WELCOME

TO

PATHOPHYSIOLOGY

UNIT 3

TOPIC :

- **Endocrine system :** Diabetes, thyroid diseases, disorders of sex hormones

Endocrine system

Diabetes

→ Diabetes Mellitus is a inherited or acquired disease occurs due to defect in insulin secretion or insulin action or both , in which blood sugar level is high for long time.
→ It is also called Hyperglycemia.
→ Diabetes means pass through , and mellitus means sweet,
→ So we can say abnormal passing of sugar through blood or urine is called Diabetes mellitus.

Normal range of blood sugar level

	normal people	diabetes patients target
Before meals	72-99 mg/dl	80-130mg /dl
2 hours after meals	less than 140/ mg/dl	less than 180mg/dl

Types of Diabetes

- **Type 1 Diabetes :** This type of diabetes occurs due to severe reduction in production of Insulin because of autoimmune destruction of beta cells of Pancreas . This occurs in younger age usually . (before 35-40 years)
- **Type 2 diabetes :** This type of diabetes occurs due to the resistances to the action of Insulin . Or cells do not respond to insulin . This occurs in older age usually .
- **Gestational Diabetes :** During pregnancy , placenta generate hormones that alter the function of insulin.

Etiology

1) Type 1 Diabetes :

- Autoimmune destruction of beta cells of pancreas.
- Any disease in pancreas
- Age
- Genetic factors
- Beta blockers and Thiazide drugs if used for long term

2) Type 2 Diabetes

- Insulin does not function properly.
- Resistances to insulin function
- Obesity.
- lack of physical activity
- Genetic factors

Pathogenesis

Type 1 diabetes	Type 2 Diabetes
Immune attack on beta cells ↓	Poor response of cells to insulin ↓
Severe decrease in insulin production ↓	Decrease function of Insulin ↓
Increase blood sugar level ↓	Increase blood sugar level ↓
Type 1 Diabetes Mellitus	Type 2 Diabetes Mellitus

Clinical Manifestations

- Presence of sugar in urine
- Increase thirst
- Increase frequency of urination
- Extreme hunger
- Fatigue
- Blurred vision
- Headache
- Frequent infection
- Delay in healing of cuts and wounds
- Itchy skins

Non Pharmacological managements

- ❖ Physical Activity
- ❖ Diet (should avoid carbohydrates , salt in excess amount)
- ❖ Should avoid Sweats

Pharmacological managements

- **Type 1 diabetes :** It is insulin dependent , insulin is administered to treat this type of diabetes .
- **Type 2 diabetes**
  - **Hypoglycemic agents**
    - Sulfonylurea : they stimulate the release of insulin from pancreas , : Tolbutamide ,chlorpropamide , glibenclamide
    - Biguanides : prevent liver from production of glucose , : metformin , phenformin
    - α Glucosidaese Inhibitors : it prevent the absorption of carbohydrates form intestine : Acarbos , miglitol

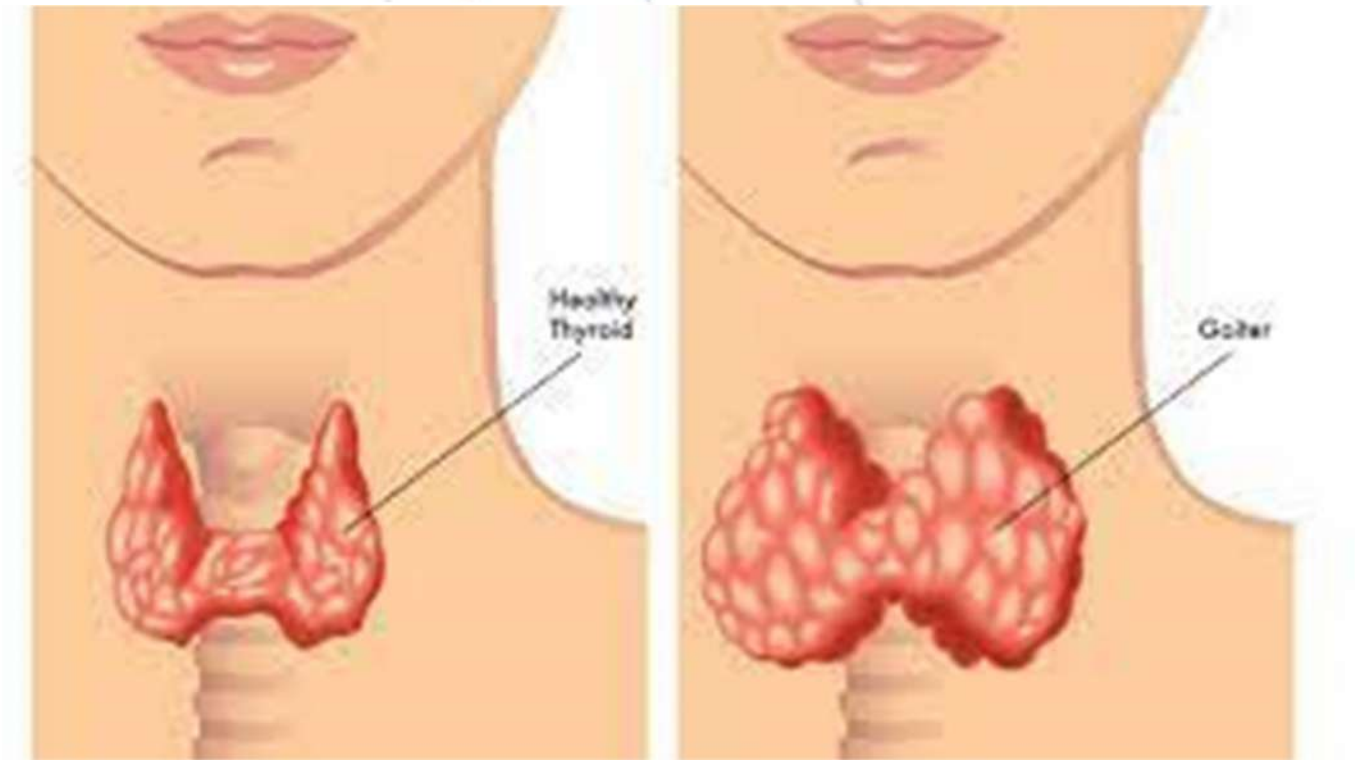
Thyroid Disorder (Hypo and hyperthyroidism)

→ The thyroid gland, usually located below and anterior to the larynx, consists of two bulky lateral lobes connected by a relatively thin isthmus.

→ The thyroid is divided by thin fibrous septae into lobules composed of about 20 to 40 evenly dispersed follicles, lined by a cuboidal to low columnar epithelium.

Hypothyroidism

→ Lake of Thyroid Hormones (TH) in blood circulation about 20% to 40 % which slow down the metabolism is called Hypothyroidism.



Etiology :

- There are two types of etiology of Hypothyroidism , primary (Problem in thyroid gland) , secondary (problem in Pituitary gland)

Primary :

- Autoimmune disorder
- Dietary iodide deficiency.
- Anti-thyroid drugs
- Lithium therapy
- Radioactive iodine (RAI) uses.

Secondary :

- low secretion of TSH.
- Damage of pituitary gland.

Pathogenesis of Hypothyroidism

Primary or secondary causes
Autoimmune disorder ↓
decreased production of TH ↓
lake of TH in blood ↓
Hypothyroidism ↓

Clinical manifestation

- Constipation
- Depression
- Feeling tiredness
- high blood cholesterol level
- Dry skin
- Excessive forgetfulness
- Heavy and frequent menstrual cycle

- Tingling in hands
- Loss of sexual desire
- Gaining weight

Non Pharmacological Management

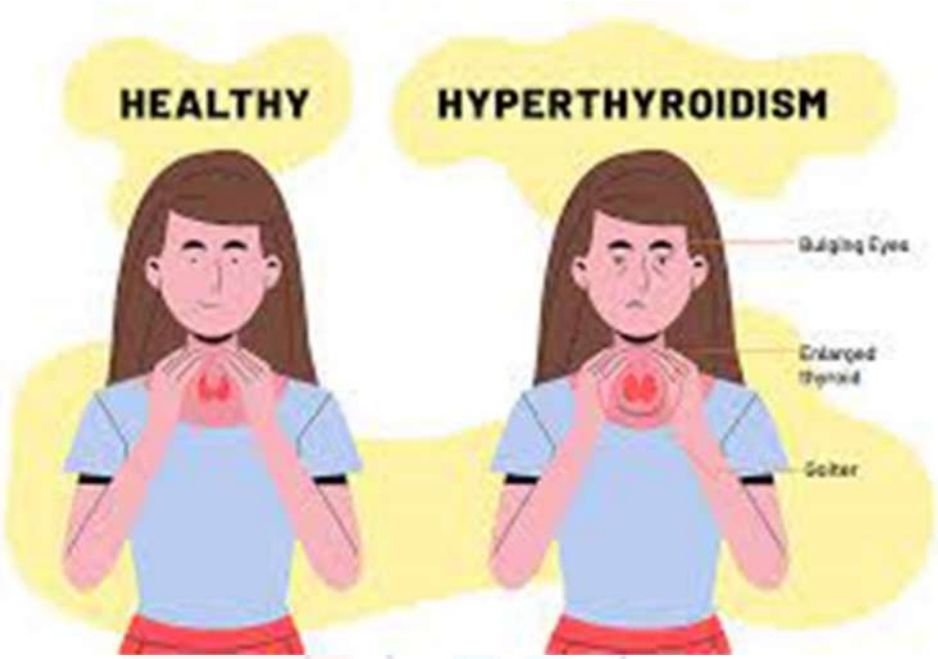
- Exercise
- Stress management
- Diet (Increase intake of foods , fruits , vegetables are rich in iodine , zinc , iron copper selenium , Vitamin A , D.

Pharmacological Management

- Levothyroxine (T_4)
- Liothyronine (T_3)
- Combination Of T_4 and T 3

Hyperthyroidism

→ A condition in which thyroid gland produces more Thyroid Hormones (TH) than requirement of the body is called Hyperthyroidism.



Etiology

- Graves 's Disease : It is an immune system disorder in which thyroid produce excess amount of Thyroid hormones.
- Infection of Thyroid gland.
- Excess consumption of Iodine
- Pituitary gland disorder

Pathogenesis of Hyperthyroidism

Thyroid gland disorder ↓
Increases production of TH ↓
High level of TH in Blood ↓
Hyperthyroidism

Clinical Manifestation

- Weight Loss
- Increased appetite
- Changes in menstrual
- Restless
- Diarrhoea
- Excess sweating
- Sleep problems
- Swollen in thyroid gland etc.

Non Pharmacological Management

- Exercise
- Stress management
- Diet (decrease intake of foods , fruits , vegetables are rich in iodine , zinc , iron copper selenium , Vitamin A , D.

Pharmacological Management

- **Hormone Inhibitors :** Methimazole , Propylthiouracil .
- **Beta Blockers :** Propranolol (these drugs provide relief from hyperthyroid symptoms till the anti-thyroid drugs become effective .
- **Glucocorticoids :** They inhibit the conversion of T_4 to T_3 (T_3 is more power full Hormone)
- **Radioactive Iodine :** These drugs destroy thyroid cells and control thyroid hormones . the dosage of RAI should be given carefully , otherwise cause hypothyroid .

Disorders of Sex Hormones

→ Sex hormones include androgens (e.g., testosterone) and estrogens and progesterone.
→ These hormones regulate reproductive development, sexual function, and secondary sexual characteristics.
→ Disorders occur due to hormonal imbalance, gland dysfunction, tumors, genetic defects, or exogenous hormone use.

Classification of Sex Hormone Disorders

➢ Sex hormone disorders arise due to excess or deficiency of androgens, estrogens, or progesterone and affect the reproductive, endocrine, and secondary sexual characteristics in both males and females.

FEMALES

Disorder	Description
1. Polycystic Ovary Syndrome (PCOS)	Hormonal imbalance → ↑ androgens, irregular periods, ovarian cysts, infertility
2. Amenorrhea	Absence of menstruation (primary or secondary); due to hypothalamic, pituitary, or ovarian causes
3. Hirsutism	Excessive hair growth in male-like pattern due to ↑ androgens (as in PCOS or adrenal tumors)
4. Hypogonadism	Deficiency of estrogen and progesterone → delayed puberty, infertility, osteoporosis
5. Premature Ovarian Failure (POF)	Early loss of ovarian function before age 40, leading to menopause-like symptoms
6. Hyperprolactinemia	Excess prolactin inhibits ovulation → infertility, amenorrhea, galactorrhea

MALES

Disorder	Description
1. Erectile Dysfunction	Inability to achieve or maintain erection sufficient for sexual activity
2. Gynecomastia	Enlargement of male breast tissue due to imbalance between estrogen and testosterone
3. Hypogonadism	Low testosterone levels → ↓ libido, infertility, muscle loss, fatigue
4. Precocious Puberty	Early onset of puberty due to excess androgens or pituitary stimulation
5. Delayed Puberty	Late or absent sexual maturation → often due to hypogonadism
6. Infertility	Low sperm count or impaired sperm function due to hormonal or testicular dysfunction

Erectile Dysfunction (ED)

→ Erectile Dysfunction (ED), also known as impotence, is defined as the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance.

It is a common condition, especially in aging males, and may be a sign of underlying health issues like cardiovascular disease or diabetes.

Etiology (Causes)

Physical (Organic) Causes

- **Vascular diseases:** Atherosclerosis, hypertension
- **Neurological disorders:** Spinal cord injury, Parkinson's, multiple sclerosis
- **Endocrine disorders:** Diabetes mellitus, hypogonadism, hyperprolactinemia
- **Medications:** Antihypertensives, antidepressants, antipsychotics
- **Surgery or trauma:** Pelvic surgery, prostatectomy
- **Substance abuse:** Alcohol, smoking, narcotics

Psychological Causes

- Stress
- Anxiety
- Depression
- Relationship problems
- Performance anxiety

Pathogenesis

1. **Sexual stimulation** → activates **parasympathetic nerves** → release **nitric oxide (NO)**
2. NO stimulates **cGMP production** → causes **relaxation of smooth muscle** in penile arteries
3. Increased **blood flow into corpora cavernosa** → erection
4. In ED, there is a **failure in this pathway** due to **vascular, neurological, hormonal, or psychological** causes

Clinical Manifestations

- Inability to **achieve or maintain erection**
- Reduced **sexual desire (libido)**
- Anxiety or depression related to sexual performance
- Relationship problems
- Signs of underlying conditions like **diabetes or heart disease**

Non-Pharmacological Management

- **Lifestyle changes**:
  - Stop smoking
  - Reduce alcohol intake
  - Lose weight
  - Regular exercise
- **Psychological counseling** for anxiety, depression, or relationship issues
- **Vacuum erection devices (VEDs)**
- **Penile implants** (in severe, unresponsive cases)

Pharmacological Management

Drug Class	Examples	Mechanism
PDE-5 inhibitors	Sildenafil (Viagra), Tadalafil, Vardenafil	↑ cGMP → vasodilation → erection
Hormonal therapy	Testosterone (if hypogonadism present)	Corrects hormonal imbalance
Prostaglandin analogs	Alprostadil (intracavernosal/intraurethral)	Directly dilates penile arteries
Dopamine agonists	Apomorphine (rarely used)	Stimulates sexual arousal centers in brain

Gynecomastia

→ Gynecomastia is a condition characterized by benign enlargement of male breast tissue, usually due to an imbalance between estrogen and androgen levels.
→ It is not breast cancer and commonly occurs during neonatal period, puberty, and old age due to normal hormonal changes.
→ It may be unilateral or bilateral and is usually soft and mobile under the nipple.

Etiology (Causes)

Physiological Causes

- **Neonatal**: Due to maternal estrogen transfer
- **Pubertal**: Temporary hormonal imbalance
- **Senile (Elderly men)**: ↓ testosterone with aging

Pathological Causes

- **Hormonal imbalance**: ↓ Androgens / ↑ Estrogens
- **Testicular failure**: Klinefelter syndrome, mumps orchitis
- **Liver disease**: Cirrhosis (increased estrogen)
- **Thyroid disorders**: Hyperthyroidism
- **Chronic kidney disease**

Drug-induced Gynecomastia

- Spironolactone
- Cimetidine
- Ketoconazole
- Anti-androgens (e.g., flutamide)
- Estrogens, anabolic steroids
- Digoxin
- Marijuana, alcohol

Pathogenesis

- Normal male breast tissue has low estrogen and high androgen influence
- In gynecomastia, ↑ estrogen or ↓ testosterone
- Leads to proliferation of glandular breast tissue
- Results in visible breast enlargement

Clinical Manifestations

- Enlargement of breast tissue (soft, tender mass behind nipple)
- Bilateral or unilateral
- Nipple sensitivity or pain
- Psychological embarrassment or anxiety
- No signs of malignancy (if symmetrical, mobile, no lymphadenopathy)

Non-Pharmacological Management

- Reassurance (pubertal gynecomastia resolves in 6–18 months)
- Avoid offending drugs or substances
- Weight loss in obese individuals
- Psychological counseling (for body image issues)
- Surgical treatment:
  - Subcutaneous mastectomy
  - Liposuction (if persistent or severe)

Pharmacological Management

Drug Class	Examples	Mechanism
Anti-estrogens	Tamoxifen, Clomiphene	Block estrogen receptors
Aromatase inhibitors	Anastrozole, Letrozole	Prevent conversion of androgens → estrogens
Androgens (rarely used)	Testosterone (if deficient)	Restore androgen:estrogen balance