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Tamil Nadu, India

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Course Code: BC303CR

UNIT – V

DISORDERS OF ENDOCRINE SYSTEM

Dr. KALAIARASI A
Dept. of Biochemistry
BDU. Trichy

BLOOD AND COAGULATION , DISTURBANCE OF BLOOD CLOTTING MECHANISM, SYSTEMATIC ANALYSIS OF HEMORRHAGIC DISORDERS COAGULATION AND PROTHROMBIN TIME

Introduction to Blood and Coagulation

Overview of Blood Composition

- Red Blood Cells (RBCs)
- White Blood Cells (WBCs)
- Platelets
- Plasma

What is Coagulation

- The process of blood clot formation
- Prevents excessive bleeding

Normal Coagulation Mechanism

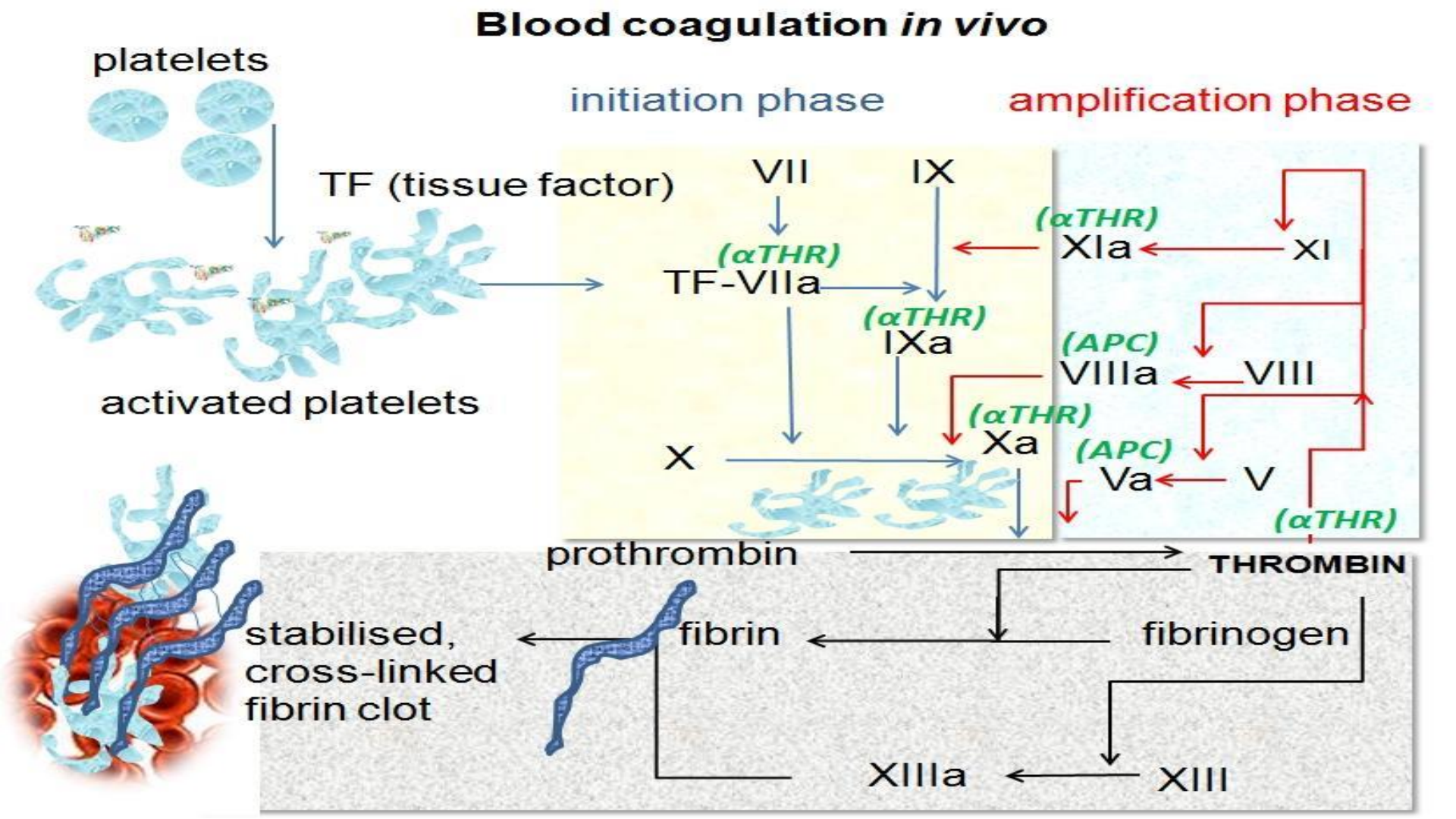
Coagulation Cascade

- ❏ Intrinsic Pathway
- ❏ Extrinsic Pathway
- ❏ Common Pathway

Steps of Clot Formation

- ❏ Vasoconstriction
- ❏ Platelet Plug Formation
- ❏ Activation of Clotting Factors
- ❏ Fibrin Mesh Formation
- ❏ Clot Retraction and Repair
- ❏ Fibrinolysis (Clot Breakdown)

Blood coagulation *in vivo*



Extrinsic and Intrinsic pathway

extrinsic pathway

The extrinsic pathway is one of the two primary pathways that initiate blood coagulation, the other being the intrinsic pathway. It is faster than the intrinsic pathway and is triggered by external trauma that causes blood to escape from the blood vessels.

Intrinsic pathway

The intrinsic pathway is the second of the two main pathways (along with the extrinsic pathway) that lead to blood coagulation. It is activated by damage to the blood vessel wall and involves factors that are already present in the bloodstream,

Disturbances in Blood Clotting Mechanism

Inherited Clotting Disorders

- ❏ Hemophilia A & B (Factor VIII and IX deficiencies)
- ❏ Von Willebrand Disease

Acquired Disorders

- ❏ Vitamin K Deficiency
- ❏ Liver Disease
- ❏ Disseminated Intravascular Coagulation (DIC)
- ❏ Anticoagulant Medications (e.g., Warfarin, Heparin)

Hemorrhagic Disorders

Symptoms of Hemorrhagic Disorders

- ❏ Frequent bruising
- ❏ Excessive bleeding after injury
- ❏ Nosebleeds
- ❏ Heavy menstrual bleeding

Clinical Assessment

- ❏ Family history of bleeding disorders
- ❏ Detailed patient history and physical examination

Laboratory Diagnosis

Tests for Hemorrhagic Disorders

- **Complete Blood Count (CBC):** Platelet levels
- **Prothrombin Time (PT):** Measures extrinsic pathway
- **Activated Partial Thromboplastin Time (aPTT):** Measures intrinsic pathway
- **Fibrinogen Levels**
- **Clotting Factor Assays**
- **Genetic Testing** (e.g., for Hemophilia or von Willebrand Disease)

Prothrombin Time (PT)

What is PT?

- Measures the time it takes for blood to clot via the **extrinsic and common pathways**.

Normal PT Range: 10-13 seconds

INR (International Normalized Ratio)

- Standardizes PT results across different labs
- Normal INR: 0.8-1.1 (without anticoagulants)

Prothrombin Time (PT) Test: Procedure

Steps in PT Testing

- Blood sample collection in sodium citrate tube
- Centrifugation to separate plasma
- Addition of thromboplastin and calcium chloride
- Measurement of clotting time

Clinical Significance

- Prolonged PT: Indicates Vitamin K deficiency, liver disease, or anticoagulant use.
- Shortened PT: Rare, but may indicate a hypercoagulable state.

Hemorrhagic Disorders – Example Conditions

Hemophilia

- Affects clotting factors VIII or IX
- Diagnosed with prolonged aPTT and normal PT

Von Willebrand Disease

- Deficiency in von Willebrand factor (vWF)
- Prolonged bleeding time, normal or slightly prolonged aPTT

Liver Disease

- Both PT and aPTT prolonged due to impaired clotting factor production

Management of Hemorrhagic Disorders

Treatment Approaches

- Factor replacement therapy (for Hemophilia)
- Vitamin K supplementation (for Vitamin K deficiency)
- Desmopressin (for von Willebrand Disease)
- Managing underlying liver disease
- Adjustments in anticoagulant medications

Conclusion

- Blood coagulation is vital to prevent excessive bleeding.
- Disturbances can lead to either excessive bleeding or unwanted clot formation.
- Systematic assessment through clinical history, lab tests like PT, and specific assays is essential for diagnosis.
- Proper treatment can manage or correct coagulation disorders.

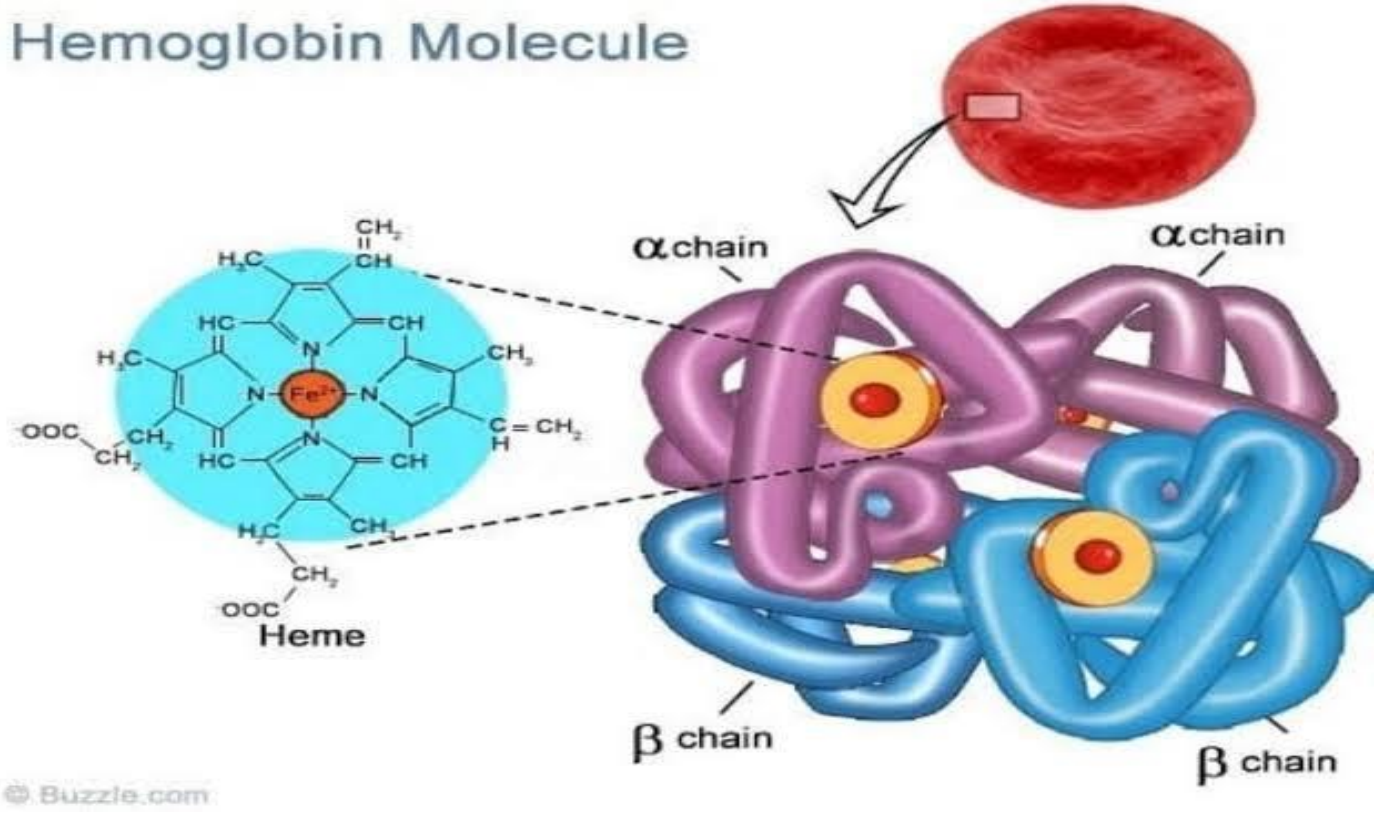
Hemoglobin and their structure abnormal hemoglobin and identification

Hemoglobin (heterotetramer protein)

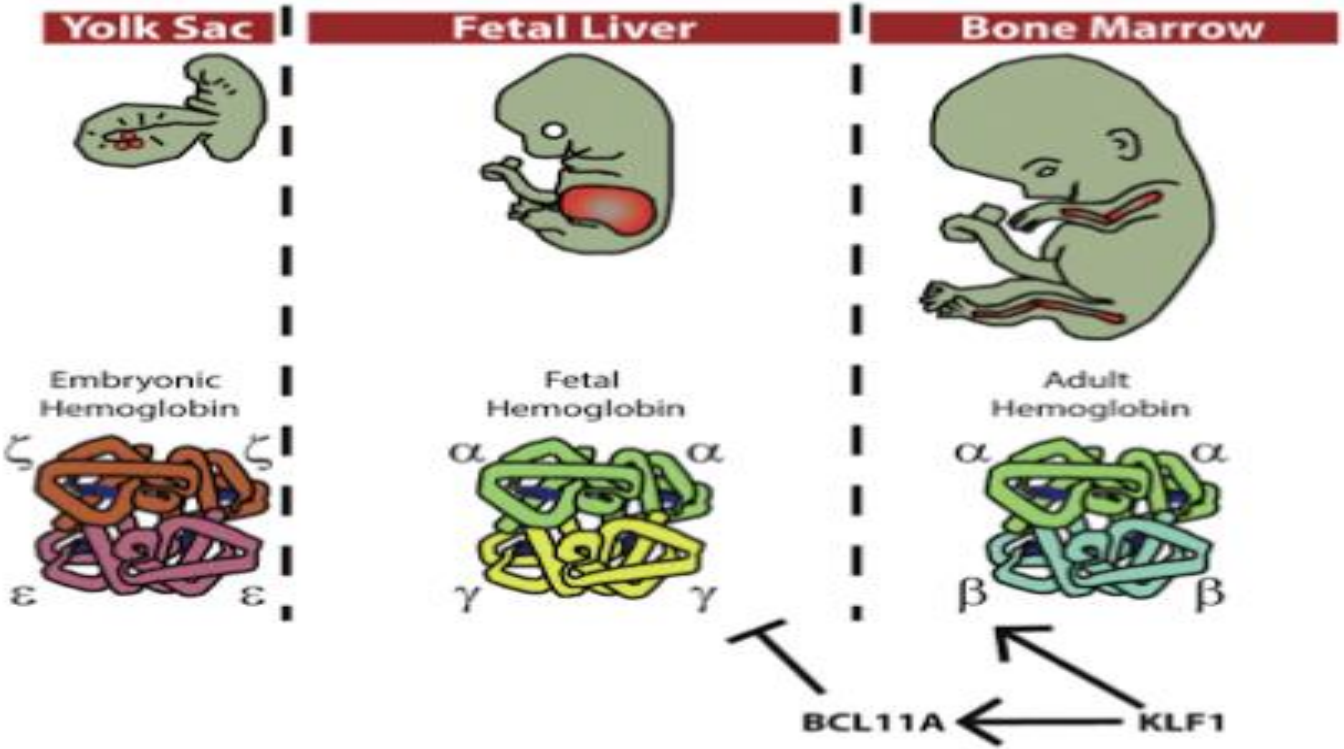
1. Hemoglobin is a protein found in red blood cells (RBCs) that is responsible for transporting oxygen from the lungs to the rest of the body and returning carbon dioxide from the tissues back to the lungs.

2. Key functions and characteristics of hemoglobin include
3. Oxygen Transport: Hemoglobin binds to oxygen in the lungs and releases it in tissues where it is needed.
4. Carbon Dioxide Transport: Hemoglobin also helps carry carbon dioxide, a waste product of metabolism, back to the lungs for exhalation.
5. Buffering: Hemoglobin plays a role in regulating blood pH by binding to hydrogen ions

Structure of hemoglobin



Hemoglobin varies during development:



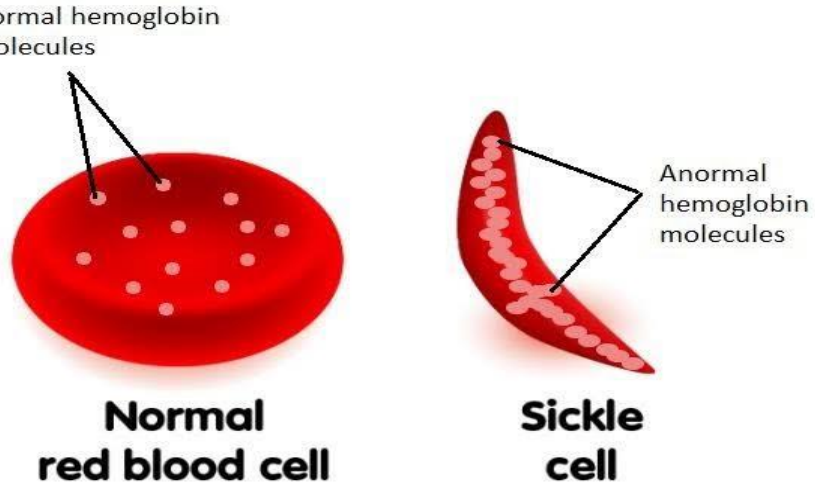
ANEMIA

1. Anemia is when you have low levels of healthy red blood cells to carry oxygen throughout your body.

2. What causes anemia?
3. Many things can cause it. For example, iron-deficiency anemia is the most common type of anemia. You can develop this type if you don’t get enough iron from the food you eat, or if you lose blood from an injury or illness. Healthcare providers classify anemia as being acquired or inherited.
4. symptoms
5. Symptoms that may occur first include:
6. Feeling weak or tired more often than usual, or with exercise.
7. Headaches.
8. Problems concentrating or thinking.
9. Irritability.
10. Loss of appetite.
11. Numbness and tingling of hands and feet.

Abnormal hemoglobin

1. Normal, healthy red blood cells are flexible, so they can move easily through blood vessels. But abnormal hemoglobin can change the size and shape of your red blood cells. This can cause the cells to clu ult to carry oxygen in yo



Abnormal hemoglobin their identification

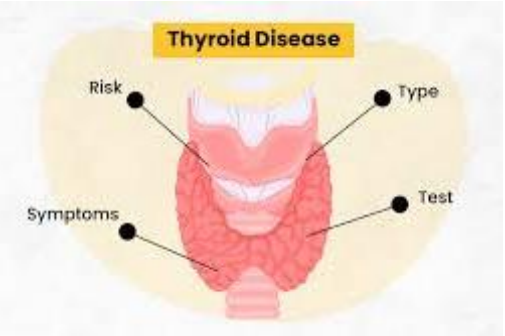
- Hemoglobin electrophoresis
- HPLC analysis
- Isoelectric Focusing (IEF):
- Capillary Electrophoresis:

Endocrine system :Laboratory Investigations and investigations related to disorders of thyroid , pituitary, adrenal cortex

Thyroid Gland Disorders: Laboratory Investigations

- **Hypothyroidism (Underactive Thyroid):**
- **TSH (Thyroid Stimulating Hormone)**:
  - The most sensitive test for hypothyroidism. Elevated TSH with low T3 and T4 levels indicates primary hypothyroidism.
  - **Primary Hypothyroidism**: The thyroid gland is not producing enough hormones, so TSH increases as the pituitary attempts to stimulate the thyroid.
- **Free T4 (FT4) and Free T3 (FT3)**:
  - **Free T4** and **Free T3** are the biologically active forms of thyroid hormones. A low Free T4 (FT4) with a high TSH typically confirms hypothyroidism.
  - In **secondary hypothyroidism** (due to pituitary dysfunction), both TSH and T4 levels are low.
- **Thyroid Antibodies**:
  - **Anti-thyroid peroxidase (TPO) antibodies** are often elevated in autoimmune hypothyroidism, especially in **Hashimoto's thyroiditis**.
  - **Thyroglobulin antibodies** may also be elevated in certain cases of autoimmune thyroiditis.
- **Thyroid Ultrasound**:
  - Helps detect structural abnormalities like **goiter**, **nodules**, or **cysts**.
  - Useful in cases of suspected **Hashimoto's thyroiditis**, where the thyroid may become enlarged or irregular in shape.

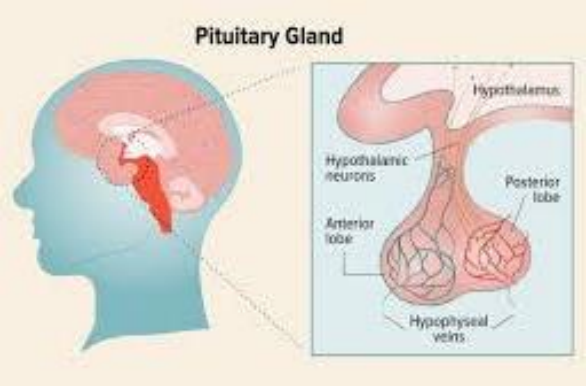
- **Hyperthyroidism (Overactive Thyroid):**
- **TSH**:
  - Low TSH with high Free T4 and Free T3 levels indicates **primary hyperthyroidism** (Graves' disease is the most common cause).
- **Free T3 and Free T4**:
  - Elevated Free T3 and Free T4 levels confirm hyperthyroidism.
- **Thyroid Antibodies**:
  - **TRAb (Thyroid Receptor Antibodies)** are often positive in **Graves' disease**, an autoimmune cause of hyperthyroidism.
- **Radioactive Iodine Uptake (RAIU)**:
  - A **high uptake** suggests **Graves' disease** or **toxic multinodula goiter**.
  - A **low uptake** may suggest thyroiditis or an iodine deficiency.



Pituitary Gland Disorders: Laboratory Investigations

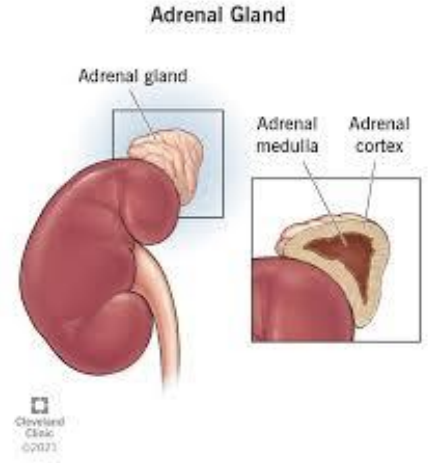
- **Hypopituitarism (Underactive Pituitary**
  - Low levels of these hormones suggest **hypopituitarism**, which may be caused by pituitary tumors, trauma, or radiation.
- **Stimulation Tests**:
  - **ACTH Stimulation Test**: Used to test adrenal insufficiency. In a healthy person, ACTH should stimulate cortisol production; no increase in cortisol indicates pituitary dysfunction.
  - **Growth Hormone Stimulation Test**: Often performed using **insulin tolerance test (ITT)** or **GHRH** stimulation. Low growth hormone response indicates pituitary insufficiency.
- **MRI/CT Imaging**:
  - **Pituitary MRI** is the gold standard for detecting tumors or structural abnormalities in the pituitary gland.

- **Hyperpituitarism (Excess Pituitary Hormones):**
- **Prolactin**:
  - Elevated prolactin levels may suggest a **prolactinoma** (a benign pituitary tumor). Symptoms include galactorrhea and amenorrhea.
- **Growth Hormone (GH)**:
  - **Acromegaly** (due to excess GH, typically caused by a pituitary adenoma) is diagnosed by measuring GH levels and performing an **Oral Glucose Tolerance Test (OGTT)**. Failure to suppress GH after glucose ingestion is diagnostic.
- **ACTH and Cortisol**:
  - **Cushing's disease** (pituitary origin) can be diagnosed by **ACT levels**, **24-hour urinary free cortisol**, or the **Dexamethasone suppression test**.
- **MRI/CT Imaging**:
  - For detecting pituitary adenomas or other structural causes.



Adrenal Cortex Disorders: Laboratory Investigations

- **Cushing's Syndrome (Excess Cortisol):**
- **24-hour Urinary Free Cortisol**:
  - Elevated levels suggest **Cushing's syndrome**. Urine is collected over a 24-hour period to measure cortisol excretion.
- **Low-Dose Dexamethasone Suppression Test**:
  - A normal response is a decrease in cortisol levels after taking dexamethasone. In **Cushing's syndrome**, cortisol production is not suppressed.
- **ACTH**:
  - **Low ACTH** suggests **adrenal tumor** (adrenal cortisol overproduction).
  - **High ACTH** indicates **Cushing's disease** (pituitary adenoma).
- **Salivary Cortisol**:
  - Late-night salivary cortisol is used to assess the circadian rhythm of cor production. Elevated levels at night are indicative of **Cushing's syndron**

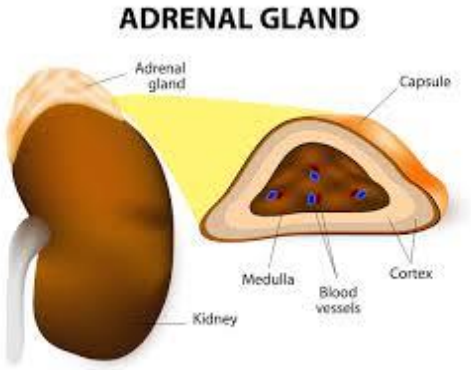


- **Addison's Disease (Adrenal Insufficiency):**
- **Morning Serum Cortisol**:
  - Cortisol is normally highest in the morning. Low levels may indicate **Addison's disease**.
- **ACTH Stimulation Test**:
  - A failure to increase cortisol levels after administering synthetic ACTH confirms **Addison's disease**.
  - Elevated ACTH levels with low cortisol suggest primary adrenal insufficiency.
- **Electrolyte Imbalances**:
  - **Hyponatremia**, **hyperkalemia**, and **hypoglycemia** are classic signs of **Addison's disease**.
- **Hyperaldosteronism (Excess Aldosterone):**
- **Plasma Renin Activity (PRA) and Aldosterone**:
  - **Primary hyperaldosteronism** is characterized by **low renin** and **high aldosterone** levels.
- **Saline Infusion Test**:
  - Failure to suppress aldosterone after intravenous saline infusion confirms **primary hyperaldosteronism**.
- **CT/MRI Imaging**:
  - Imaging is used to identify **adrenal adenomas** or **hyperplasia** of the adrenal glands.

ENDOCRINE SYSTEM:ADRENAL MEDULLA,TESTES,OVARIES-PLASMA AND URINARY ASSAYS OF HORMONES RELATED TO VARIOUS ENDOCRINE DISORDERS

ADRENAL GLAND

Adrenal Medulla:



- Inner portion of the adrenal gland
- It is a small organ that sits on top of each kidney.
- The adrenal medulla produces hormones that help the body respond to stress, such as during the fight-or-flight response.
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Function –Produces hormones that control the body's response to stress

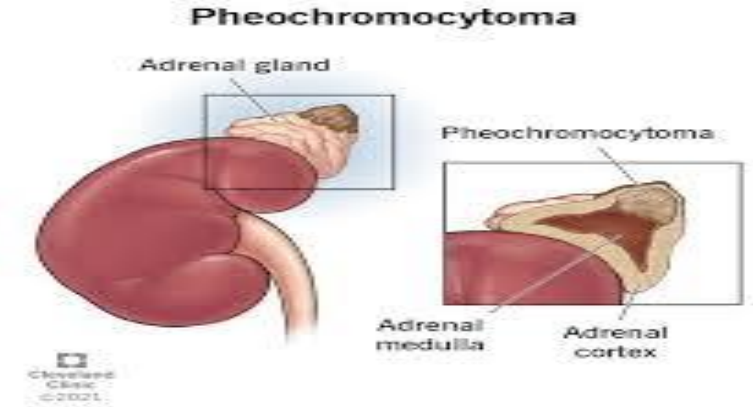
Main hormones –Epinephrine (adrenaline) and norepinephrine (noradrenaline)

Regulation –Regulated by the sympathetic nervous system

DISORDER OF ADRENAL MEDULLA

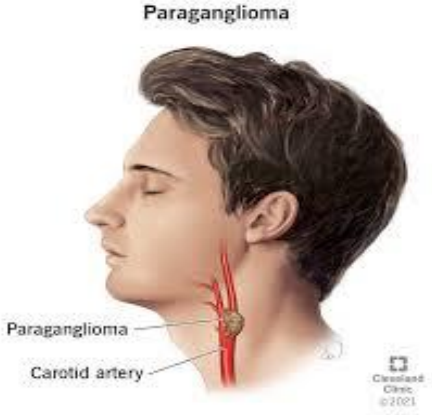
Pheochromocytoma

Pheochromocytoma is a rare tumor of the adrenal medulla that produces excess catecholamines (adrenaline and noradrenaline), it may occur in person of any age (mostly in people with hypertension)



PARAGANGLIOMA

Paraganglioma is a rare tumor that arises from paraganglia, clusters of neuroendocrine cells found throughout the body. These tumors can be either functional (producing hormones) or non-functional.



Types

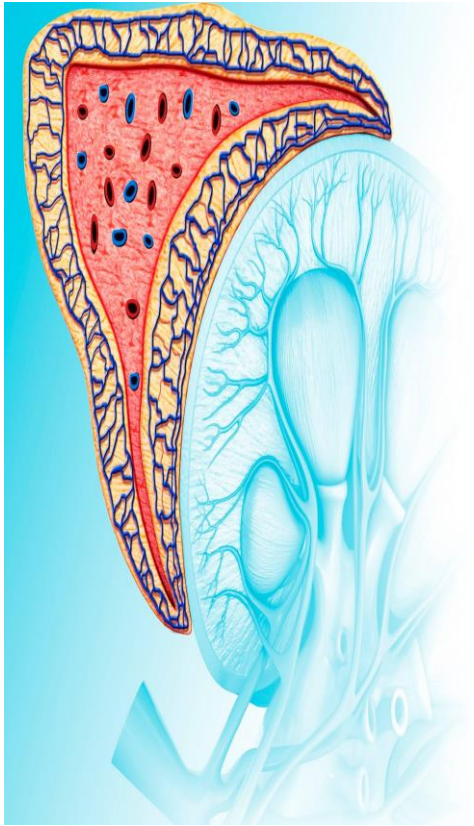
- **Functional Paragangliomas**: These tumors secrete catecholamines, similar to pheochromocytomas, leading to symptoms like hypertension and palpitations.

- **Non-Functional Paragangliomas**: These tumors do not produce significant hormones and may present with symptoms related to mass effect, such as pain or pressure.

ADRENAL MEDULLARY HYPERPLASIA

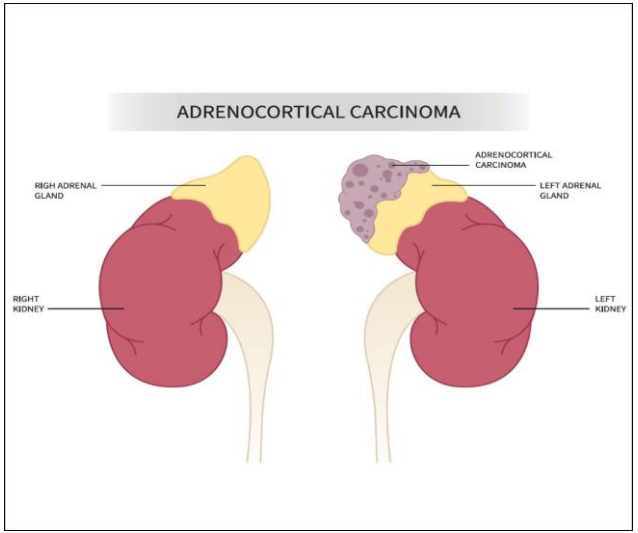
Adrenal medullary hyperplasia is a condition characterized by an increase in the number of cells in the adrenal medulla, leading to its enlargement.

- This can result in excess production of catecholamines (adrenaline and noradrenaline).



ADRENAL CARCINOMA

- Adrenal carcinoma, also known as adrenal cortical carcinoma (ACC).
- It is a rare and aggressive cancer that originates in the adrenal cortex, the outer layer of the adrenal glands.
- This type of cancer can produce hormones and may lead to significant hormonal imbalances.



Symptoms

- **Hypertension**: Persistent or episodic high blood pressure.
- **Palpitations**: Rapid or irregular heartbeat.
- **Headaches**: Severe headaches, often described as pounding or throbbing.
- **Sweating**: Excessive sweating (hyperhidrosis).
- **Anxiety or Panic Attacks**: Episodes of intense anxiety or feelings of panic.
- **Weight Loss**: Unexplained weight loss despite normal appetite.

Diagnosis

- **Blood and Urine Tests**: Elevated levels of catecholamines or their metabolites (like metanephrines) are indicative.
- **Imaging Studies**: CT or MRI scans to locate the tumor.
- **Genetic Testing**: May be performed if there's a family history of related conditions.

Treatment

- **Surgery**: The primary treatment is surgical removal of the tumor.
- **Medications**: Before surgery, patients may require medications (like alpha-blockers) to manage hypertension and prevent complications.

TESTES

The testes (or testicles) are the male reproductive organs responsible for producing sperm and hormones, primarily testosterone. They are located in the scrotum and play a critical role in male fertility and overall hormonal balance.

Common Disorders

1. **Cryptorchidism**: A condition where one or both testes fail to descend into the scrotum. This can lead to infertility and increases the risk of testicular cancer.
    - **Symptoms**: Absence of one or both testes in the scrotum, potential swelling, and possible fertility issues later in life.
2. **Testicular Torsion**: A medical emergency where the spermatic cord twists, cutting off blood supply to the testis.
    - **Symptoms**: Sudden severe pain in the scrotum, swelling, nausea, vomiting, and sometimes fever.

3.Epididymitis: Inflammation of the epididymis, often caused by infection.

- **Symptoms**: Pain and swelling in the scrotum, tenderness, fever, and sometimes discharge from the urethra.

4.Orchitis: Inflammation of the testes, often due to viral or bacterial infections.

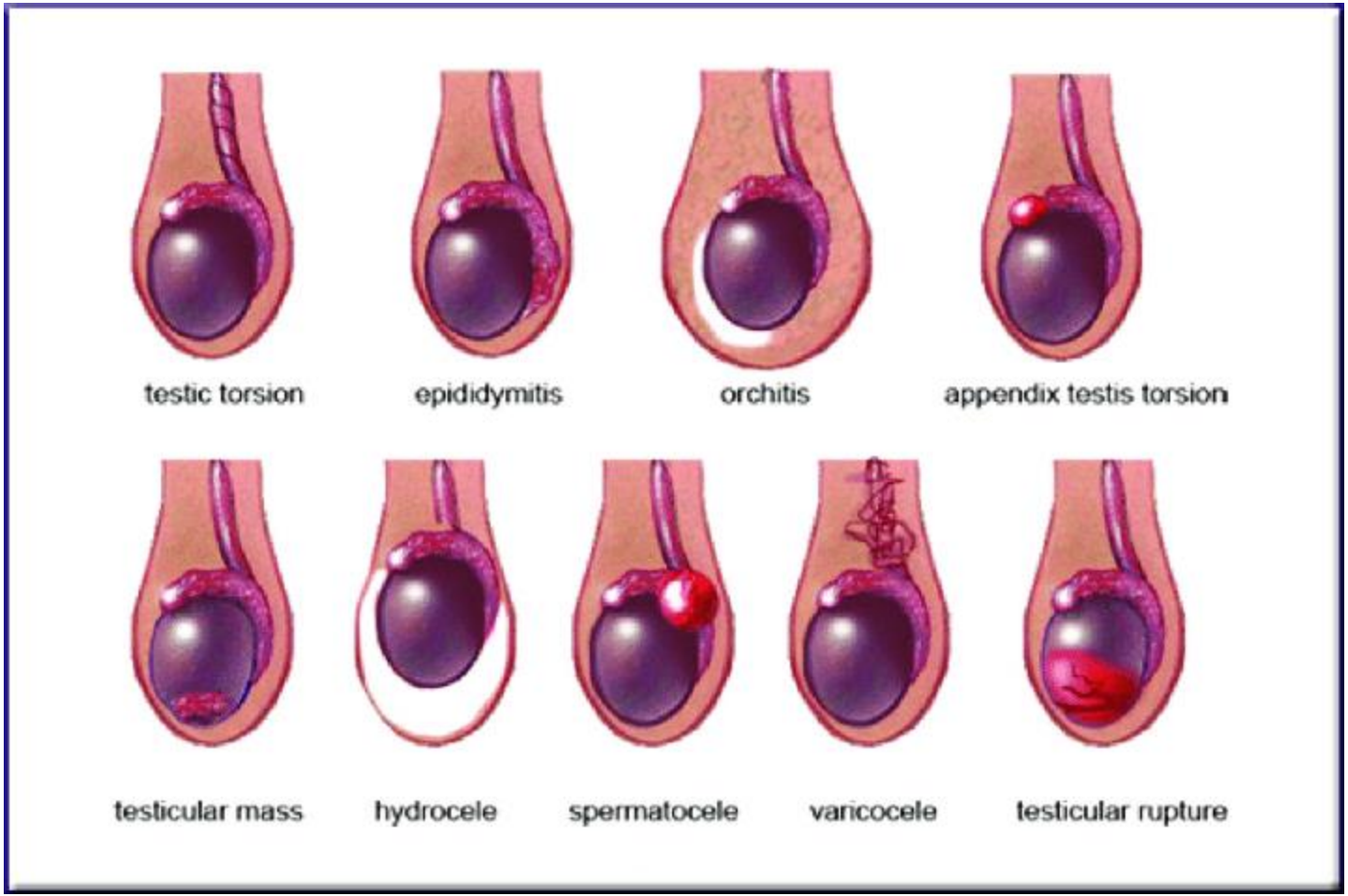
- **Symptoms**: Pain and swelling in the testes, fever, and sometimes a rash (if viral).

5.Testicular Cancer: A malignant growth that can arise from germ cells or other tissues within the testes.

- **Symptoms**: A lump or swelling in the testicle, pain or discomfort in the scrotum, heaviness in the scrotum, and changes in size or shape.

6.Varicocele: Enlarged veins within the scrotum, similar to varicose veins.

- **Symptoms**: Often asymptomatic, but can cause dull pain or a feeling of heaviness in the scrotum


testic torsion
epididymitis
orchitis
appendix testis torsion
testicular mass
hydrocele
spermatocele
varicocele
testicular rupture

Diagnosis

- **Physical Examination**: Doctors assess size, shape, and tenderness.
- **Ultrasound**: Imaging used to examine abnormalities or masses.
- **Blood Tests**: To check hormone levels and identify tumor markers in cases of cancer

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Treatment

- **Surgery**: For conditions like cryptorchidism, torsion, and varicocele.
- **Antibiotics**: For infections like epididymitis and orchitis.
- **Chemotherapy/Radiation**: For testicular cancer, depending on the stage and type.

OVARIES

The ovaries are the female reproductive organs responsible for producing eggs (ova) and hormones, including estrogen and progesterone. They play a crucial role in the menstrual cycle, fertility, and overall hormonal balance.

Common Disorders

1. **Polycystic Ovary Syndrome (PCOS)**: A hormonal disorder characterized by enlarged ovaries with multiple small cysts.
    - **Symptoms**: Irregular or absent menstrual periods, excessive hair growth (hirsutism), acne, weight gain, and fertility issues.
2. **Ovarian Cysts**: Fluid-filled sacs that develop on the ovaries. Most are benign and may resolve on their own.
    - **Symptoms**: Often asymptomatic, but can cause pelvic pain, bloating, or pressure if large or ruptured.

3. Ovarian Cancer: Malignant tumors that develop in the ovaries.

- **Symptoms**: Bloating, pelvic or abdominal pain, difficulty eating, frequent urination, and changes in menstrual patterns.

4. Premature Ovarian Failure (POF): The loss of normal ovarian function before age 40, leading to reduced hormone production and infertility.

- **Symptoms**: Irregular or absent periods, hot flashes, night sweats, and infertility.

5. Endometriosis: A condition where tissue similar to the lining of the uterus grows outside of it, often affecting the ovaries.

- **Symptoms**: Painful periods, pain during intercourse, pelvic pain, and infertility.

Disorders

Polycystic Ovary Syndrome (PCOS)

Ovarian Cysts

Ovarian Cancer

Primary Ovarian Insufficiency (POI)

Osteoporosis

Diagnosis

- **Physical Examination**: Assessment of symptoms and pelvic exam.
- **Ultrasound**: Imaging to evaluate ovarian structure and identify cysts or tumors.
- **Blood Tests**: To check hormone levels and tumor markers (e.g., CA-125 for ovarian cancer).

Treatment

- **Lifestyle Changes**: For conditions like PCOS, weight management and exercise can help.
- **Medications**: Hormonal contraceptives for regulating menstrual cycles, pain relief for endometriosis, and fertility treatments as needed.
- **Surgery**: For large cysts, endometriosis, or ovarian tumors.

plasma and urinary assays of hormones related to various endocrine disorders

Plasma and urinary assays are essential diagnostic tools for evaluating hormonal levels and diagnosing various endocrine disorders.

1. **Cortisol:**

Cortisol is a steroid hormone produced by the adrenal glands, specifically in the adrenal cortex. It is often referred to as the "stress hormone" because its levels increase in response to stress.

Assays:

- **Plasma Cortisol**: Plasma cortisol refers to the concentration of cortisol, a steroid hormone, present in the blood. Cortisol is produced by the adrenal cortex and plays a crucial role in various bodily functions, including metabolism, immune response, and stress regulation
- .Measured in blood, often at specific times (e.g., morning and late-night) to assess diurnal variation.
- **Urinary Free Cortisol**: Collected over 24 hours to measure total cortisol excretion.

Disorders:

- **Cushing's Syndrome**: Elevated cortisol levels.
- **Adrenal Insufficiency**: Low cortisol levels.

2. Thyroid Hormones (TSH, T3, T4)

- **Assays**:
  - **Plasma Thyroid-Stimulating Hormone (TSH)**: First-line test for thyroid function.
  - **Free T4 and Total T3**: Measured to assess thyroid hormone levels.
- **Disorders**:
  - **Hypothyroidism**: Elevated TSH, low T4.
  - **Hyperthyroidism**: Low TSH, elevated T4/T3.

3. Insulin and Glucose

- **Assays**:
  - **Plasma Insulin**: Measured during fasting or after a glucose tolerance test.
  - **Fasting Blood Glucose**: Assesses blood sugar levels.

- **Disorders**:
  - **Diabetes Mellitus**: Elevated glucose and possibly high insulin.
  - **Insulinoma**: Elevated insulin levels.

4. Adrenal Hormones (Aldosterone, Catecholamines)

- **Assays**:
  - **Plasma Aldosterone**: Measured alongside plasma renin activity to evaluate the renin-angiotensin system.
  - **Urinary Catecholamines**: Measured in a 24-hour urine sample (includes epinephrine and norepinephrine).
- **Disorders**:
  - **Primary Hyperaldosteronism (Conn's Syndrome)**: High aldosterone levels.
  - **Pheochromocytoma**: Elevated catecholamine levels.

5. Sex Hormones (Estrogen, Testosterone)

- **Assays**:
  - **Plasma Testosterone**: Measured in both men and women.
  - **Urinary Estrogen**: Often assessed in 24-hour urine samples for total estrogen metabolites.
- **Disorders**:
  - **Polycystic Ovary Syndrome (PCOS)**: Elevated androgens (testosterone).
  - **Hypogonadism**: Low testosterone levels.

6. Parathyroid Hormone (PTH)

- **Assays**:
  - **Plasma PTH**: Measured to assess parathyroid function.
- **Disorders**:
  - **Primary Hyperparathyroidism**: Elevated PTH with high calcium levels.
  - **Secondary Hyperparathyroidism**: Elevated PTH with low calcium levels.

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