WELCOME

TO

PATHOPHYSIOLOGY

UNIT 3

TOPIC :

- **Nervous system :** Epilepsy, Parkinson's disease, stroke, psychiatric disorders: depression, schizophrenia and Alzheimer's disease.

Nervous system

Epilepsy

→ Epilepsy is a nervous system disorder due to abnormal electrical activity in brain cells, it is also called seizure and convulsant.

→ This disorder results contraction , involuntary movement , shaking of the body etc.

Classification of seizures

- Seizure is classified on the basis of behavioural and electrophysiologic pattern of activity as

1. **Partial (Focal seizures)**
   - ⇨ It mainly appears in only one hemisphere.
   - ⇨ That means symptoms only happen in a specific part or on one side of your body. But focal seizures can sometimes spread and become generalized seizures.
     a) Simple partial seizures with motor, sensory, or autonomic symptoms.
     b) Complex partial seizures.

c) Partial seizures with secondary generalization.

2. **Generalized seizures**

⇨ These are seizures that happen in both hemispheres of your brain side. These seizures tend to cause more severe effects and symptoms.

a. Absence seizures.
b. Tonic- clonic seizures.
c. Other (Myoclonic, tonic, clonic, atonic)

Etiology

- Brain injury
- High fever
- lake of oxygen to brain
- Brain tumor
- Genetic brand disorder
- Stroke (reduce blood supply to brain)

Pathogenesis

Due to etiological factors
↓
Neuronal cell membrane altered
↓
Repeated Action potential
↓
Rapid generation of electrical Impulses
↓
spread to other cell of brain
↓
The abnormal electrical impulses reach to skeletal muscles
↓
Epilepsy

Clinical Manifestation

- Recurrent of seizure
- Sudden stiffness due to unknown reason
- Sudden falling due to unknown reason
- Sudden bouts of chewing due to unspecific reason
- Rpetitive involuntary movement
- Changes in sense of smell touch and sound

Non Pharmacological Management

- Ketogenic diet is useful in children are suffering from seizure . ketogenic diet is a high -fat adequate protein , and low carbohydrates diet for example fish , meat , eggs , seafood etc

Pharmacological managements

- Benzodiazepines— ex- clonazepam, lorazepam, diazepam.
- Barbiturates— ex- phenobarbital, desoxyphenobarbital.
- Deoxy barbiturates— ex- primidone.
- Hydantoin— ex-phenytoin, ethotoin.
- Aliphatic carboxylic Acid— ex- valproic acid, magnesium valproate.
- Oxazolidine derivatives— ex- trimethadione, paramethadione.
- Cyclic GABA Analogues— ex- gabapentin, pregabalin.
- Iminostilbene— carbamazepine, oxcarbazepine.
- Other drugs— ex- levetiracetam, parampanel, brivaracetam, lacosamide

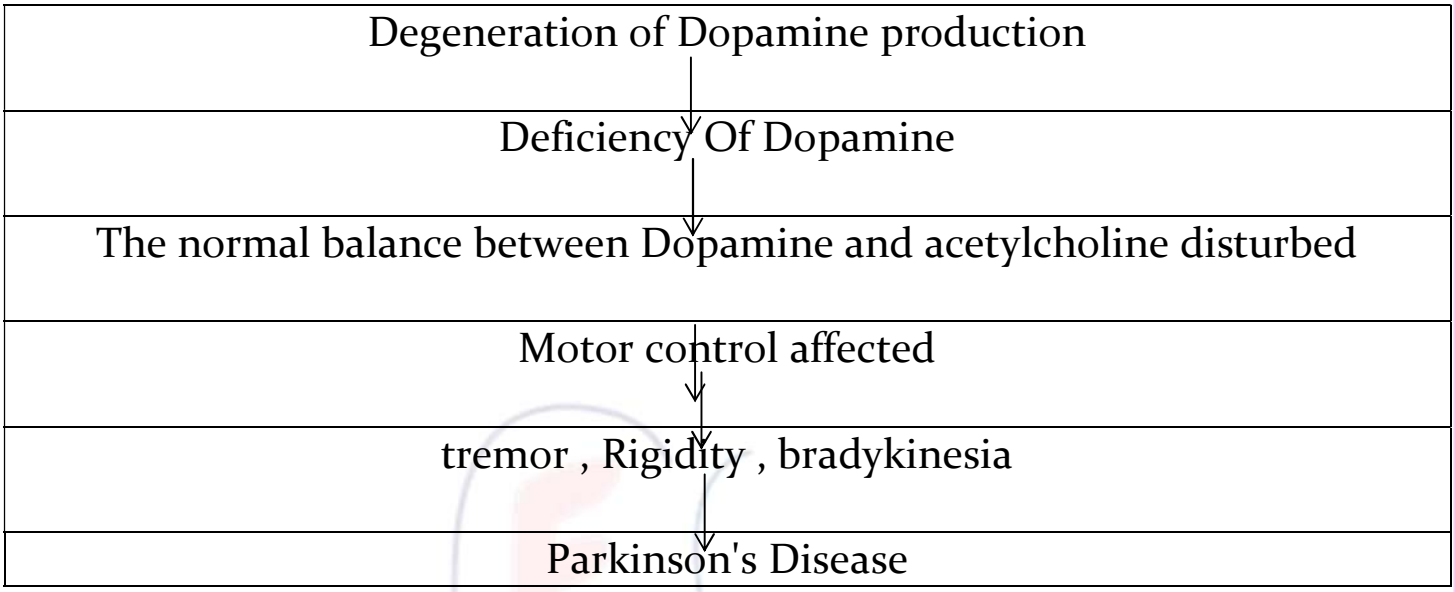
Parkinson's Disease

→ It is a chronic, progressive , neurodegeneration disorder. in which slows down the voluntary movement of body parts (bradykinesia) , muscles tone changed (rigidity) and tremor at rest.

Etiology

- Genetic factors
- Advancing age : above 60 year mostly scene
- Head injury
- Drugs : like neuroleptics ,antiemetics etc.
- Exposure to toxin.
- Low production of Dopamine

Pathogenesis of Parkinson 's Disease



Clinical Manifestation

- Slow moment
- Tremor / trembling
- Low volume of speech
- Dropping of saliva
- Constipation
- Tendency to fall backwards
- Depression

Non Pharmacological Management

- Avoid and discard the all activities which cause/induce the depression, stress, sleep disorders etc.
- Follow and change the diet plans according to own demand or prescription by any RMP
- Practice the yoga, meditation, physical exercise regularly. Ventilation is one of the reasons which leads to brain disorders and cardiac disorders also
- Practice of herbal/natural medicine other than allopathic.
- Do such all activities which makes you happy and cheerful.

Pharmacological Management

- **Levodopa :** It converts into dopamine when reach to the brain . It is the most effective drug For PD.
- **Dopamine agonist :** Bromocriptine , ropinirole : They work like dopamine on dopaminergic receptors.
- **MAOI :** Selegiline , Rasagline.
- **Anti-cholinergic drugs :** Benztropine , Procyclidine.

Stroke

→ Stroke is a condition in which blood supply to the brain reduced or stops due to blockage or hemorrhage.

→ In stroke condition brain function is stopped due to the death of brain cell.

→ Stroke is also called brain attack and cerebrovascular accident (CVA).

Types

- **Islamic stroke :** Blood flow to the brain reduced due to narrowed or blocked arteries of brain by Thrombus(lipid deposition) or embolus (blood clot).
- **Haemorrhagic stroke :** Blood flow is disturbed due to leakage of blood vessels of brain.

Etiology

- Blockage in brain arteries
- Leakage in blood vessels
- Diabetes mellitus
- Smoking
- Inactivity

- Obesity
- Alcoholism
- Estrogen use
- Advancing age
- Family history

Pathogenesis

Due to Etiological Factors (Blockage)
↓
Reduced Blood Supply
↓
Death of brain cell
↓
loss of brain functions
↓
Stroke

Clinical Manifestations

- Dizziness
- Loss of control and coordination
- Difficulty in speaking and understanding
- Paralysis in face, leg, arms , mostly on one side of the body
- Blurred vision
- Severe headache

Non Pharmacological Management

- ❖ Early Contact to doctor
- ❖ Early Diagnosis

Pharmacological Management

- Emergency treatment with medications
- Alteplase Injection : it is given by vein in arm , it dissolves the blood clot and restore the blood flow
- Anticoagulant drugs : these drugs prevent further blood clot .Heparin , warfarin.

Emergency Procedure for removal of clot

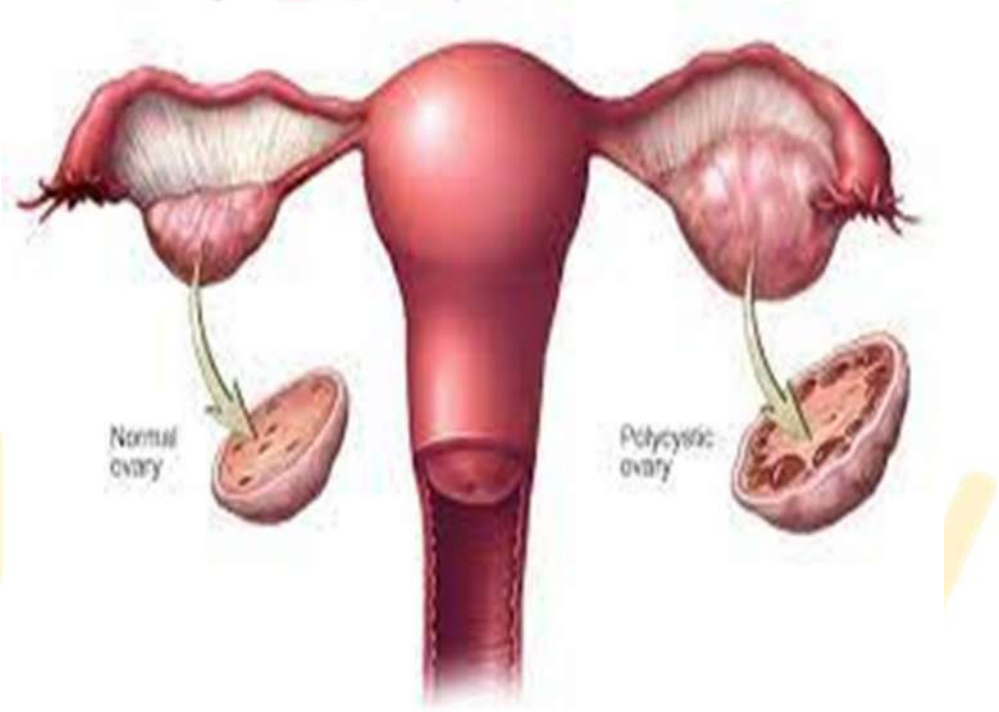
1) Surgical Procedure
2) **Mechanical clot removal :** Using a catheter a small device is move into the brain , which removes the clot either by grabbing it or by breaking it .

Polycystic Ovary Syndrome (PCOS)

→ Polycystic ovarian syndrome (PCOS) is a condition of hormonal imbalancewhen ovaries (that produces and releases eggs) produce excessive male hormones.

→ In PCOS, the ovaries produce abnormally high levels of androgens and causeimbalance in reproductive hormones.

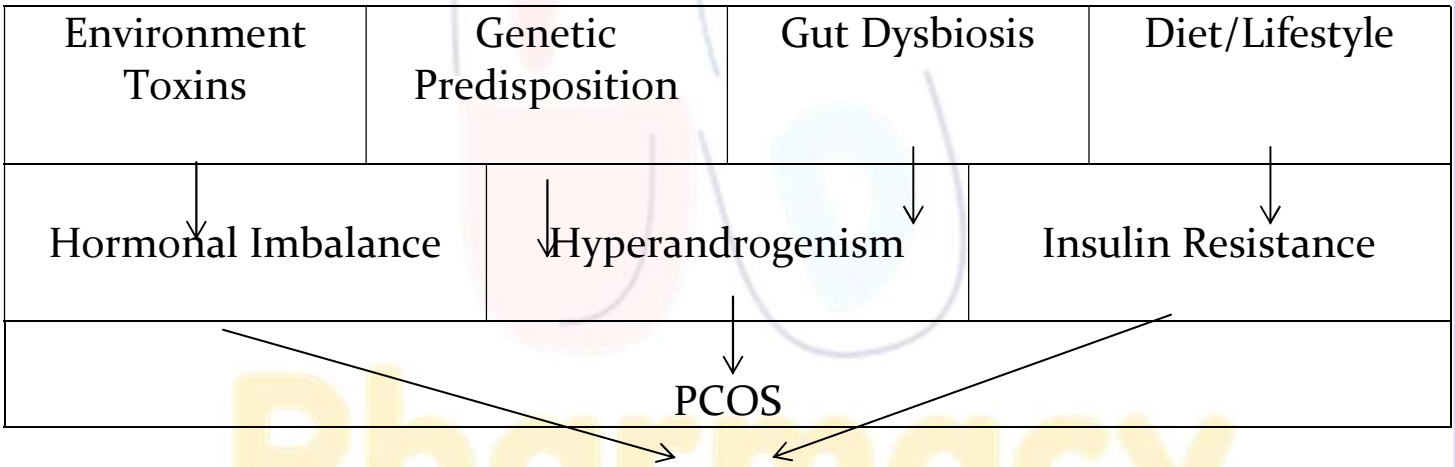
→ Thus, PCOS patients experience irregular menstrual cycles, missed periods, and erratic ovulation. Anovulation (lack of ovulation) may lead to the development of small cysts on the ovaries



Etiology

- Genetic
- Environmental factor(climate , diet , pollution , smoking, alcoholism etc)
- High level of androgens (Male hormone : testosterone) it leads to irregular MC and prevent evolution and this can lead to development of cyst .
- Insulin resistance : high level of insulin causes excess production of androgens which cause PCOS .

Pathogenesis



Clinical Manifestation

- Irregular Periods
- Abnormal hair growth
- Acne
- Obesity
- Cyst
- Thinning of hair
- Infertility

Non Pharmacological Managements

- ❖ Weight loss
- ❖ Low calorie diet
- ❖ Moderate exercise
- ❖ Enough sleep
- ❖ Stress reduction

Pharmacological Managements

- ◈ **Oral contraceptives :** Birth control pills containing a combination of estrogen and progestin can regulate menstrual cycles and reduce androgen levels, which can improve symptoms of PCOS.
- ◈ **Anti-androgens :** Drugs like spironolactone and flutamide : can block the effects of androgens (male hormones) in the body, which can reduce symptoms such as acne and excess hair growth.
- ◈ **Metformin :** This medication is typically used to treat type 2 diabetes, but it can also be helpful for women with PCOS who have insulin resistance. Metformin can help regulate menstrual cycles and lower androgen levels.
- ◈ **Gonadotropins :** Women with PCOS who are trying to conceive may benefit from injections of gonadotropins, which can stimulate ovulation.
- ◈ **Clomiphene citrate :** This medication is an oral fertility drug that can help women with PCOS ovulate and conceive.
- ◈ **Letrozole :** This medication is also used to stimulate ovulation in women with PCOS who are trying to conceive

Amenorrhea

Amenorrhea is a condition characterized by the **absence of menstruation** in females of reproductive age.
It is not a disease itself but a symptom of various underlying physiological or pathological conditions.

Types of Amenorrhea

→ **Primary Amenorrhea :** When a girl has not started menstruating by age 15 (with normal secondary sexual features) or by age 13 (without secondary sexual features).
→ **Secondary Amenorrhea :** When a woman who has previously had regular periods experiences absence of menstruation for 3 months or more.

Etiology (Causes)

Primary Amenorrhea

- Genetic Disorders: Turner syndrome (45, XO)
- Hypothalamic dysfunction
- Müllerian agenesis (absence of uterus/vagina)
- Androgen Insensitivity Syndrome
- Pituitary disorders

Secondary Amenorrhea

- Pregnancy (most common cause)
- Polycystic Ovary Syndrome (PCOS)
- Hypothyroidism
- Hyperprolactinemia
- Stress, anorexia, excessive exercise
- Premature ovarian failure (early menopause)
- Asherman's syndrome (intrauterine adhesions)

Pathogenesis

Normal menstrual cycle depends on the hypothalamic-pituitary-ovarian-uterine axis:
Hypothalamus → GnRH → Pituitary → FSH & LH → Ovaries → Estrogen & Progesterone → Menstruation

In Amenorrhea:

Disruption at any level →

No hormone production or improper hormone response →

⊖Absence of menstruation

Clinical Manifestations

- Absence of menstruation
- Infertility
- Delayed puberty (in primary)
- Headache, visual disturbances (if pituitary tumor present)
- Galactorrhea (milky nipple discharge due to high prolactin)
- Acne or hirsutism (in PCOS)
- Hot flashes and vaginal dryness (in ovarian failure)

Non-Pharmacological Management

- Lifestyle correction: balanced diet, stress reduction, moderate exercise
- Nutritional support (for anorexia or underweight patients)
- Counseling: psychological support in adolescents or infertility cases
- Monitor menstrual history and sexual development

Pharmacological Management

Cause	Drug/Treatment
PCOS	Oral contraceptive pills (to regularize periods), Metformin
Hyperprolactinemia	Dopamine agonists: *Bromocriptine, Cabergoline*
Hypothyroidism	Levothyroxine
Premature ovarian failure	Hormone replacement therapy (HRT)
Pituitary tumor	Surgery or dopamine agonists
Asherman's syndrome	Surgical removal of adhesions (hysteroscopy)

Psychiatric disorders

Depression

→ Depression is a common mood disorder characterized by a persistent feeling of sadness, hopelessness, and loss of interest in daily activities.
→ It affects a person's thoughts, behavior, emotions, and physical health, often interfering with personal and social functioning.

Types of Depression

- **Major Depressive Disorder (MDD)** – Classic clinical depression
- **Persistent Depressive Disorder (Dysthymia)** – Long-term, low-grade depression
- **Bipolar Depression** – Depression as a phase of Bipolar Disorder
- **Postpartum Depression** – After childbirth
- **Seasonal Affective Disorder (SAD)** – Occurs during specific seasons (usually winter)
- **Psychotic Depression** – Includes depressive symptoms with psychosis (delusions/hallucinations)

Etiology (Causes)

Biological Causes

- Imbalance of neurotransmitters: ↓ serotonin, dopamine, norepinephrine

- Genetic predisposition (family history)
- Hormonal imbalances (e.g., cortisol, thyroid hormones)

Psychosocial Causes

- Chronic stress or trauma (abuse, loss of loved ones)
- Unemployment, relationship issues
- Low self-esteem or pessimistic thinking

Medical & Drug-related Causes

- Chronic illnesses: diabetes, cancer, heart disease
- Neurological disorders: stroke, Parkinson's, dementia
- Substance abuse: alcohol, drugs
- Side effects of medications (e.g., steroids, beta blockers)

Pathogenesis

- Stress or other triggers lead to neurotransmitter imbalance (↓ serotonin/dopamine)
- Affects brain regions: prefrontal cortex, hippocampus, amygdala
- Leads to emotional and behavioral symptoms of depression
- Chronic cases alter brain structure and hormone regulation (↑ cortisol)

Clinical Manifestations (Symptoms)

- Persistent sad or empty mood
- Loss of interest or pleasure in most activities (anhedonia)
- Fatigue or decreased energy
- Sleep disturbances (insomnia or hypersomnia)
- Appetite or weight changes
- Feelings of worthlessness, guilt, or helplessness
- Difficulty in thinking, concentrating, or making decisions
- Psychomotor changes (agitation or retardation)
- Suicidal thoughts or attempts

Non-Pharmacological Management

- **Psychotherapy** (Talk therapy)
  - *Cognitive Behavioral Therapy (CBT)* – most effective
  - *Interpersonal Therapy (IPT)*
- **Lifestyle modifications**:
  - Regular exercise
  - Adequate sleep and nutrition
  - Avoid alcohol and drugs
  - Social support from family and friends
- **Electroconvulsive Therapy (ECT)** – for severe, treatment-resistant depression
- Mindfulness meditation and stress reduction techniques

Pharmacological Management

Drug Class	Examples	Mechanism
SSRIs (Selective Serotonin Reuptake Inhibitors)	Fluoxetine, Sertraline, Citalopram	↑ Serotonin levels in brain
SNRIs (Serotonin-Norepinephrine Reuptake Inhibitors)	Venlafaxine, Duloxetine	↑ Serotonin and norepinephrine
TCAs (Tricyclic Antidepressants)	Amitriptyline, Imipramine	Block reuptake of serotonin and norepinephrine
MAOIs (Monoamine Oxidase Inhibitors)	Phenelzine, Tranylcypromine	Inhibit breakdown of neurotransmitters
Atypical antidepressants	Bupropion, Mirtazapine	Varying mechanisms
Mood stabilizers or antipsychotics	In severe or bipolar depression	Used adjunctively with antidepressants

Schizophrenia

→ Schizophrenia is a chronic and severe psychiatric disorder that affects a person's thinking, feeling, perception, and behavior.
→ It is characterized by delusions, hallucinations, disorganized speech, and impaired social functioning.
→ The onset is usually in late adolescence or early adulthood.

Types of Schizophrenia

1. **Paranoid Type**: Dominated by delusions and hallucinations
2. **Disorganized Type**: Speech and behavior are disorganized; inappropriate affect
3. **Catatonic Type**: Abnormal motor activity (rigid posture, mutism)
4. **Undifferentiated Type**: Symptoms don't fit a specific subtype
5. **Residual Type**: Absence of prominent positive symptoms but continued negative symptoms

Etiology (Causes)

Biological Factors

- **Genetic predisposition** (family history of schizophrenia)
- **Neurochemical imbalance**:
  - ↑ **Dopamine** (main neurotransmitter involved)
  - Also involves serotonin, glutamate, and GABA

- **Brain structure abnormalities**:
  - Enlarged ventricles
  - Decreased gray matter volume

Psychosocial Factors

- Childhood trauma
- Stressful life events
- Poor family environment

Drug-Induced Triggers

- Cannabis
- Amphetamines
- LSD
- Cocaine

Pathogenesis

- Genetic/environmental trigger
- Leads to dopaminergic hyperactivity in certain brain pathways (especially mesolimbic)
- Causes positive symptoms (hallucinations, delusions)
- Hypoactivity in other pathways (e.g., prefrontal cortex) leads to negative symptoms (apathy, social withdrawal)

Clinical Manifestations (Symptoms)

Positive Symptoms *(excess/distortion of normal functions)*:

- **Delusions** (false, fixed beliefs – e.g., persecution, grandeur)
- **Hallucinations** (usually auditory – hearing voices)
- **Disorganized speech** (e.g., incoherence, word salad)
- **Disorganized or catatonic behavior**

Negative Symptoms *(loss of normal functions)*:

- **Affective flattening** (reduced emotional expression)
- **Alogia** (poverty of speech)
- **Avolition** (lack of motivation)
- **Social withdrawal**

Cognitive Symptoms:

- Poor attention
- Impaired working memory
- Difficulty in executive functions

Non-Pharmacological Management

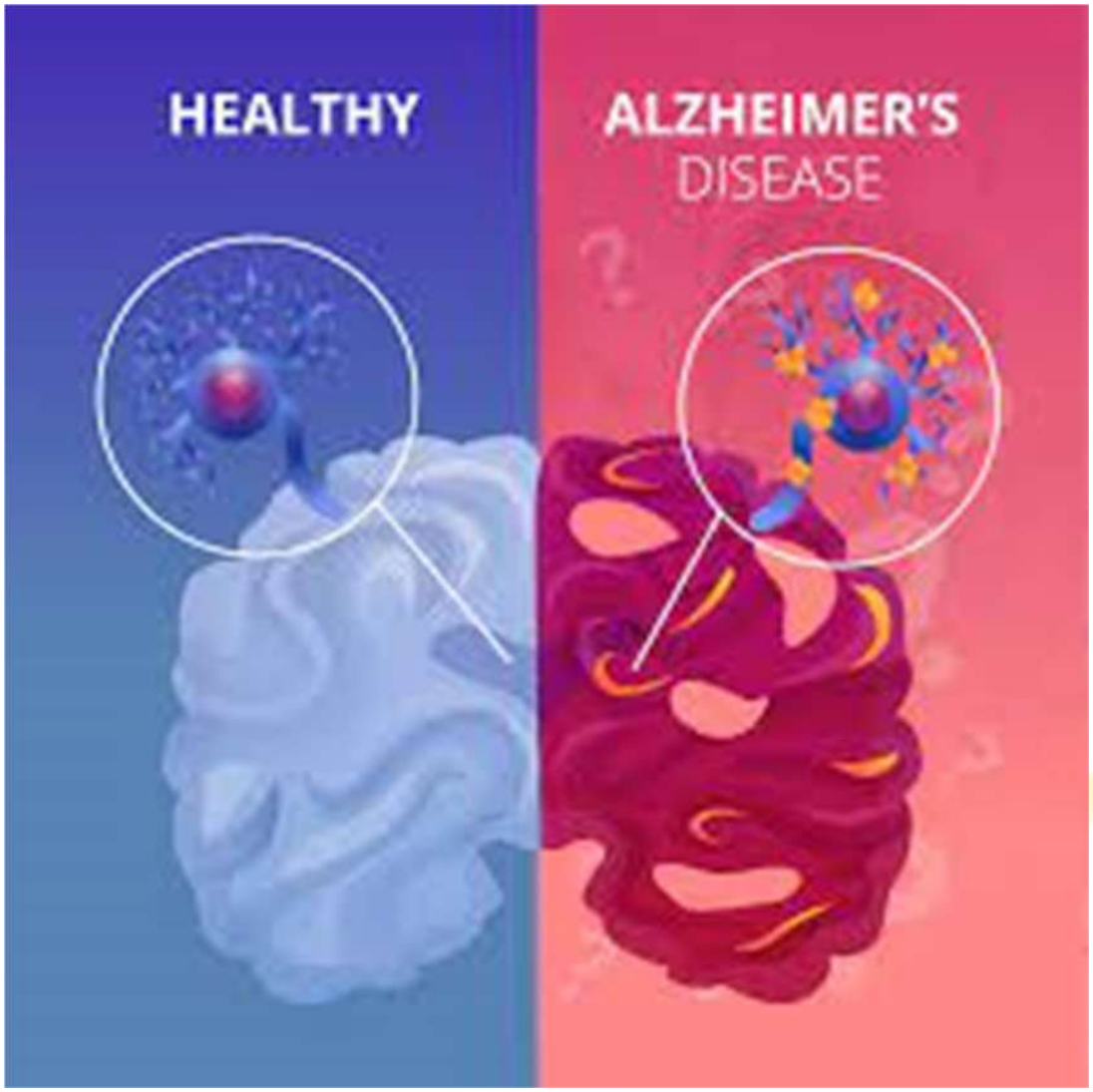
- **Psychosocial interventions**:
  - Family therapy
  - Cognitive Behavioral Therapy (CBT)
  - Social skills training
  - Supported employment/rehabilitation
- **Electroconvulsive Therapy (ECT)**: In severe or treatment-resistant cases

Pharmacological Management

Drug Class	Examples	Effects
Typical Antipsychotics	Haloperidol, Chlorpromazine	Mainly control positive symptoms, risk of extrapyramidal side effects (EPS)
Atypical Antipsychotics	Risperidone, Olanzapine, Clozapine, Aripiprazole	Control both positive and negative symptoms, fewer EPS
Depot injections	Fluphenazine decanoate, Risperidone LAI	Long-acting, used for non-compliant patients

Alzheimer 's Disease

→ Alzheimer's disease is a chronic irreversible neurodegeneration disease which gradually destroy the ability to think, remember, and learn ,and involves memory loss.



Etiology

- Neurochemical factor
- Genetic factors
- Environmental factors
- Head injury
- Smoking
- Advancing age (above 65 years).

Pathogenesis

Degeneration of neurochemicals ↓
due to etiological factors ↓
deficiency of neurochemicals ↓
Alzheimer disease

Clinical Manifestation

- Loss of memory
- Placing object at unusual place
- Confusion about events, time and place
- Asking the same question repeatedly
- Problem to perform familiar work
- Getting lost of or wandering
- Problem in sleeping
- Behaviour changes like agitation , anxiety
- Poor thinking or understanding
- Difficulty in recognising family members or friends
- Difficulty in speaking during choosing the right words.

Non Pharmacological Management

- ❖ Avoid and discard the all activities which cause/induce the depression, stress, sleep disorders etc.
- ❖ Follow and change the diet plans according to own demand or prescription by any RMP
- ❖ Practice the yoga, meditation, physical exercise regularly. Ventilation is one of the reasons which leads to brain disorders and cardiac disorders also
- ❖ Practice of herbal/natural medicine other than allopathic.
- ❖ Do such all activities which makes you happy and cheerful.

Pharmacological Management

- ◈ **Chonilesterase Inhibitors :** Donepezil , galantamine.
- ◈ **Glutametergic Drugs :** Gabapentin , Lamotrigine