disorders.
- They primarily work by blocking Dopamine (D_2) receptors in the brain, especially in the mesolimbic pathway, reducing positive symptoms of schizoprenia (like hallucinations and delusions).

MOA

- Typical (first-generation) antipsychotics primarily work by blocking Dopamine (D_2) receptors in the brain, particularly in the mesolimbic pathway.
- This antagonism reduces the overeactivity of dopamine, which is thought to contribute to positive symptoms of psychosis, such as hallucinations and delusions.
- In addition to D_2 blockade, many typical antipsychotics also have varying degress of blocking activity at other receptors, including:
  - Noradrenergic receptors
  - Cholinergic (muscarinic) receptors
  - Histaminergic (H1) receptors

PHARMCOKINETICS

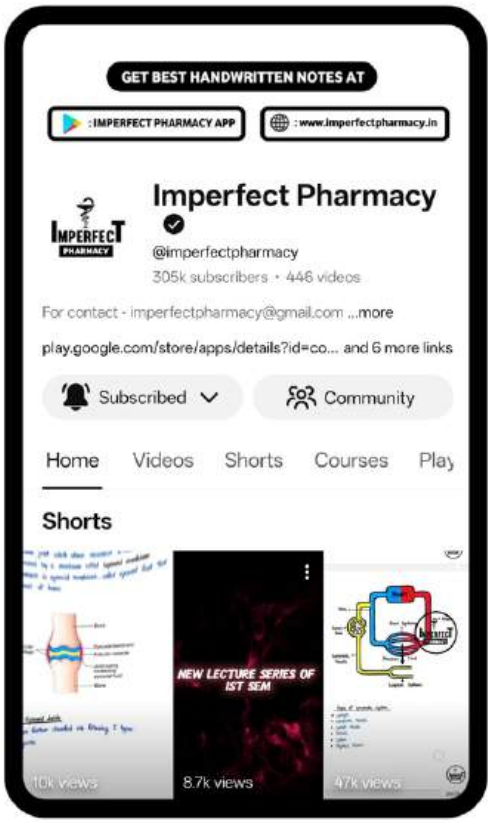
Absorption - Oral; also available in IM/Depot forms.

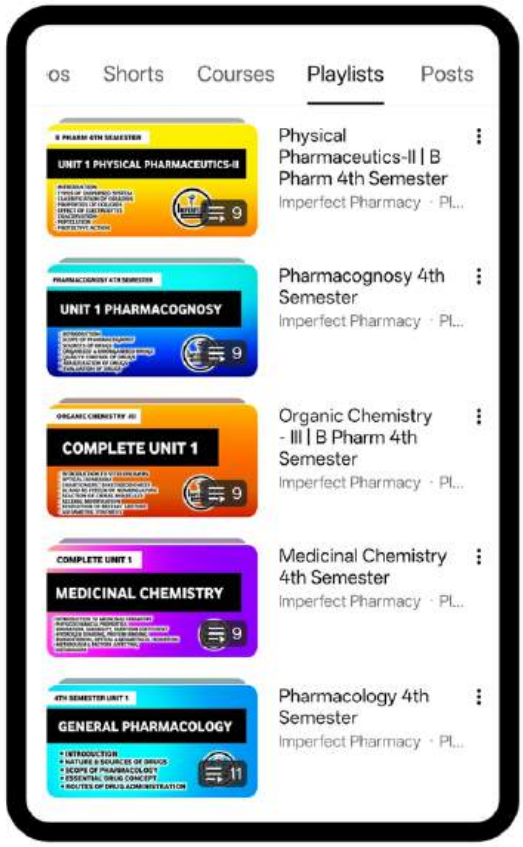
Distribution - Highly lipophilic → accumulate in fat, brain; high protein binding

Metabolism - Liver (CYP450 enzymes); active metabolites possible

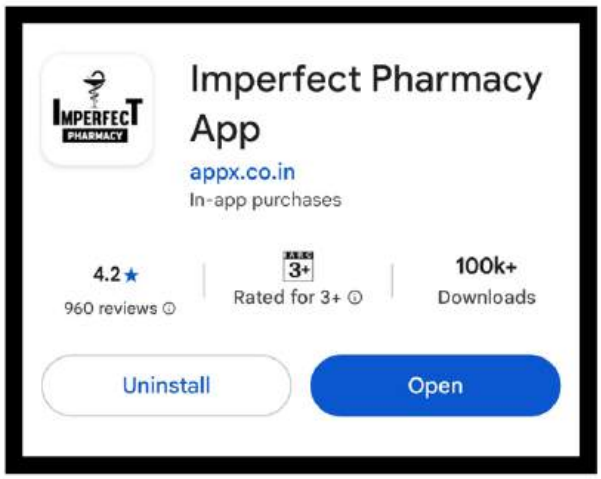
Excretion - Mostly via urine, some feces.

FOR LECTURE VIDEOS VISIT OUR CHANNEL





FOR MORE CONTENT : VISIT OUR APP



Clinical Uses

- Schizoprenia (especially positive symptoms)
- Acute psychosis
- Mania (bipolar disorder)
- Nausea and vomiting (e.g. prochlorperazine)

Adverse Effects

① Extrapyramidal Symptoms (EPS) - Dystonia, Parkinsonism, Akathisia, Tardive dyskinesia

② Neuroleptic Malignant Syndrome (NMS) - Serious life threatening

③ Hyperprolactinemia - Galactorrhea, Amenorrhea, ~~Gity~~ Gynecomastia

④ Sedation - Due to H_1 histamine blockade

⑤ Orthostatic Hypotension - Due to α_1 - adrenergic blockade

⑥ Anticholinergic Effects - Dry mouth, Constipation, Blurred vision, Urinary retention

ATYPICAL ANTIPSYCHOTICS

- Atypical antipsychotics Drugs (also called second- generation) are a class of medications used primarily to treat schizoprenia and bipolar disorder.
- They differ from typical (first - generation) antipsychotics by having:
  - Lower risk of extrapyramidal symptoms (movement disorders)
  - Broader receptor activity, especially targetting serotonin and dopamine receptors.

MECHANISM OF ACTION

Atypical antipsychotics work through dual antagonism:

1. Dopamine D_2 receptor antagonism - Reduces positive symptoms (like hallucinations and delusions) by blocking dopamine receptors in the mesolimbic pathway.

2. Serotonin 5-HT2A receptor antagonism: Helps reduce negative symptoms (like apathy, withdrawl) and lowers the risk of extrapyramidal side effects by modulating dopamine release in the nigrostriatal and mesocostical pathways.

Some atypical antipsychotics also affects other receptors:

- Histamine ⟶ Sedation, weight gain
- Muscarinic ⟶ anticholinergic effects
- α_1 - adrenergic ⟶ orthostatic hypotension

PHARMACOKINETICS

- **Absorption** - Generally well- absorbed orally ; some affected by food (e.g. ziprasidone is better absorbed with food)
- **Distribution** - Highly protein- bound and widely distributed
- **Metabolism** - Extensively metabolized in liver, mainly by CYP450 enzymes.
- **Excretion** - Metabolites are excreted in urine and feces.

USES

- Schizoprenia (Positive & negative symptoms)
- Bipolar disorders (manic and depressive episodes)
- Major depressive disorder (adjunct)

EXAMPLE

- Clozapine
- Risperidone
- Olanzipine
- Aripiprazole
- Ziprasidone etc.

ADVERSE EFFECTS

- Hyperglycemia
- Hypotension
- Dizziness
- Constipation
- Dry mouth
- Tachycardia
- Insomnia etc.

ANTIPARKINSONIAN DRUGS

Antiparkinsonian drugs are medications used to treat parkinson's disease (PD) — a progressive neurological disorder that affects movement due to the deficiency of dopamine in the brain, especially in the substantia nigra.

PARKINSON'S DISEASE

- Caused by degeneration of dopaminergic neurons in the substantia nigra pars compacta.
- Leads to an imbalance between dopamine (↓) and acetycholine (Ach ↑) in the basal ganglia.
- Charactarized by :
  - Tremor (Resting)
  - Rigidity
  - Bradikinesia (slowness of movement)
  - Postural instability

PARKINSON'S DISEASE

- Parkinson's Disease (PD) is a neurodegenerative disorder in which Dopamine producing neurons in a brain structure called Substantia Nigra are damaged & die over time leading to a number of motor problems & mental disabilities.
- It is named on a British Physician Dr. James Parkinson, who first discovered it.
- Parkinson's Disease result from an insufficiency of Dopamine in the brain & thus categorised as movement disorder.
- It is one of the most common progressive movement neurological disorder.
- Symptoms of Parkinson's Disease appears when approxiamately 70% of dopamine producing cells are damaged.

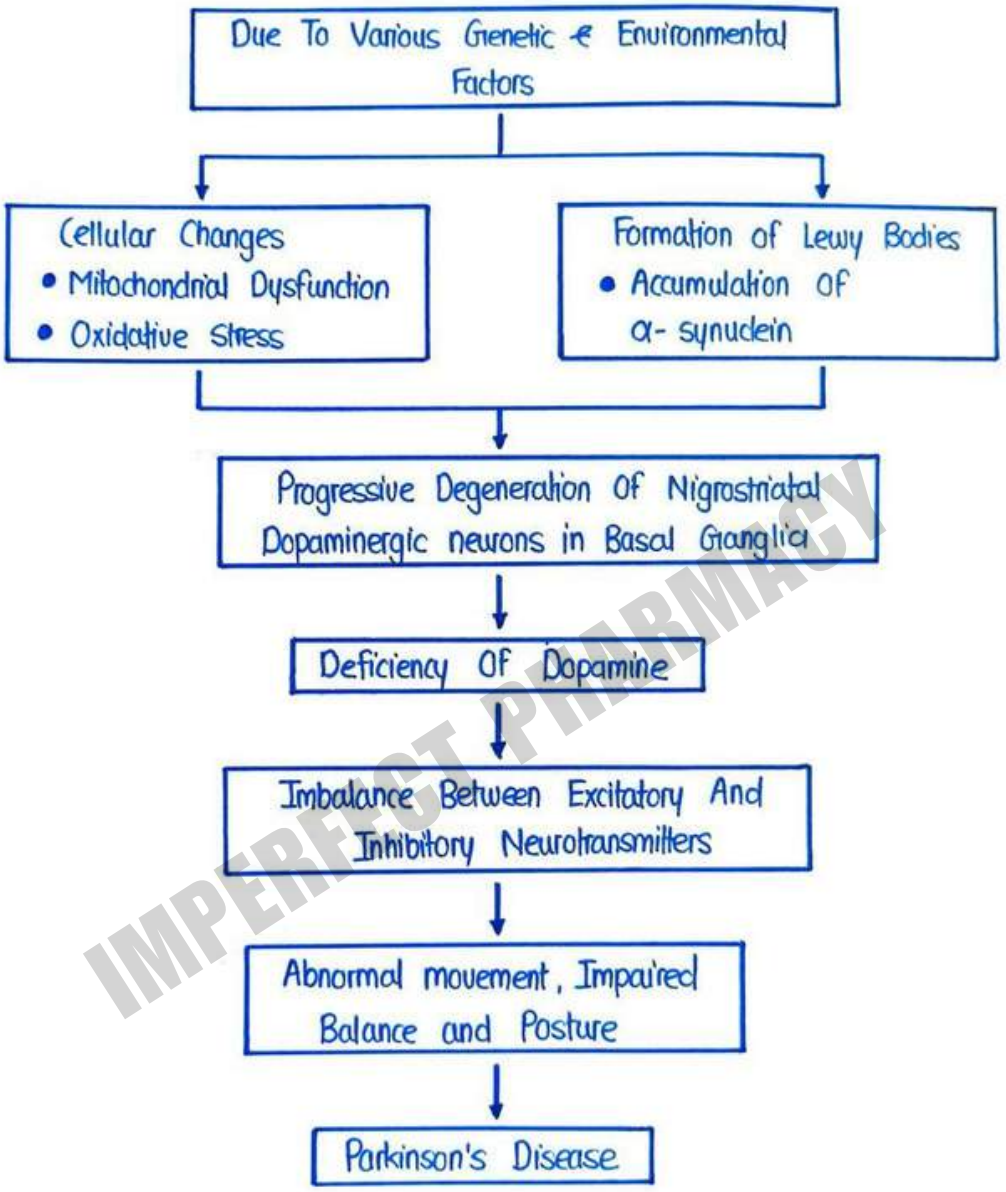
CAUSES / ETIOLOGY

- The major cause of PD is degeneration of neuronal cells in the area called Substantia Nigra lies in Basal Ganglia.
- These neurons produce Dopamine, a neurotransmitter involved in regulating movement & coordination.
- The exact cause of this neuron loss is not fully understood but both Genetic & Environmental Factors are beleived to play a role.

- Genetic Factors
- Mitochondrial Dysfunction
- Neuroinflammation
- Certain Medications
- Head Injury

PATHOGENESIS

The pathogenesis of Parkinson's Disease can be explained as follows :



Symptoms

- Rigidity
- Akinesia
- Tremors
- Posture Instability
- Bradykinesia
- Reduced Facial Expression
- Speech Disorder

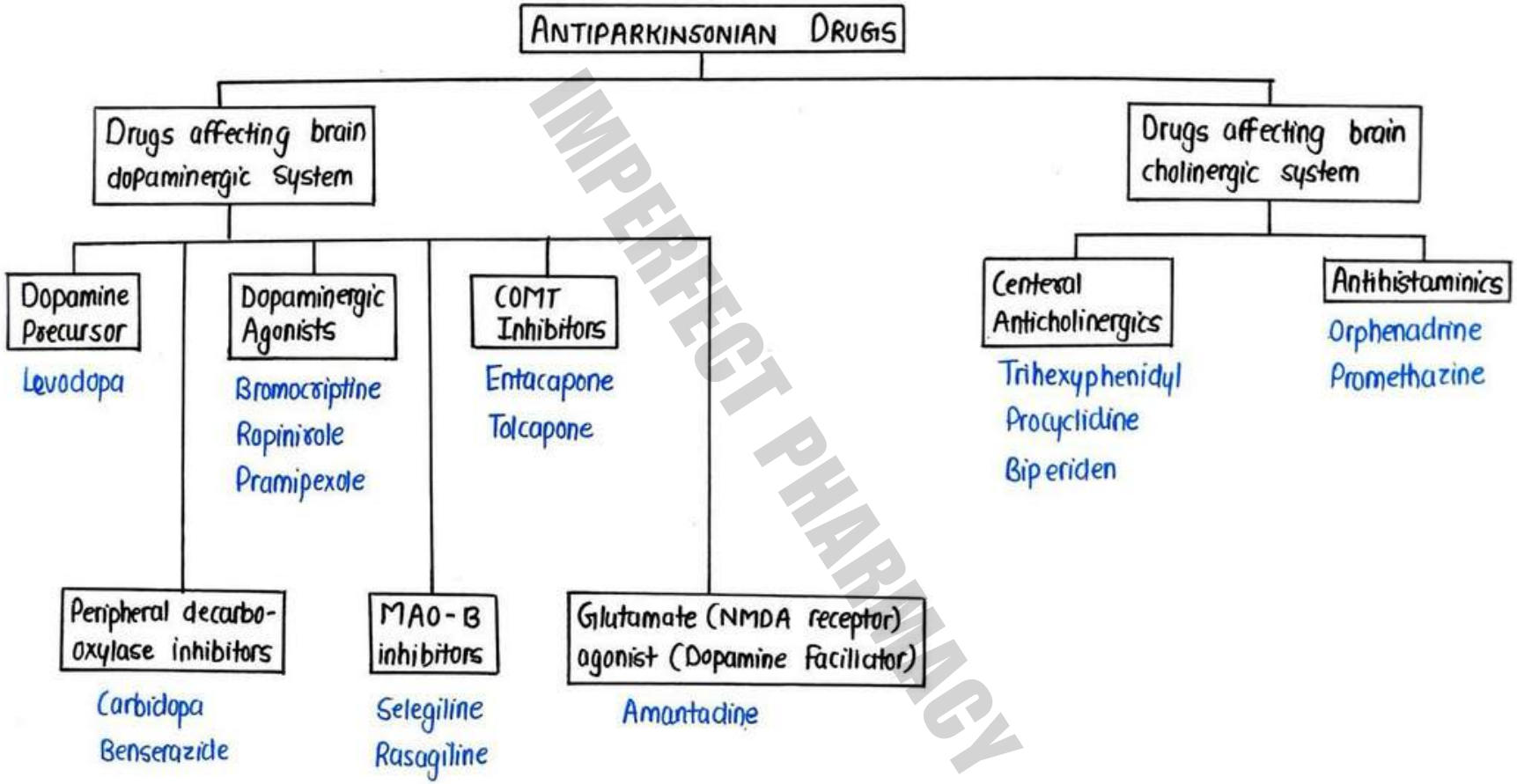
Complications

- Depression / Anxiety
- Social Isolation
- Sleep Disturbances
- Mobility Issues
- Sexual Dysfunction

Treatment

There is no permanent cure for Parkinson's Disease, Treatment is mainly focuses on managing symptoms & improving quality of life.

- Levodopa
- Carbidopa
- Anticholinergic Drugs
- Lifestyle Modifications
- Psychological Support



Drugs Affecting Brain Dopaminergic System

These drugs aim to restore dopamine levels or enhance dopaminergic activity in the brain, which is deficient in Parkinson's disease.

① Dopamine Precursor

Levodopa :
- It is the most effective drug for parkinson's disease.
- It crosses blood brain barrier and is converted to dopamine in brain.
- Administered with a peripheral decarboxylase inhibitor to prevent conversion to dopamine outside the brain (which causes side effects like nausea).

② Peripheral Decarboxylase Inhibitors

Carbidopa, Benserazide :
- Inhibit DOPA decarboxylase in periphery.
- Prevent premature conversion of Levodopa to dopamine outside the CNS.
- Allow more Levodopa to reach the brain → increased effectiveness, reduced side effects.

③ Dopaminergic Agonists

Bromocriptine, Ropinirole, Pramipexole :
- Directly stimulate dopamine receptors in the brain.
- Used as adjuncts to Levodopa or in early-stage parkinson's.
- Useful when Levodopa's effects wears off.

④ MAO-B Inhibitors

Selegiline, Rasagiline:
- Inhibit MAO-B enzyme, which breaks down dopamine in the brain.
- Increases dopamine availability.
- Can be used alone in early stages or with Levodopa.

⑤ COMT Inhibitors

Entacapone, Tolcapone:
- Inhibit COMT enzyme, which metabolizes Levodopa in the periphery and CNS.
- Prolong the effect of Levodopa.
- Often used in combination therapy with Levodopa & Carbidopa.

⑥ Glutamate (NMDA Receptor) Agonist / Dopamine Faciliator

Amantadine:
- Enhances releases of dopamine and inhibits reuptake.
- Also has antiglutamatergic properties (modulates NMDA receptors).
- Used for mild parkinson's or to reduce Levodopa-induced dyskinesia.

Drugs Affecting Brain Cholinergic System

- These drug help restore the balance between dopamine and acetycholine in the brain.
- In Parkinson's disease, dopamine levels are reduced, and acetycholine activity becomes dominant, contributing to symptoms like tremors and rigidity.
- These drugs inhibit cholinergic acitivity (i.e., they have anticholinergic effects).

① Central Anticholinergics

- These drugs block muscarinic acetylcholine receptors in the CNS, especially in the striatum, helping to reduce tremors and muscle rigidity.
- Ex - Trihexyphenidyl, Procyclidine, Biperiden etc.

Mechanism : Blockade of central muscarinic receptors ⟶ reduces excitatory cholinergic tone ⟶ restores balance with dopamine.

Indications :
- Mainly used in younger patients for tremor-predominant Parkinson's.
- Less effective on bradykinesia.

Side effects :
- Dry mouth
- Blurred vision
- Constipation
- Urinary retention
- Confusion or memory loss etc.

② Antihistaminic With Anticholinerngic Activity

- These drugs are H_1 antihistamines that also have centeral anticholinergic properties, making them useful in mild parkinsonism or drug-induced extrapyramidal symptoms (EPS).
- Ex-
  - Orphenadrine
  - Promethazine

Mechanism : They block centeral muscarinic receptors in addition to histamine H_1 receptors, thus reducing tremors and stiffness.

Uses :
- Milder cases of Parkinsonism
- Drug-induced Parkinson-like side effects (eg. due to antipsychotics)

Side effects :
- Sedation (due to antihistaminic effect)
- Dry mouth, Dizziness, Blurred vision (due to anticholinergic effect)

ALZHIEMER'S DISEASE

- Alzheimer's Disease is an irreversible, progressive neurodegenerative disease in which there is a loss of intellectual functions & memory of the patient.
- It is the most common cause of Dementia.
- It was first introduced by Alois Alzheimer in 1907.
- It commonly occurs in older age.
- Alzheimer's Disease typically worsen over time, patient slowly lose his memory, thinking ability & eventually interfares with person's ability to carry out simple tasks.

CAUSES

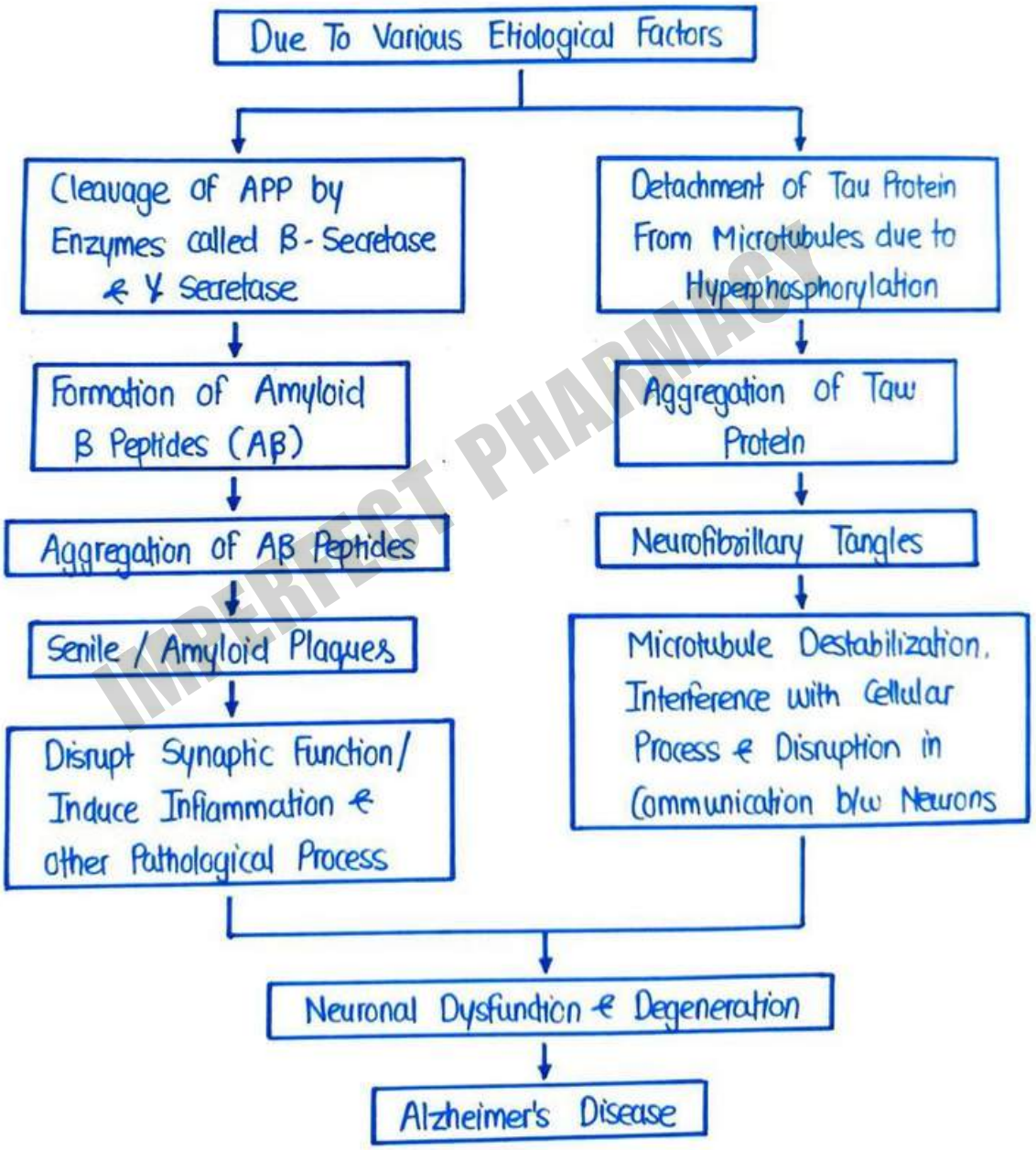
The exact causes of Alzheimer's Disease are not fully understood but several factors are believed to contribute to its development as follows:

- Genetic Factors
- Downsyndrome
- Family History
- Age
- Brain Trauma
- Viral Infections
- Myocardial Infarction
- Hypertension
- Smoking
- Obesity
- Diabetes

PATHOGENESIS

There are two major pathogenic changes are seen in Alzheimer's Patient through which we can explain its pathogenesis, although its not fully understood how they cause Neurodegeneration.

① Senile Plague : Accumulation of β-Amyloid Protein
② Neurofibrillary Tangles : Tangles of Tau Protein



Symptoms

- Loss of Memory Function
- Poor Judgement
- Confusion
- Changes in Mood / Behaviour
- Depression / Anxiety

Complications

- Inability to Perform Daily Task
- Loss of Mobility
- Malnutrition / Dehydration
- Pneumonia
- Death

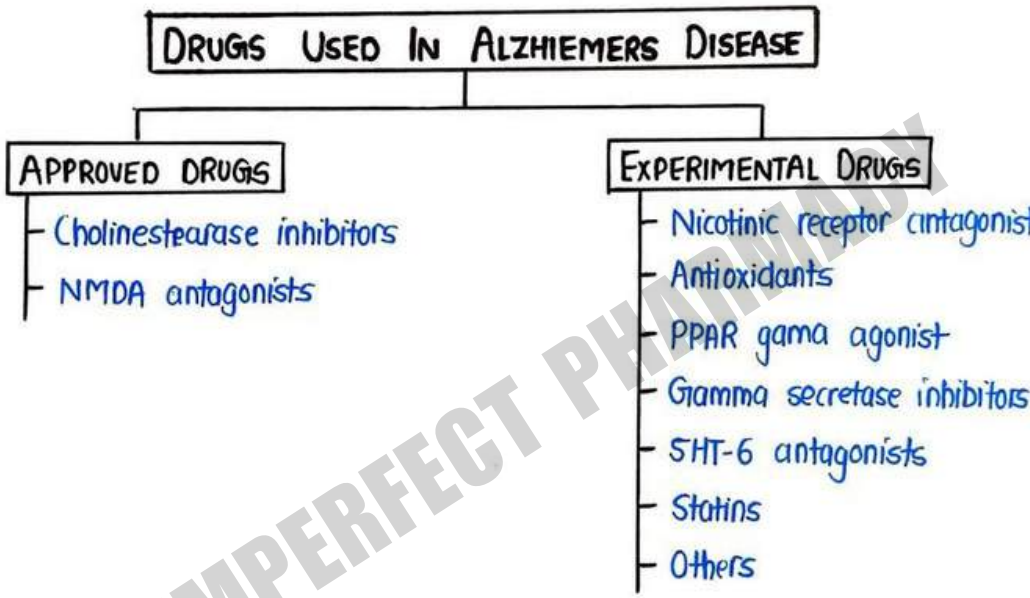
Treatment

There is no permanent cure for this disease, treatment is mainly focuses on managing symptoms & slowing down progression.

- Cholinesterase Inhibitors
- Memantine (NMDA receptor agonist)
- Counselling Therapy
- Lifestyle Medications

ANTIALZHIEMER DRUGS

Antialzhiemer drugs are a class of drugs used to treat symptoms or slow the progression of Alzhiemer's disease, a neurodegenerative disorder charactarized by progressive memory loss, cognitive decline, and behaviour changes.



① CHOLINESTERASE INHIBITORS

- Cholinesterase inhibitors are the main drugs used in the early stages of Alzhiemer's disease.
- In Alzhiemer's, there is a deficiency of acetycholine, a brain chemical important for memory and thinking.
- These drugs increase acetylcholine levels and help improve symptoms.

Mechanism of Action (MOA)

- These drugs inhibits the enzyme acetycholinesterase, which normally breaks down acetycholine.
- As a result, acetylcholine leves increase in the brain.
- This helps in improving cognitive functions like memory, attention and learning.

Pharmacokinetics

DRUG	ABSORPTION & ROUTE	METABOLISM
Donepezil	Well absorbed orally	Liver (CYP450 enzymes)
Rivastigmine	Oral & transdermal patch	By esterases (non - CYP)
Galantamine	Oral	Liver (CYP450)

Therapeutic Uses

- Used in mild to moderate Alzhiemer's disease.
- Donepezil is also used in severe stages.
- May help improve memory, daily activities, and delay worsening.

Adverse Effects

- Nausea, Vomiting, Diarrhea
- Dizziness and Headache
- Muscle cramps, fatigue
- Bradycardia (slow heart rate)
- Insomnia (sleep disturbance)

② NMDA Receptor Antagonist

- Memantine is the main drug in this class.
- It is used in moderate to sever Alzhiemer's disease.
- In AD, excess glutamate overstimulates neurons, leading to cell damage (excitotoxicity).
- Memantine helps protect brain cells.

Mechanism of action (MOA)

- Memantine blocks NMDA receptor, which are activated by Glutamate.
- This prevents overstimulation and protects neurons from damage.
- It helps to slow the progression of Alzhiemer's and may improve memory and behaviour.

ADME

- Given orally, well absorbed.
- Low liver metabolism.
- Excreted unchanged in urine.
- Moderate half-life (~ 60 - 80 hrs).

Uses

- Moderate to severe Alzhiemer's disease.
- Often used alone or with cholinesterase inhibitors for better results.

Adverse effects

- Dizziness, Headache
- Confusion
- Constipation
- Rarely: Hallucinations, Agitation etc.

Example

- Mirtazapine
- Bupropion
- Trazodone
- Atomoxetine etc.

DEPRESSION

- Depression is defined as Mood Disorder that causes a persistent feeling of sadness & loss of interest.
- It is a very common but serious mental illness.
- It is a significant risk for suicide.
- It affect how you think, feel & handle daily activities, often resulting in emotional & physical problem.

TYPES OF DEPRESSION

There are several types of depression recognized by mental health professionals as follows:

① Major Depressive Disorder
② Persistent Depressive Disorder
③ Bipolar Disorder
④ Seasonal Affective Disorder
⑤ Psychotic Depression
⑥ Postpartum Depression
⑦ Premenstrual Depression

① MAJOR DEPRESSIVE DISORDER

- It is a serious & most common type of depression.
- It is characterized by persistent feeling of sadness, hopelessness & loss of interest in daily activities.

② Persistent Depressive Disorder

- It is a chronic form of depression lasting for at least 2 years.
- Symptoms of PDD is a milder compare to MDD but persistent over a longer period.

③ Bipolar Depression

- It is also known as Maniac Depressive Illness.
- It involves periods of extreme mood swings that includes Emotional Highs (Mania) & Lows (Depression).

④ Seasonal Depression

- It typically occurs during winter months when natural sunlight is reduced.
- It typically gets away with spring & summer.

⑤ Psychotic Depression

- It includes severe depressive symptoms along with psychotic features such as Hallucination (seeing or hearing things that aren't there) or Delusions (strongly held false beliefs).

⑥ Postpartum Depression

- It is experienced by some women after giving birth.
- It can occur during pregnancy & upto 1 year after having a baby.

⑦ Premenstrual Depression

- It causes emotional & physical symptoms similar to depression, occurs in the week or before menstruation, it improves after menstruation.

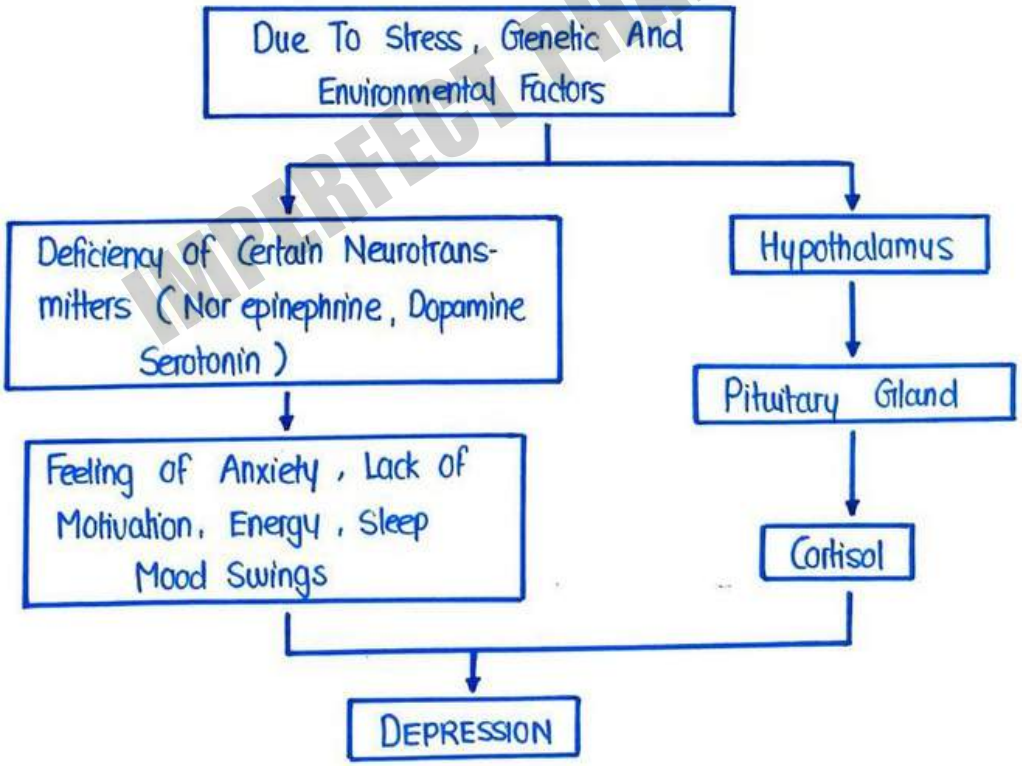
CAUSES

- Genetic Factors
- Imbalance of Neurotransmitters
- Environmental Factors
- Medical Conditions
- Certain Medications
- Social Isolation
- Childhood Trauma

PATHOGENESIS

There are 2 major Hypothesis available to explain pathogenesis of depression

① Monoamine Hypothesis
② Neuroendocrine Hypothesis



Sign & Symptoms

- Persistent Sadness
- Hopelessness
- Lack of Interest
- Feeling of Guilt / Worthlessness
- Sleep Disturbances / Oversleep
- Lack of Confidence
- Low Self Esteem
- Lack of Concentration
- Forgetfullness
- Irritability
- Lack of Energy
- Suicidal Thoughts

Complications

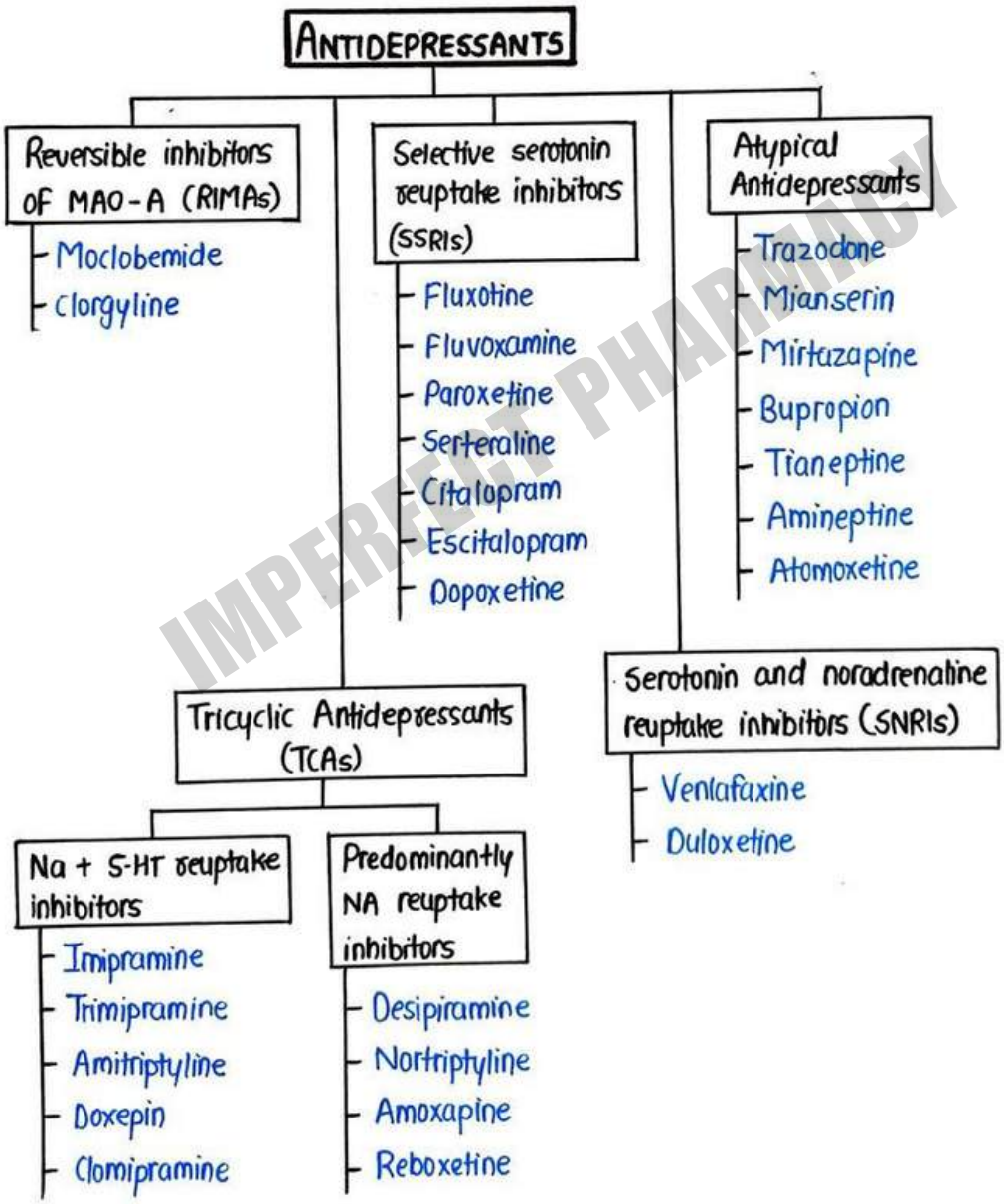
- Suicide
- Social Isolation
- Relationship Issues
- Premature Death

Treatment

- Counselling Therapy
- Antidepressants
- Exercise / Healthy Diet
- Mindfullness
- Social Connections

ANTIDEPRESSANTS

Antidepressant are drugs that help to relieve the symptoms of depressive disorders by correcting chemical imbalances of neurotransmitters in the brain, particularly serotonin, norepinepherine, and dopamine.



① Reversible Inhibitors of MAO-A (RIMAs)

- Older class but improved safety than older MAO inhibitors.
- They reversibly inhibit MAO-A enzymes.
- Example- Moclobemide,

MOA - Blocks MAO-A enzyme ⟶ prevents breakdown of 5-HT & NA ⟶ ↑ levels in brain.

ADME-
- Orally, well absorbed
- Hepatic metabolism
- Short duration due to reversible binding

Uses-
- Atypical depression
- Social Phobia etc.

Adverse effects -
- Less risk of cheese action
- Insomnia
- Dizziness etc.

② Selective Serotonin Reuptake Inhibitors (SSRIs)

- Most commonly prescribed antidepressant.
- Safer and fewer side effects.
- Example - Fluoxetine, Setraline etc.

MOA - Block serotonin (5-HT) reuptake ⟶ increase serotonin in synapse ⟶ improve mood.

ADME -
- Good oral absorption
- Hepatic metabolism
- Fluoxetine has long half-life (taken once daily)

Uses -
- Major depression
- OCD
- Panic disorder
- Anxiety etc.

Adverse effects -
- Nausea
- Sexual dysfunction
- Insomnia etc.

③ Tricyclic Antidepressants (TCAs)

- Oldest class of antidepressants.
- Effective but more side effects.

A.) NA + 5-HT Reuptake inhibitors

Examples - Amitriptyline, Imipramine, Clomipramine etc.

MOA - Block uptake of serotonin + noradrenaline + increased levels

ADME - Lipophilic, oral, hepatic metabolism

Uses - Depression, Nerve pain, enuresis etc.

Adverse effects - Sedation, Dry mouth, Weight gain, Cardiac toxicity etc.

B.) Predominantly NA reuptake inhibitors

Examples - Nortriptyline, Desipramine

MOA - Mainly block norepenepherine reuptake

Same ADME and Uses as above.

Adverse effects - Less sedation, but still anticholinergic effects etc.

④ SEROTONIN - NOREPENEPHRINE REUPTAKE INHIBITORS (SNRIs)

- Modern class, similiar to TCAs but with fewer side effects.
- Examples - Venlafaxine, Duloxetine etc.

MOA - Block reuptake of both 5-HT & NA → increased neurotransmission

ADME -
- Good oral absorption
- Liver metabolism
- Short half-life.

Uses -
- Depression
- Anxiety
- Neuropathic pain (especially duloxetine). etc

Adverse effects -
- Nausea
- Increased blood pressure (venlafaxine)
- Sexual dysfunction etc.

⑤ Atypical Antidepressants

- Atypical antidepressants are group of drugs that treat depression but don't belong to traditional classes like SSRIs, TCAs or MAOIs.
- They have unique mechanisms of action and are often used when first-line drugs are ineffective or not tolerated.

MOA

Drug	Mechanism Of Action
Mirtazapine	α_2 blocker → increases serotonin & NA release
Bupropion	DA & NA reuptake inhibitor
Trazodone	5-HT2 antagonists + weak SSRI + H_1 blocker
Atomoxetine	Selective NA reuptake inhibitor (NRI)

ADME (general)

- Absorbed orally
- Metabolized in liver
- Varies in half-life depending on drug

Uses

- Major depressive disorder.
- Anxiety disorders
- Insomnia (Trazodone) etc.

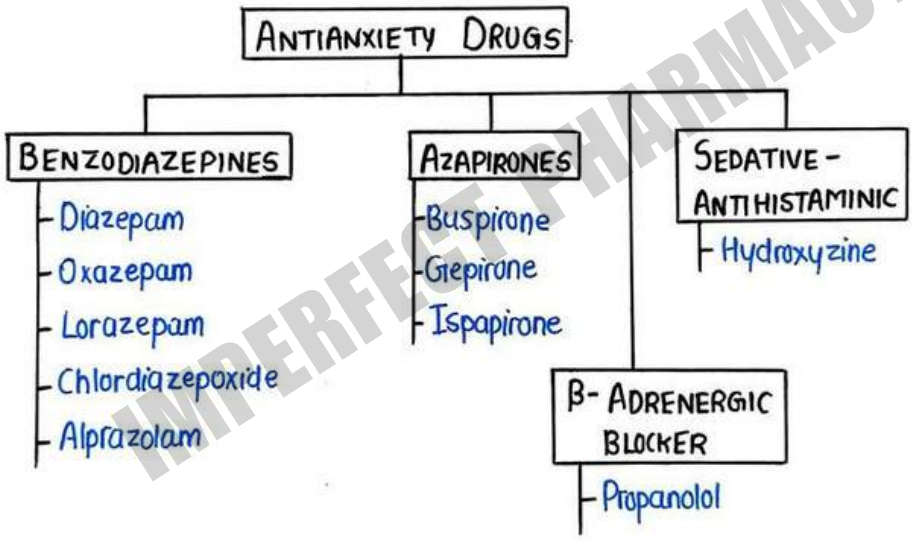
Adverse effects

- Mirtazapine: Sedation, Weight gain
- Bupropion: Insomnia, siezure risk
- Trazodone: Sedation
- Atomoxetine: Appetite loss, Insomnia etc.

ANTIANXIETY DRUGS

Antianxiety drugs, also known as anxiolytics, are group of medication used to reduce or relieve anxiety, tension, nervousness and associated physical symptoms (like restlessness), without causing significant sedation.

CLASSIFICATION



① BENZODIAZEPINES

Examples- Diazepam, Lorazepam, Alprazolam etc.

Mechanism of Action-

- These drugs enhance the effect of GABA (a calming chemical in brain).
- They bind to GABA-A receptors and chloride ion flow increases.
- This cause relaxation and reduces anxiety.

② AZAPIRONES

Example- Buspirone

Mechanism of Action-

- Act as a partial agonist at serotonin 5-HT_1A receptor.
- It helps to balance serotonin levels, which reduce anxiety slowly over time.
- It does not cause sedation or addiction.

③ SEDATIVE ANTIHISTAMINIC

Example- Hydroxyzine

Mechanism of Action-

- Blocks H_1 histamine receptors in the brain.
- This causes sedation and reduces anxiety symptoms.

④ β- ADRENERGIC RECEPTOR

Example- Propranolol

Mechanism of Action -

- Blocks beta (β) receptors in the heart and body.
- Reduces physical symptoms of anxiety like rapid heartbeat, shaking and sweating.

PHARMACOLOGY OF PROPRANOLOL

Class - Non selective β- adrenergic receptor blockers (blocks both β_1 and β_2 receptors)

Mechanism of Action (MOA) -

- Propanolol blocks β_1 receptors in the heart ⟶ decrease heart rate, decrease cardiac output
- Blocks β_2 receptors in lungs and blood vessels
- In anxiety : Reduces physical symptoms like palpitations, tremors, sweating (especially in performance anxiety).

Pharmacokinetics -

Absorption : Well absorbed orally.
Distribution : Lipid soluble ⟶ crosses blood -brain barrier.
Metabolism : Extensive first - pass metabolism in liver.
Excretion : Mainly via urine.

Uses

- Anxiety (Performance anxiety)
- Hypertension
- Angina Pectoris
- Arrhythmias etc.

Adverse effects

- Bradycardia (slow heart rate)
- Hypotension
- Fatigue, Dizziness
- Bronchospasm (avoid in asthma) etc.
- Depression

ANTI-MANICS

- Anti-manic drugs are medications used to control manic episodes in patients with bipolar disorders (also called manic-depressive illness).
- These drugs help in reducing symptoms like extreme excitement, overactivity, irritability and impulsiveness.

MAIN CLASSES OF MANIC DRUGS

① Mood Stabilizers
- Lithium (most commonly use)

② Anti convulsants (used as mood stabilizers)
- Valproic Acid
- Carbamazepine
- Lamotrigine

③ Atypical antipsychotics
- Olanzapine
- Risperidone
- Quetiapine
- Aripiprazole

USES
- Treatment of Acute mania
- Prevention of manic episodes.
- Sometimes used along with antidepressants in bipolar disorder.

HALLUCINOGENS

- Hallucinogens are a group of psychoactive drugs that cause hallucinations, meaning they make a person see, hear, or feel things that are not real.
- They also affect thoughts, emotions and perception of the time or space.

COMMON HALLUCINOGENS

NATURAL	SYNTHETIC
Psilocybin (magic mushrooms)	LSD (lysergic acid diethylamide)
Mescaline (from peyote cactus)	Phencyclidine (PCP)
Cannabis (in high doses)	MDMA (Ecstasy - mixed effects)

Mechanism Of Action

Most hallucinogens work by:

- Stimulating serotonin receptors (especially 5-HT_2A) in the brain.
- This leads to altered sensory perception and mood changes.

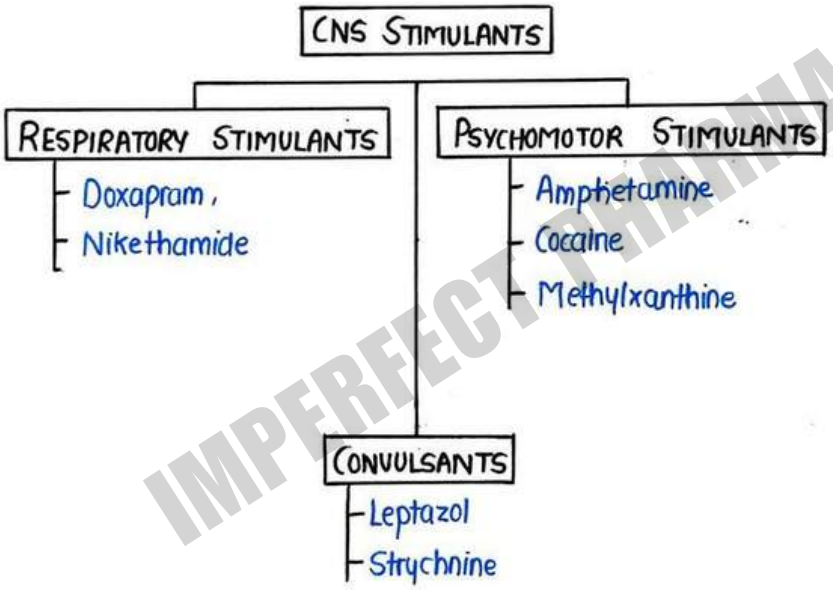
Effects (Temporary)

- Visual and auditory hallucinations.
- Altered thinking and time sense.
- Euphoria or anxiety
- Dilated pupils, increased heart rate.

CNS STIMULANTS

CNS ((entral Nervous System) stimulants are drugs that increase brain activity, resulting in enhanced alertness, wakeness, and energy levels.

CLASSIFICATION



① Respiratory Stimulants

- They stimulate the respiratory centers in the brainstem and are primarily used to treat respiratory depression.
- Example - Doxapram, Nikethamide.

- Doxapram: Stimulates breathing by activated chemoreceptors in the corotid body.
- Nikethamide: A weak CNS stimulants, previously used in respiratory depression but now largely obsolete.

② Psychomotor Stimulants

- These enhance mental activity, alertness and physical performance.
- They act mainly by increasing levels of neurotransmitter like dopamine and norepinephrine.

- Examples- Amphetamine, Cocaine, Methylxanthines.

- Amphetamine: Increases release of dopamine and norepinephrine, used in ADHD and narcolepsy.
- Cocaine: Inhibits reuptake of dopamine, norepinephrine and serotonin; also act as local anaesthetic.

METHYLXANTHINES

- Methylxanthines are naturally occuring alkaloids derived from xanthine, and they acts as mild CNS stimulants.
- Examples - • Caffiene (found in coffee, tea, cola)
  - Theophylline (found in tea : used as bronchalilator)
  - Theobromine (found in cocoa)

Mechanism of Action -
- Phosphodiesterase (PDE) inhibitors, inhibits the enzyme PDE, leading to increased levels of cyclic AMP (cAMP), which stimulates various physiological process.
- Adenosine receptor antagonism: Blocks adenosine receptors in brain, which normally have depressant effect, this leads to increased alertness and wakefulness.

Pharmacological Effects -
- CNS Stimulation
- Bronchodilation
- Mild diuretic effect
- Increased gastric acid secretion
- Cardiac stimulation etc.

Therapeutic effects -
- Caffiene : Used to relieve fatigue and drowsiness.
- Theophylline : Used in the treatment of bronchial spasm - asthma & chronic obstructive pulmonary disease (COPD).
- Theobromine: Mainly of historical interest, less potent than caffiene.

③ CONVULSANTS

- These are CNS stimulants that can induced convulsions by stimulating spinal cord and brain neurons.
- They are not used therapeutically and are mainly of toxicological interest.
- Examples - Leptazol , Strychnine etc.

- Leptazol (pentylenetetrazol) : Used experimentally to induce siezures.
- Strychnine : A toxic alkaloid that blocks glycine receptors , leading to uncontrolled reflux stimulation and convulsions.

NOOTROPICS

Nootropics (also called smart drugs) are drugs or substances that enhance cognitive function like memory, attention, learning, creativity and motivation without causing sedation or significant stimulation.

KEY FEATURES

- Improve memory and learning
- Enhance brain metabolism
- Increase mental performance
- Do not cause sedation or major side effects
- No-addictive (ideally)

EXAMPLES OF NOTROPICS

DRUG NAME	ACTION / USES
Piracetam	Enhances memory and brain metabolism
Aniracetam	Related to piracetam, improves focus
Modafinil	Promotes wakefulness, used in narcolepsy (off-label cognitive enhancer)
Selegiline	MAO-B inhibitor, used in parkinson's has cognitive benefits
Caffiene (low dose)	Mild memory and alertness booster

Opioid Analgesics

- Opioid analgesics are drugs that relieve moderate to severe pain by acting on opioid receptors (mu, kappa, detta) in the central and peripheral nervous system.
- They mimic endogenous opioids (endorphins, enkephalins).

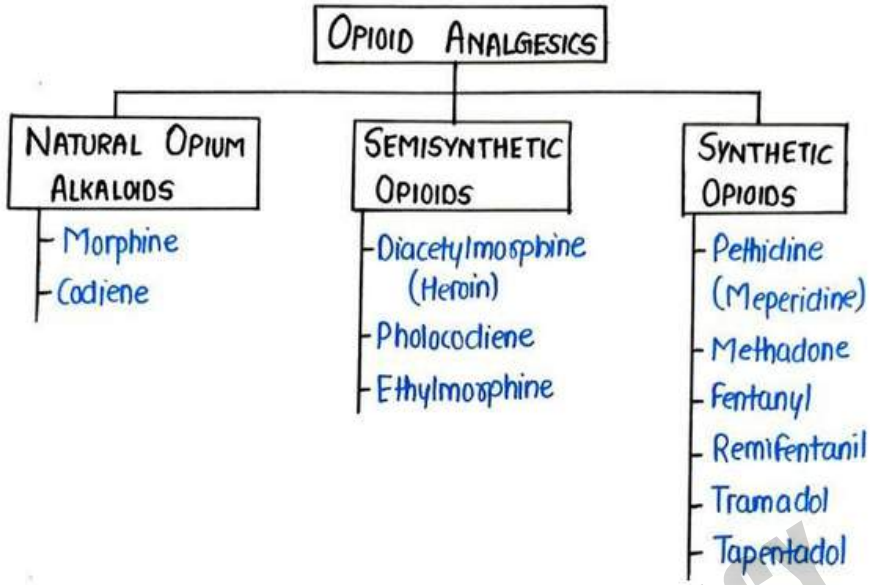
Opioid Receptor

- Opioid receptor are G-protein coupled receptors (GPCRs) present in the central and peripheral nervous system.
- They mediate the effects of opioid drugs (like morphine) and endogenous peptides (like endorphins).

Types Of Opioid Receptors

Receptor	Main Actions	Endogenous Ligand	Drugs Acting
μ (mu)	Analgesia, (supraspinal & spinal), respiratory depression, euphoria, sedation, constipation, physical dependence	Endorphins	Morphine, Fentanyl, Methadone
κ (kappa)	Spinal analgesia, dysphoria, sedation	Dynorphins	Pentazocine, Nalbuphine
δ (Detta)	Spinal analgesia, mood modulation	Enkephalins	Not many selective drugs clinically used

CLASSIFICATION



MECHANISM OF ACTION

- Opioid binds mainly to μ (mu) receptors in the brain and spinal cord.
- They inhibit pain transmission by:
  - Release of pain neurotransmitters (e.g., substance P)
  - Neuronal excitability
- Also cause euphoria, sedation and respiratory depression.

PHARMACOKINETICS

Absorption - Well absorbed orally, IM, IV.

Distribution - Cross blood-brain barrier (lipophilic drugs like fentanyl faster)

Metabolism - Liver (e.g., morphine → morphine-6-glucoronide active metabolite)

Excretion - via Renal (urine).

THERAPEUTIC USES

- Pain relief (acute & chronic)
- Pre-anaesthetic medication (e.g., Fentanyl)
- Cough suppression (codeine, pholcodiene)
- Diarrhea (Loperamide - a peripheral opioid) etc.

ADVERSE EFFECTS

- Respiratory depression
- Constipation
- Nausea, Vomiting
- Miosis (pinpoint pupils)
- Physical dependence & tolerence
- Sedation & Dizziness, etc.

Pharmacology Of Morphine

- Morphine is a natural opioid analgesic derived from opium poppy.
- It is the prototype drug of strong opioid agonists.
- Used to relieve severe pain (e.g., post-operative, cancer, trauma).

Mechanism Of Action

- Act as full agonist at μ (mu) opioid receptors in the spinal cord & brain.
- Also has weaker action on κ (kappa) and δ (delta) receptors.
- Results in:
  - ↓ Pain perception (analgesia)
  - ↓ Emotional response to pain
  - Sedation and euphoria
  - ↓ GI motility (constipation)
  - Respiratory depression

Pharmacokinetics

Absorption - Well absorbed orally and parenterally (IM/IV)

Distribution - Widely distributed; crosses BBB slowly

Metabolism - In liver via conjugation to morphine-6-glucuronide (active metabolite)

Excretion - Mostly in urine.

Therapeutic Uses

- Severe acute & chronic pain (eg, trauma, MI, cancer)
- Pulmonary edema (↓ anxiety & vasodilation)
- Cough suppression (less commonly used now)
- Diarrhea (replaced by loperamide) etc.

Adverse Effects

- Respiratory depression
- Constipation
- Nause & vomiting
- Physical dependence
- Sedation & Dizziness etc.

Opioid Antagonists

- Opioid antagonists are drugs that blocks opioid receptors (mu, kappa, detta) without activating them.
- They reverse the effects of opioid agonists like morphine, heroin, etc., especially in overdose or toxicity.

Examples

Drug Name	Duration	Uses
Naloxone	Short	Acute opioid overdose (IV only)
Naltrexone	Long	Opioid & Alcohol dependence (oral)
Nalmefene	Long	Alcohol dependence, Opioid overdose (IV)
Methylnaltrexone	Peripheral only	For opioid-induced constipation

Mechanism Of Action

- They competitively block the μ, κ, δ opioid receptors in CNS & periphery.
- Do not produce any opioid-like effect themselves.
- Rapidly reverse respiratory depression, sedation, and miosis caused by opioid overdose.

PHARMACOKINETICS

DRUG	ROUTE	ONSET	DURATION
Naloxone	IV/IM	Rapid	1-2 hr (may need repeat doses)
Naltrexone	Oral	Slow	Up to 24 hrs
Methylnaltrexone	SC	30 min	Peripheral action only

THERAPEUTIC USES

- Naloxone : Emergency treatment of opioid overdose.
- Naltrexone:
  - Maintenence therapy for opioid addicts (prevent relapse)
  - Helps reduce alcohol craving
- Methylnaltrexone : Used for opioid - induced constipation (acts only on gut)

ADVERSE EFFECTS

- Sweating
- Anxiety
- Vomiting
- Tachycardia
- Nausea
- Dizziness etc.

Drug Addiction, Drug Abuse, Drug Dependence, Drug Tolerance

Drug Addiction

Drug addiction is a chronic condition where a person loses control over the use of drug, leading to compulsive drug-seeking behaviour and continued use despite knowing its harmful effects.

Key Features

- Strong psychological craving
- Repeated, uncontrollable drug use
- Often associated with substances like opioids, cocaine, alcohol and nicotine.

Drug Abuse

Drug abuse refers to the intentional and inappropriate use of a drug for non-medical purposes, often to achieve euphoria or altered mental states.

Key Features

- Use of illegal drugs or misuse of prescription drugs.
- Leads to social, occupational, or health-related problems.
- Involves overuse or experimental use beyond therapeutic limits.

DRUG DEPENDENCE

Drug dependence is a state where the body or mind adapts to repeated drug use, and withdrawl symptoms occur when the drug is reduced or stopped.

TYPES

① Physical depedence: Involves withdrawl symptoms like tremors, sweating or nausea

② Psychological Dependence: Charactarized by emotional or mental craving for the drug

EXAMPLES

Dependence can develop with long-term use of benzodiazepine, opioids or alcohol.

Drug Tolerance

Drug tolerance is a condition where increasing doses of a drug are required to procedure the same therapeutic or euphoric effect.

Mechanism

- May be due to metabolic adaption or changes in receptor sensitivity.
- Leads to reduced response over time despite the same dosage

Examples

Common with substances like morphine, alcohol, and barbiturates.

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

IMPERFECT PHARMACY

JOIN US ON :


IMPERFECT PHARMACY


IMPERFECT PHARMACY


@IMPERFECTPHARMA


IMPERFECT PHARMACY


@IMPERFECTPHARMACY


IMPERFECT PHARMACY


IMPERFECTPHARMACY@GMAIL.COM