Name of Unit	Hematological Diseases, Endocrine System, Nervous System and Gastrointestinal System
Subject /Course name	Pathophysiology
Subject/Course ID	BP204T
Class: B.Pharm. Semester	II
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Learning Outcome of Module 03

LO	Learning Outcome	Course Outcome Code
LO 1	To understand about the Hematological Diseases: Iron deficiency, megaloblastic anemia (Vit B12 & folic acid), sickle cell anemia, thalassemia, hereditary acquired anemia, hemophilia.	BP204T.3
LO 2	To understand about the Endocrine System**:** Diabetes, thyroid diseases,	BP204T.3
LO 3	To understand about the disorders of sex hormones	BP204T.3
LO 4	To understand about the Nervous System**:** Epilepsy, Parkinson's disease, stroke,	BP204T.3
LO 5	To understand about the psychiatric disorders: depression, schizophrenia and Alzheimer's disease	BP204T.3
LO 6	To understand about the Gastrointestinal System: Peptic Ulcer	BP204T.3

Content Table

Topic
• Hematological Diseases: Iron deficiency, megaloblastic anemia (Vit B12 & folic acid), sickle cell anemia, thalassemia, hereditary acquired anemia, hemophilia. • Endocrine System: Diabetes, thyroid diseases, disorders of sex hormones • Nervous System: Epilepsy, Parkinson's disease, stroke, psychiatric disorders: depression, schizophrenia and Alzheimer's disease • Gastrointestinal System: Peptic Ulcer

HEMATOLOGICAL DISEASE

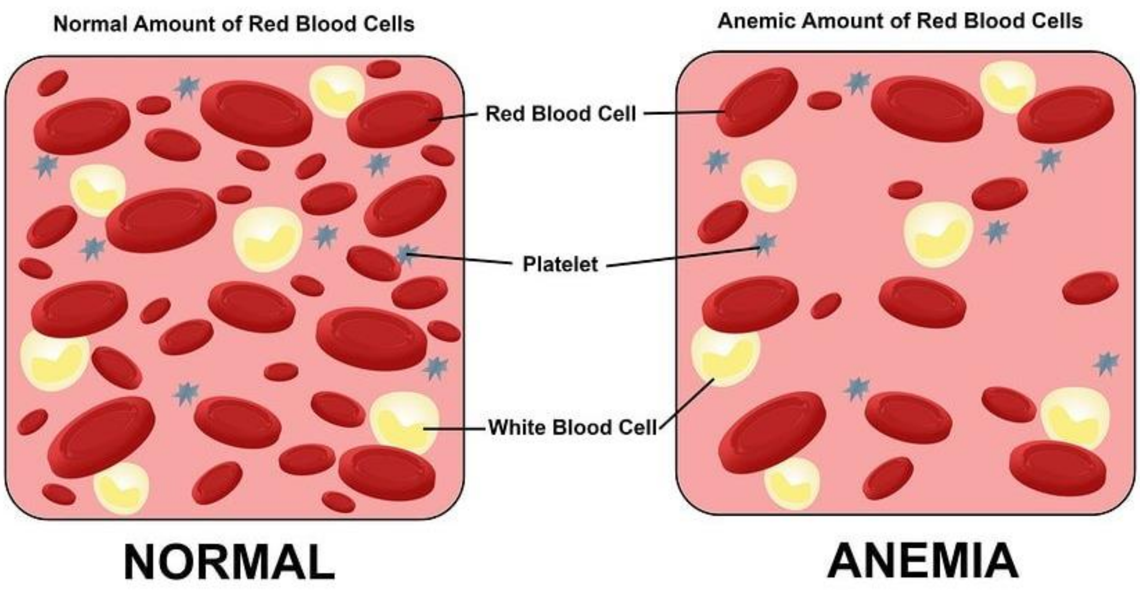
ANEMIA

Anemia derived from Greek word ***anaimia*** which means lack of blood. It is a decrease in number of red blood cell (RBCs) or less than the normal quantity of hemoglobin in the blood.

Anemia is the condition in which the oxygen carrying capacity of blood is reduced. In the anemia the total number of RBCs decreases so indirectly decreases the oxygen level so decrease the production of ATP and energy.

WHO: Anemia is the condition in which the oxygen carrying capacity insufficient to meet physiologic needs, which vary by age sex, altitude, smoking and pregnancy.

OXFORD: Anemia is defined as low hemoglobin (Hb) concentration and may be due either to a low red cell mass or increased plasma volume.



GENERAL PATHOPHYSIOLOGY OF ANEMIA:

Subnormal level of haemoglobin causes lowered oxygen carrying capacity of the blood. This, in turn, initiates compensatory physiologic adaptations such as follows:

- Increased release of oxygen from haemoglobin.
- Increased blood flow to the tissues;
- Maintenance of the blood volume; and
- Redistribution of blood flow to maintain the cerebral blood supply.

Anemia is not a single disease entity but a sign of disease. Independent of the cause, anemia is associated with a reduction in circulating Hb because of reduced number of erythrocytes or less Hb per erythrocytes. The number of erythrocytes varies with age, sex and atmospheric pressure

CAUSES:

The main causes of anemia are:

1. Blood loss
2. Lack of red blood cell production
3. High rates of red blood cell destruction

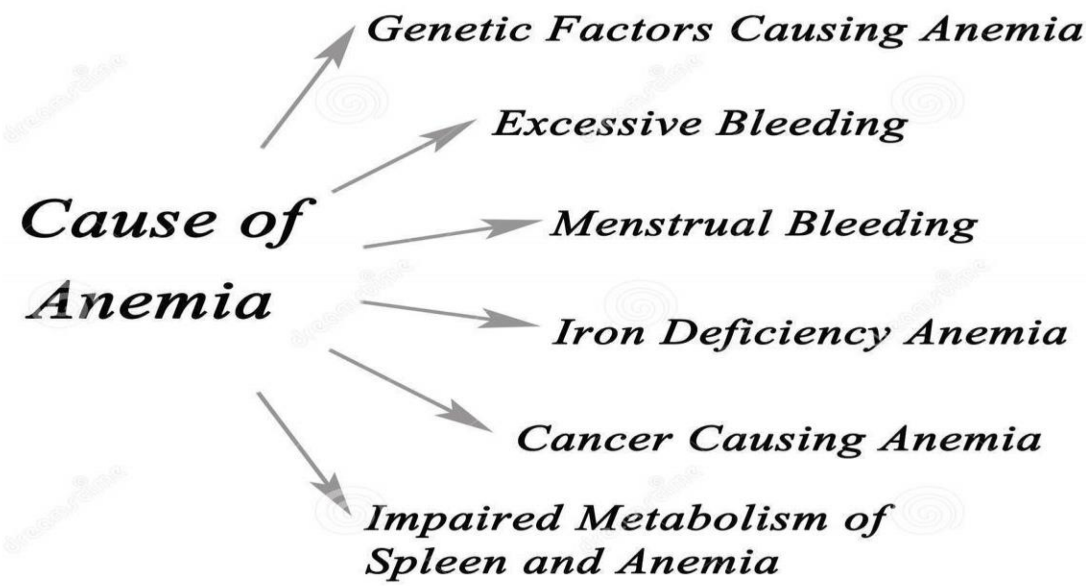
Blood Loss

Blood loss is the most common cause of anemia, especially iron-deficiency anemia.

Blood loss can be short term or persist over time.

Heavy menstrual periods or bleeding in the digestive or urinary tract can cause blood loss. Surgery, trauma, or cancer also can cause blood loss.

If a lot of blood is lost, the body may lose enough red blood cells to cause anemia.



Lack of Red Blood Cell Production

Both acquired and inherited conditions and factors can prevent your body from making enough red blood cells. "Acquired" means you aren't born with the condition, but you develop it. "Inherited" means your parents passed the gene for the condition on to you.

Acquired conditions and factors that can lead to anemia include poor diet, abnormal hormone levels, some chronic (ongoing) diseases, and pregnancy.

Aplastic anemia also can prevent your body from making enough red blood cells. This condition can be acquired or inherited.

High rates of red blood cell destruction

Both acquired and inherited conditions and factors can cause your body to destroy too many red blood cells.

Hemolytic anemia is example of a condition in which your body destroys too many red blood cells. Inherited or acquired conditions or factors can cause hemolytic anemia. Examples include immune disorders, infections, certain medicines, or reactions to blood transfusions.

The other causes for the anemia are as under:

Diet A diet that lacks iron, folic acid (folate), or vitamin B12 can prevent your body from making enough red blood cells. Your body also needs small amounts of vitamin C, riboflavin, and copper to make red blood cells. Conditions that make it hard for your body to absorb nutrients also can prevent your body from making enough red blood cells.

Hormones Our body needs the hormone erythropoietin to make red blood cells. This hormone stimulates the bone marrow to make these cells. A low level of this hormone can lead to anemia.

Diseases and disease treatments: Chronic diseases, like kidney disease and cancer, can make it hard for your body to make enough red blood cells. Some cancer treatments may damage the bone marrow or damage the red blood cells ‘ability to carry oxygen. People who have HIV/AIDS may develop anemia due to infections or medicines used to treat their diseases.

Pregnancy Anemia can occur during pregnancy due to low levels of iron and folic acid and changes in the blood. During the first 6 months of pregnancy, the fluid portion of a woman's blood (the plasma) increases faster than the number of red blood cells. This dilutes the blood and can lead to anemia.

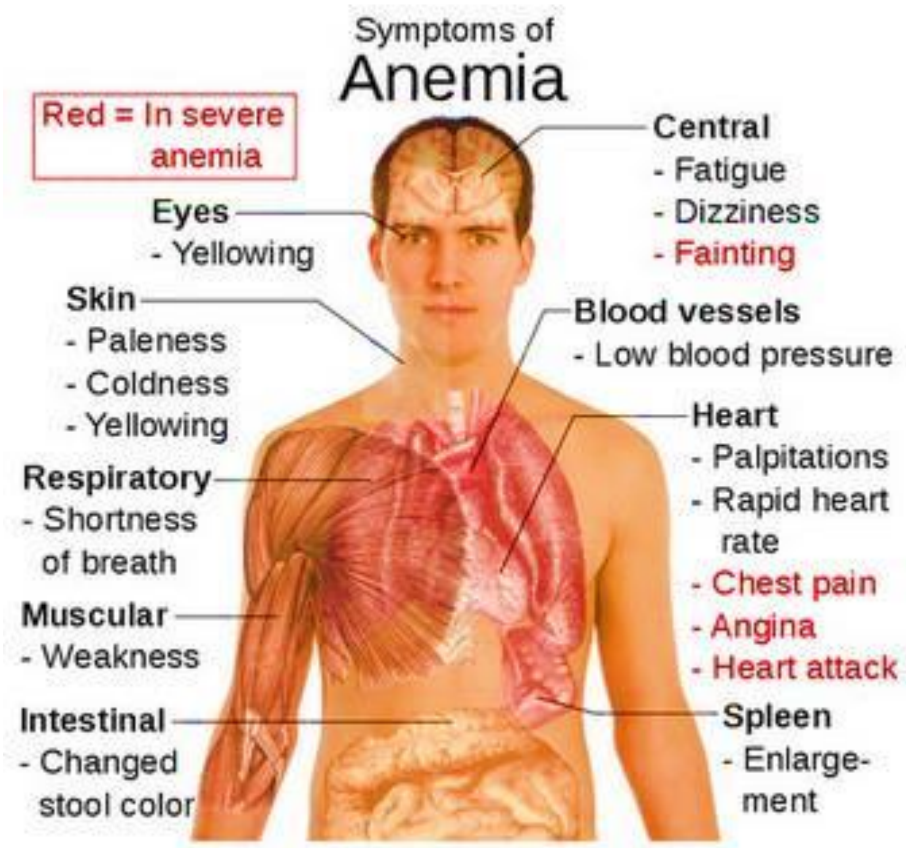
NORMAL HEMOGLOBINE VALUE AS PER AGE AND SEX:

Age & Sex	Mean Hb (g/dl)
1-3 days	16.0 – 19.0
6 Months – 2 Yrs	12.0 – 14.5
12 – 18 Yrs Male Female	 14.5 – 17.0 12.5 – 14.0
Adult Male Adult Female	15.5 – 17.0 13.0 – 15.0

Note: Atmospheric pressure:

People at high altitudes have more erythrocytes than at low altitudes.

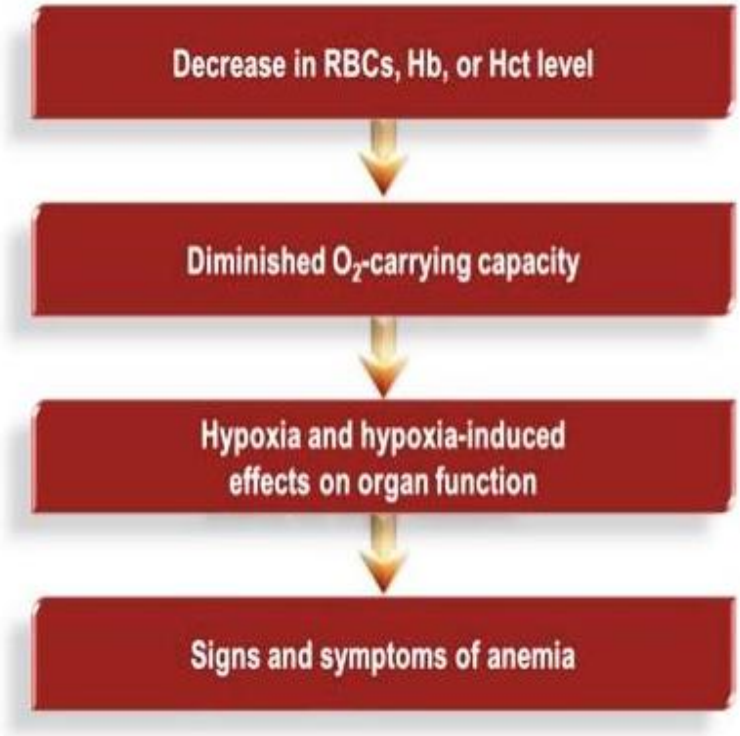
SIGNS & SYMPTOMS:



NORMAL HEMATOLOGIC PARAMETERS	
Component	**Conventional**
Hematocrit (Ratio of RBC-Blood Vol.)	
Male	45 – 52 %
Female	37 – 48 %
Hemoglobin	
Male	14 – 18 g /dL
Female	12 – 15 g/dL
Erythrocyte count	4.2 -5.9 x 106/mm
Reticulocyte count	0.5 – 1.5 %
MCV	80 – 90 fmol
MCH	27 – 30 pg
MCHC	32 – 36 g/dL
RDW	11.5 – 14.5 %

NORMAL BIOCHEMICAL PARAMETERS	
Iron	
Male	80 – 200 mcg/dL
Female	60 – 190 mcg/dL
Transferrin	170 – 370 mg/dL
TIBC	250 – 410 g/ml
Transferrin saturation	20 – 55 %
Transferrin receptors	2.8 – 8.5 mg/L
Ferritin	1.5 – 30 mcg/dL
Zinc protoporphyrin	<70 mcg/dL red cell
Folate	
Normal	2 – 10 ng/ml
Borderline	1 - 1.9 ng/ml
Vitamin B12	200 – 1000pg/ml
Methylmalonic acid	53 – 376 nmol/ L
Homocysteine	4.1 – 21.3 mcmol / L

Pathophysiology



DIAGNOSIS:

A detailed medical & medication history along with hematologic & biochemical tests is obtained.

I. Hematologic tests:

It includes blood Hb concentration, cell counts, mean corpuscular volume (MCV), Hct, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), etc.

1. MCV cell size

Microcytic anemia - < 80fL

Macrocytic anemia - >100fL

2. MCH & MCHC cell colour

Hypochromic anemia - low MCHC

Hyperchromic anemia - high MCHC

3. Red blood cell distribution width (RDW) →variation in erythrocyte size in blood sample

Iron deficiency anemia →increased RDW

4. Reticulocyte counts →bone marrow activity

Iron, B12 or folic acid therapy for respective deficiency states → reticulocytosis

5. Others: differential white cell count, platelet count, microscopic examination of peripheral blood smears & bone marrow aspirates.

II. Biochemical tests:

It includes measurement of serum vitamin conc, transport proteins, saturation of protein binding sites & storage amounts.

TYPES OF ANEMIA

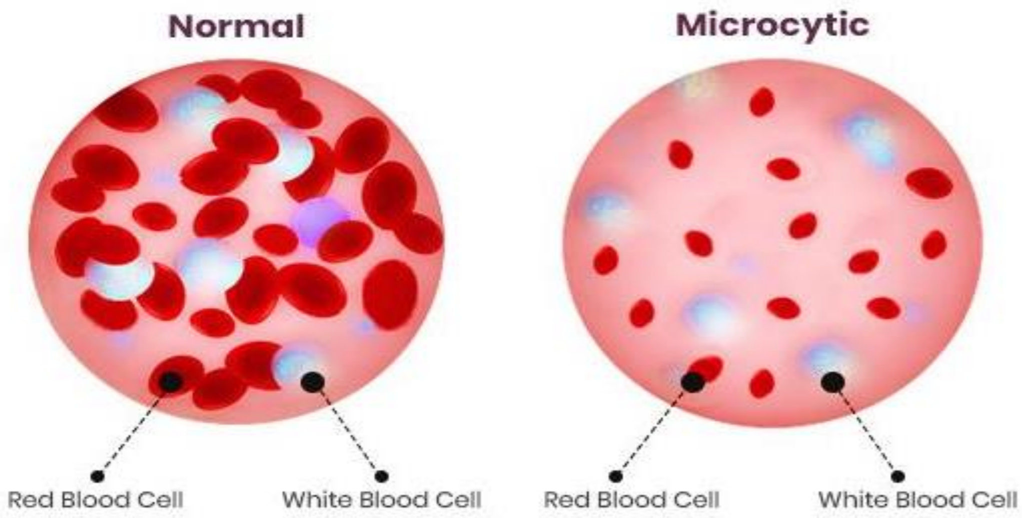
On the basis of cause

- Bleeding (blood loss)
- Hypoproliferative anemia (Inadequate production of normal blood cell)
- Hemolytic (Destruction of blood cell)

On the basis of morphology

a) **Microcytic anemia**:

If the red blood cells are smaller than normal, this is called **microcytic anemia**. The major causes of this type are iron deficiency (low level iron) anemia and thalassemia (inherited disorders of hemoglobin).

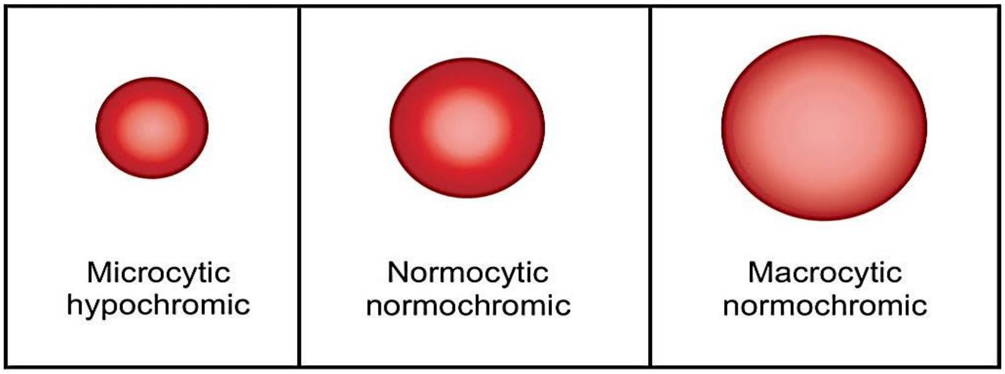


b) Normocytic anemia

If the red blood cells size are normal in size (but low in number), this is called ***normocytic anemia***, such as anemia that accompanies chronic disease or anemia related to kidney disease.

c) Macrocytic anemia

If red blood cells are larger than normal, then it is called ***macrocytic anemia***. Major causes of this type are pernicious anemia and anemia related to alcoholism.



ACCORDING TO THE CAUSE, ANEMIA IS CLASSIFIED AS UNDER:

A) IRON DEFICIENCY ANEMIA:

- It is cause by excessive loss of iron or inadequate absorption of iron.
- It is most often in female than male.
- Iron absorption is regulated by iron needs & body stores.
- When iron stores are low, higher proportion of available iron is absorbed & vice versa.
- Except, in primary hemochromatosis, thalassemia & megaloblastic anemia iron absorption remains normal & even elevated despite increased iron stores.
- It is primarily absorbed in upper duodenum.

PATHOPHYSIOLOGY OF IRON DEFICIENCY ANEMIA:

Iron is an essential element for erythropoiesis, tissue respiration & several enzyme catalyzed reactions. The average adult body contains 3 to 5 g elemental iron.

Iron is distributed in body in two forms: functional & storage.

I. Functional iron

- It exists as Hb, little as myoglobin, transferring & tissue enzymes.
- Hb is the oxygen binding protein that transports oxygen from lungs to tissues.
- Myoglobin, a hemo protein in muscle accepts oxygen from hemoglobin in the peripheries & acts as an oxygen store in muscle. If oxygen supply is limited, it releases oxygen to cytochrome oxidase leading to oxidative phosphorylation.

- Transferrin is a specific iron binding protein that transports iron through plasma & extravascular spaces. Each molecule of transferrin binds 2 molecules of iron in ferric state. The TIBC is high in iron deficiency & low in iron overload.

Predisposing Factor

Sex (Menstruation)

Precipitating Factors

Inadiquate iron intake & faulty diet

Blood loss

Pregnancy

↓

↓ Intake of iron rich foods, with blood loss

↓

Iron in body is used up

↓

Decreased iron reserves needed for hemoglobin production

↓

Decreased RBC production due to lack of hemoglobin

↓

Decreased Oxygen and Hemoglobin

II. Storage iron:

- It is in the form of ferritin & hemosiderin, which is located in parenchymal cells of liver & reticulo endothelial cells of the bone marrow, spleen & liver.
- Low iron stores are an early sign of iron deficiency & may help differentiate between iron deficiency anemia & other causes of anemia.

DAILY IRON NEEDS:

Recommended daily allowances of iron:

Category	Age (Yrs.)	Iron (mg)
Infants	0 – 0.5	6
	0.5 – 1	10
Children	1 – 10	10
Boys & men	11 - 18	12
	> 19	10
Girls & women	11 – 50	15
	> 51	10
Pregnant women		30
Lactating women		15

FACTORS ASSOCIATED WITH IRON ABSORPTION:

Promoting absorption

Inorganic iron: ferrous form is better absorbed than ferric iron & organically bound iron.

Ascorbic acid: Convert ferric iron to ferrous iron

Acids Gastric: HCl promotes the release & conversion of dietary iron to the ferrous form

Chelates Iron: chelated to low mol wt sub (sugars, amino acids, succinates) facilitates iron binding to the intestinal mucosa

Clinical states: Iron deficiency, increased erythropoiesis, pregnancy, anoxia & pyridoxine deficiency.

Reducing absorption

Alkaline: Antacids, alkaline pancreatic secretions containing phosphate convert iron to insoluble ferric hydroxide

Dietary: Dietary phosphates & phytates in cereals & tannins in tea probably complex iron

Clinical states: Chronic diarrhea, steatorrhea, adequate iron stores, decreased erythropoiesis, acute or chronic inflammation

FACTORS ASSOCIATED WITH IRON DEFICIENCY:

Factor Association

Dietary: Starvation, poverty, vegetarianism, religious practice, food pads

Blood loss:

Women & Girls: Menstruation, postmenopausal bleeding, pregnancy

General: Peptic ulcer, drug induced gastritis, carcinomas of colon & stomach, ulcerative colitis, hemorrhoids, renal or bladder lesions, hookworm infestations, frequent blood donation, athletic training, widespread bleeding disorders

Malabsorption: Celiac disease, inflammation partial & total gastrectomy, chronic

Increased requirements: Rapid growth, pregnancy

SIGNS & SYMPTOMS:

- Developmental delays
- Behavioral disturbances
- Altered central nervous system development
- Impaired work capacity
- Preterm delivery
- Delivery of low birth weight baby
- Others like brittle or spoon shaped nails, angular stomatitis, atrophic tongue & pharyngeal & esophageal webs causing dysphagia & atrophic gastric mucosa.

DIAGNOSIS:

- Medical history, full blood count & peripheral smears.
- Blood Hb concentrations & erythrocyte numbers are normal in mild cases.
- As deficiency worsens MCV & erythrocyte count & Hb decreases & RDW increases.
- Hypochromia or poikilocytosis shown when Hb conc are 7.0 g/dl or less for women & g/dl or less for men.
- Absence of stainable iron in bone marrow aspirates is ultimate proof of deficiency but is painful & expensive so not used routinely.
- After hemorrhage or iron therapy reticulocytes increase.

PREVENTION:

It can be done by identifying the underlying cause of iron deficiency & correcting it through diet or supplementation.

Dietary manipulation:

Food fortification is best recommended.

When dietary iron supplementation is not possible or adequate, oral supplementation should be initiated.

B) MEGALOBLASTIC ANEMIA/PERNICIOUS ANEMIA:

It is cause by insufficient of hemopoiesis.

In this condition stomach decreases the production of intrinsic factors because they decrease the absorption of vitamin B12.

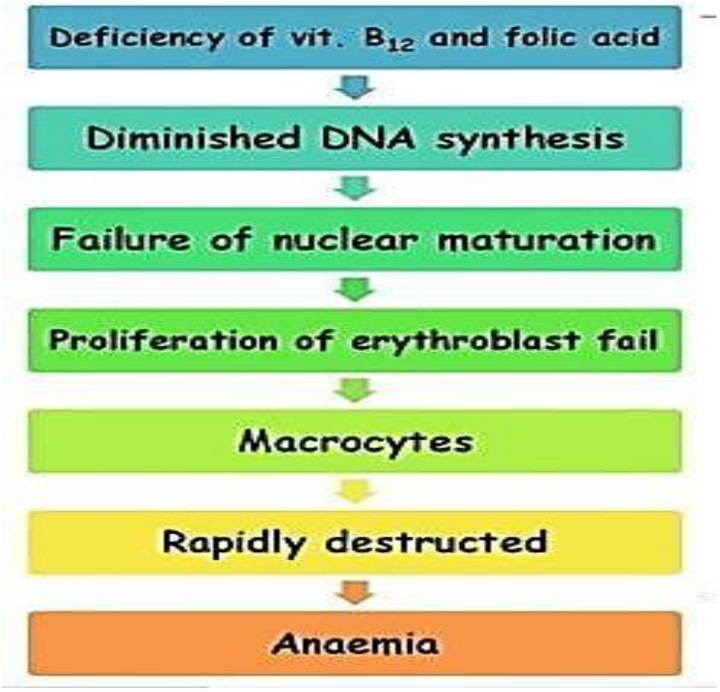
It is a sub class of the macrocytic anemias.

It is characterized by a lowered blood Hb mass due to reduced erythropoiesis secondary to defective DNA synthesis in the developing erythroid cells of the bone marrow.

CAUSES:

It can be mainly due to deficiencies of ***vitamin B12 and folate.*** It can be by drug induced interferences, either direct or indirect, i.e. with DNA synthesis or nutritional status.

PATHOPHYSIOLOGY OF MEGALOBLASTIC ANEMIA



1. VITAMIN B12 DEFICIENCY MEGALOBLASTIC ANEMIA:

Stages of vitamin B12 deficiency anemia:

Stage	B12 Concentration	MCV	Hb	Signs & Symptoms
Normal	Normal	Normal	Normal	None
Negative balance	Normal	Normal	Normal	None
Depletion of stores	Slight decrease	Normal	Normal	Possible
B12 deficient erythropoiesis	Mod decrease	Increased	Normal	Possible
B12 deficiency anemia	Severe decrease	Increased	Decreased	Probable

Vitamin B12 Needs:

1. Daily requirement for humans is 0.5 to 1 mcg.
2. The total body stores amount to 2-5 mg mainly into liver.

ETIOLOGY:

I Dietary→ inadequate intake.

II Impaired transport→ Transcobalamin II deficiency

III Malabsorption:

Pernicious anemia: It is a B12 malabsorption caused by the loss of gastric IF secretion. Its an auto immune reaction against gastric parietal cells.

Gastric disorders: gastrectomy (absolute deficiency of IF), atrophic gastritis, achlorhydria, vagotomy, partial gastrectomy & the use of H 2 receptor antagonists (prevent release of vitamin from food).

Intestinal problems: Zollinger – Ellison syndrome, surgical resection or bypass of the ileum, Crohn's disease, celiac disease, lymphomas, Whipple's disease, bacterial overgrowth.

Drug induced: colchicine, PAS, neomycin, H2 blockers, proton pump inhibitors, ethanol, Cholestyramine, etc decrease vitamin B12 absorption.

PATHOGENESIS OF MEGALOBLASTIC ANAEMIA DUE TO VIT B12:

- Vit B 12 is well absorbed from GIT in a sequence by three different binding proteins i.e. R proteins, IF, & transcobalamin II (TCII).

- Extravascular R proteins also known as cobalophilins, are the first binding proteins for
- B12.
- The cobalamin remains bound to R protein in the upper small intestine until pancreatic proteases viz, trypsin partially degrade the complex releasing B12.
- Then B12 binds to IF, a specific B12 binding glycoprotein.
- The IF – B12 complex is highly resistant to proteolysis, passes down the small intestine to the distal ileum where it attaches to specific receptors.
- This attachment with receptor is not energy dependent but requires extracellularcalcium & pH higher than 5.4.
- The majority of B12 in the circulation binds to intravascular R protein i.e. transcobalamin I (haptocorrin).
- But transcobalamin II (TCII) is a functional binding protein responsible for releasing B12 to the tissues.
- Patients with TC II deficiency may have normal serum B12 concentration as binding to
- TC I compensates for it.
- Features of severe B12 deficiency occur as TCI – B12 complex does not deliver the vitamin to the tissues.

Another mechanism of absorption is diffusion, which is a potential method of providing oral B12 therapy to people with low IF levels (pernicious anemia

DIAGNOSIS:

Measurement of holo - TC to differentiate between B12 deficiency or TC II deficiency.

But clinically not used because of limited assay availability.

TC II saturation→It decreases in early B12 deficiency.

Assessment of metabolite production – **MMA & Hcy** where MMA is more specific for B12 deficiency. But MMA also increases in renal disease so renal function should be assessed.

MCV > 100 fL indicating macrocytosis indicates its deficiency.

Evaluating smear for megaloblastic changes viz, neutrophil hypersegmentation & oval shaped erythrocytes, generally differentiates a B12 or folate deficiency from other causes. If iron deficiency occurs with vit B12, the MCV may appear normal but the blood smear should show both megaloblastic & microcytic cells.

2. FOLATE DEFICIENCY MEGALOBLASTIC ANEMIA:

Folate deficiency occurs in stages, with depletion of stores leading to deficiency that can result in megaloblastic anemia & other hematologic abnormalities.

Role of folate deficiency is evaluated in pregnancy, heart disease, stroke & peripheral arterial disease.

SIGNS & SYMPTOMS:

They are similar to those of other anemia's.

In addition may cause megaloblastosis, glossitis, diarrhoea & weight loss.

EPIDEMIOLOGY:

- Malnutrition
- In alcoholics due to poor diet & altered absorption.
- In pregnancy folate needs increase thrice the normal requirement due to large increase in nucleic acid synthesis associated with growth of the fetus, placenta & uterus & with increased maternal erythrocyte mass.
- Folate needs also increase during malignancy, increased erythropoiesis, conditions causing rapid cell turnover, chronic hemolytic anemia, exfoliative dermatitis, generalized psoriasis or extensive burns.
- Drugs can also cause folate deficiency by either reducing absorption or by altering metabolism

PATHOPHYSIOLOGY OF FOLATE RELATED MEGALOBLASTIC ANEMIA:

- Dietary folate is usually in polyglutamate form, which must be converted to monoglutamate form for absorption.
- Active absorption of dietary folate occurs mainly in the proximal part of the small intestine.
- Synthetic folate is already in monoglutamate form & has greater stability & better absorption.
- Folic acid from formulations is completely absorbed in the upper duodenum, even in the presence of malabsorption.
- The principle circulating form is extensively protein bound & undergoes enterohepatic cycling but not reabsorbed from the bile.
- Reduced form of folate (tetrahydrofolate) are cofactors for transformylation reactions in the biosynthesis of purines & thymidylates of nucleic acids.

- Folate deficiency, so leads to defective DNA synthesis resulting in megaloblast formation & bone marrow suppression.
- It is needed in Hcy metabolism or any other methylation reactions.

FOLATE NEEDS:

The minimum daily requirement of folate is 50 to 100 mcg/day in general & in pregnancy an additional 400 mcg/ day is recommended.

The average amount stored in the body is 5 to 10 mg, one half of which is found in liver.

DIAGNOSIS:

- Serum or erythrocyte **folate concentrations** are assessed where erythrocyte folate concentration reflects tissue status & is a better indicator of depletion.
- **Hcy concentration** is increased in deficiency. (also increased in B12 deficiency & decreased renal function)
- A blood smear & hematologic evaluation show macrocytosis with megaloblastosis. also shown by B12 deficiency).

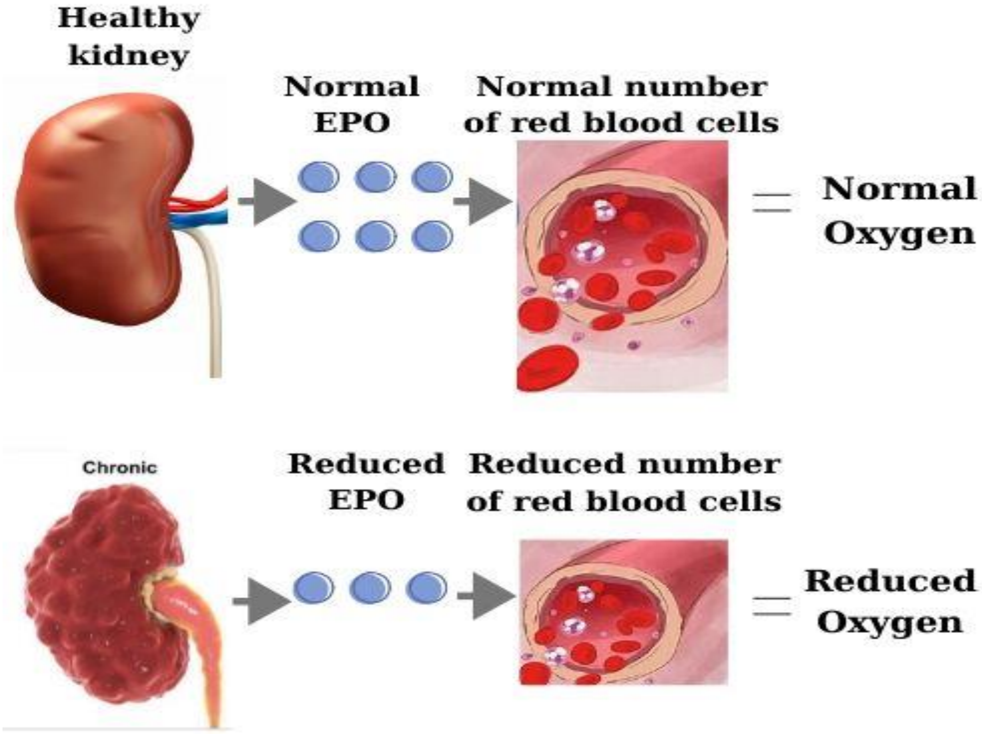
C. ANEMIA OF RENAL FAILURE

- The severity of the anemia correlates with the extent of uremia.
- Most of the patients with serum creatinine concentration higher than 310mcmol/L & 97% of those on maintenance dialysis are affected.
- The cells are normochromic & normocytic but often are irregular in shape.

PATHOPHYSIOLOGY:

- It is a multifactorial process but primarily due to reduced secretion of erythropoietin by the diseased kidneys.
- Accumulation of the inhibitors of erythropoiesis reduced RBC life span & chronic blood loss.
- Parathyroid hormone & the polyamine spermine have been implicated in reducing marrow responsiveness to erythropoietin.
- Erythrocyte survival also decreases to an average of one-half of normal uremia due to mild, chronic hemolysis.
- Chronic blood loss both from a GI source & during hemodialysis may also contribute to it.

- Others: folic acid deficiency caused by losses to the dialysate, the accumulation of fat sol vit A, aluminum toxicity caused by long term hemodialysis & the use of aluminum containing phosphate binders & osteitis fibrosa, a complication of hyperparathyroidism in which myelofibrosis reduces viable erythroid cellular mass.



D. APLASTIC ANEMIA

Aplastic anemia is distinguished by hypocellularity of the bone marrow & subsequent pancytopenia that is unrelated to malignancy or myeloproliferative disease.

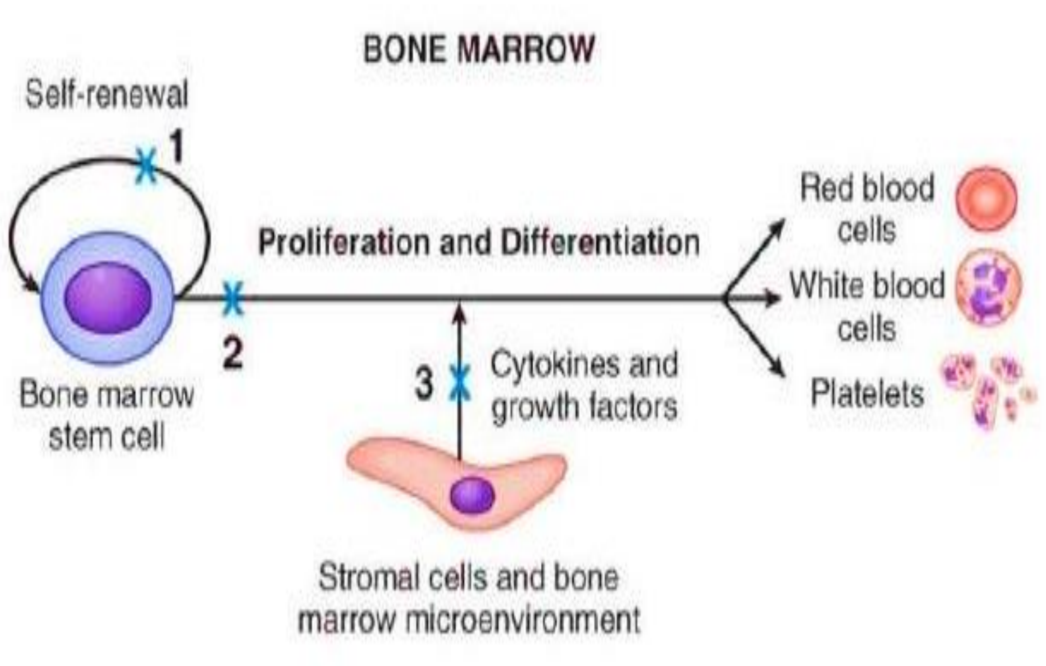
The characteristic anemia, neutropenia & thrombocytopenia result from failure of the pluripotent stem cells due to congenital or acquired process.

ETIOLOGY:

It is mostly idiopathic.

Myelosuppression is a component of several congenital disease but is more commonly acquired after exposure to : drugs (chloramphenicol, anticonvulsants, acetazolamide, etc), chemicals (arsenic, benzene, ethanol, etc), viral (HIV, influenza, rubella etc), others (ionizing radiation, pregnancy, mycobacterial infection, etc.)

PATHOPHYSIOLOGY:



It develops when hematopoiesis is interrupted because of deficient or defective stem cells.

Others : immune mediated suppression of stem cell function, disturbances in the bone marrow microenvironment, & alterations in the cellular or humoral interactions that normally sustain hematopoiesis.

CLINICAL PRESENTATION:

Pallor & fatigue initially mild but more pronounced when accompanied by bleeding due to thrombocytopenia.

Ecchymoses & petechiae

Fever due to infection caused by underlying neutropenia.

DIAGNOSIS:

Peripheral blood - number of morphologically normal cells.

Erythrocytes – normochromic, normocytic or slightly macrocytic

Reticulocyte count, absolute granulocyte count -

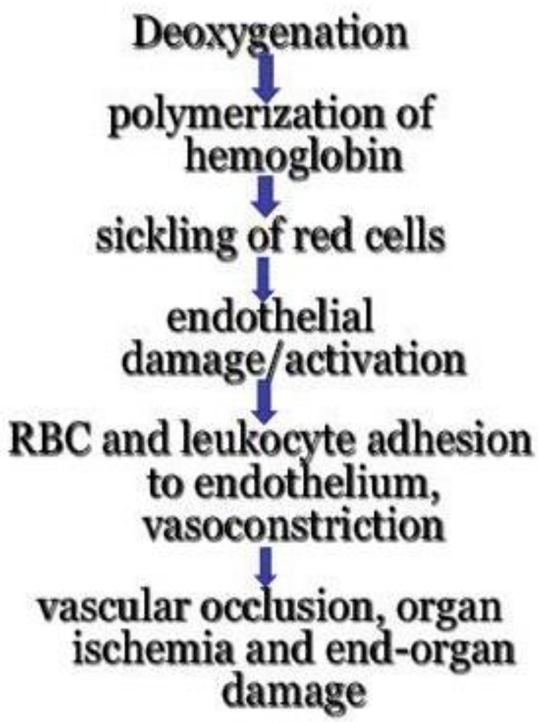
Bone marrow biopsy – extensive areas of hypocellularity interspersed with small patches of hematopoietic cells.

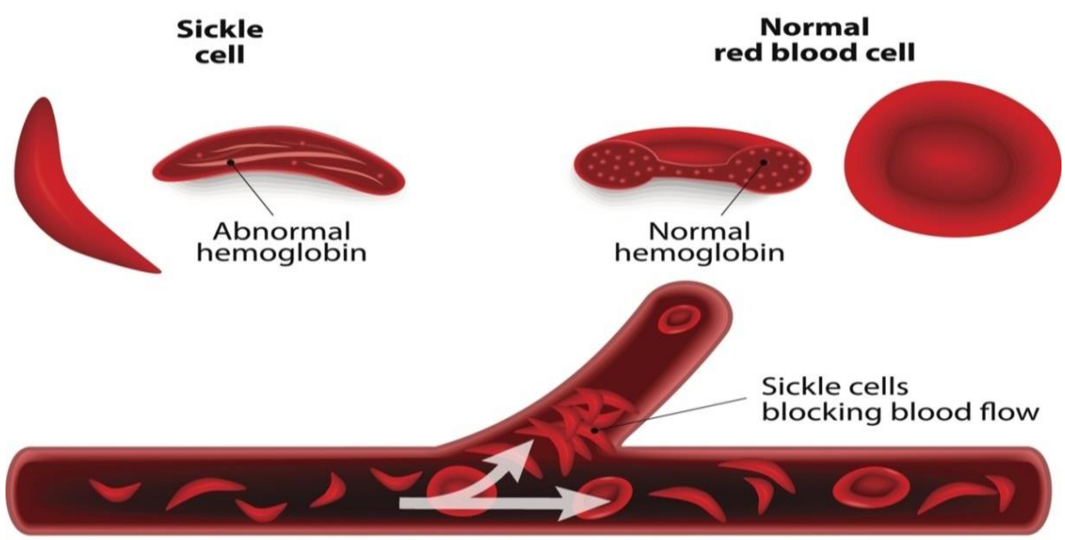
E. SICKLE CELL ANEMIA:

The term sickle cell disease encompasses a variety of hemoglobinopathies, including sickle cell anemia, sickle Hb C (SC) disease, & sickle cell thalassemia.

Although the clinical presentations of all are often similar, the manifestations of sickle cell are more severe & so mainly considered.

PATHOPHYSIOLOGY:





CLINICAL PRESENTATIONS

Constitutional

Impaired growth & development

Increased risk of infection viz meningitis, pneumonia, septicemia

Hematologic

Hemolytic anemia

Aplastic crises

Splenic sequestration crises

Vasoocclusive :

Cardiovascular:

Cardiac enlargement, Systolic murmur

Ocular: Retinopathy, Secondary glaucoma

Painful crises

Skin & skeletal : Arthropathy, Aseptic necrosis Leg ulcers

Genitourinary: Hematuria, Impotence, Priapism Renal insufficiency

Neurologic: Cerebral thrombosis Intracerebral hemorrhage, Seizures Subarachnoid haemorrhage

GI: Autosplenecetomy Gallstones / cholecystitis Hepatic insufficiency, Intrahepatic cholelithiais

Pulmonary: Infarction, Acute chest syndrome Chronic obstructive disease

DIAGNOSIS:

Hb electrophoresis---types & proportion of Hb present.

Is rapid & inexpensive screening test

It establishes the patients genotype.

If both parents have the AS genotype there is a 1 in 4 chance that their child will havehomozygous SS disease.

Prenatal diagnosis also possible

F. THALASSEMIAS:

It is an inherited disease.

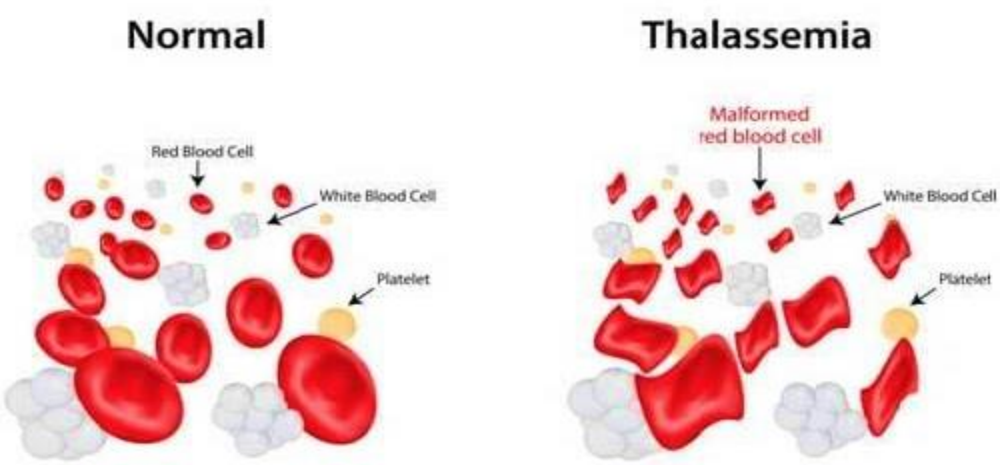
Thalassemia is also the hemolytic anemia in which hemoglobin production is decreased.

The RBCs are small, pale and short lived.

It required the blood transfusion for life.

Hemolytic disease of the newborn Rh+ antibodies of a sensitized Rh– mother cross the placenta and attack and destroy the RBCs of an Rh+ baby.

Rh– mother becomes sensitized when exposure to Rh+ blood causes her body to synthesize Rh+ antibodies.



The drug RhoGAM can prevent the Rh– mother from becoming sensitized

Thalassemia is a group of hereditary disorders of Hb synthesis characterized by impaired production of one or more of the normal polypeptide chains of globin.

The most prevalent thalassemia syndromes are those that involve diminished or absent synthesis of the α or β globin chains of HbA1.

PATHOPHYSIOLOGY:

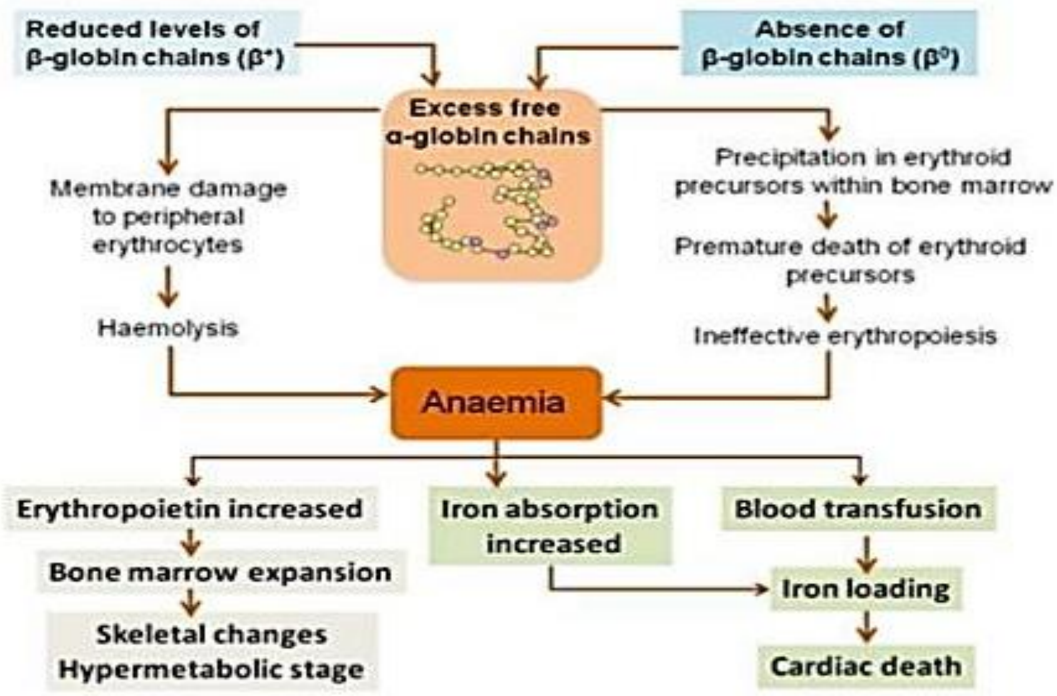
The thalassemia syndromes are collectively one of the most common genetic disorders of the human. Reduced production of normal $\alpha 2$ $\beta 2$ tetramer of HbA1 results in the production of smaller erythrocytes with a low Hb content.

The synthesis & accumulation of excess normal globin chains within the red cells lead to the formation of unstable aggregates, which may precipitate & cause cell membrane damage

These deformed cells undergo premature destruction either in the bone marrow (Extravascular hemolysis) or the peripheral circulation (intravascular hemolysis).

Chronic hemolysis is a primary complication of the clinically significant α & β thalassemia syndromes. (Hb H disease & β thalassemia major).

The ineffective erythropoiesis & microcytic, hypochromic anemia described earlier are associated with a compensatory →in the absorption of dietary iron.



CLINICAL PRESENTATION:

This may contribute to the iron overload due to blood transfusion therapy.

In erythropoietic activity in the bone marrow& in extramedullary sites.

In severe form, excessive erythropoiesis causes significant bone marrow hypertrophy, growth retardation, lymphadenopathy & hepatosplenomegaly.

Bone marrow expansion in untreated patients leads to skeletal deformities & fragility

i. α – THALASSEMIA :

Four genes are involved in the production of α globin chains, with one pair occurring on each DNA strand (αα/αα).

The most common form of it result from deletion of one or more of these genes.

Excess production of β & chains result in the formation of unstable & nonfunctional

4 (Hb Bart's) & β4 (Hb H) tetramers.

ii. β-THALASSEMIA:

It results from faulty mRNA transcription of the β gene.

Excess of α-chain accumulate & cause membrane damage in RBC precursors.

So premature destruction of the cells in the bone marrow or peripheral blood.

α- & β- chain production is usually unaffected & so levels of Hb A2 (α2 β 2).

Heterozygous

Minima Normal None None

Minor (trait) >100 Mild anemia Genetic/medical counseling

Homozygous

Intermedia 70 - 100 Mod – sev anemia, impaired growth & splenomegaly

Intermittent blood transfusion & chelation therapy

Major 20 - 70 Sev anemia, abnormal skeletal growth, splenomegaly, iron load complications

Chronic blood transfusion & chelation therapy

G. HEMOLYTIC ANEMIAS:

It is caused by an increased rate of RBC destruction.

It can be because of the production of the defective or damaged RBC's (megaloblastic anemias, thalassemias, sickle cell anemias) or drug induced.

CLASSIFICATION:

1. INHERITED:

a. Globin synthesis defect

Sickle cell anemia

Thalassemia

Unstable Hb disease

b. Erythrocyte membrane defect

Hereditary spherocytosis

Hereditary elliptocytosis

Hereditary stomatocytosis

c. Erythrocyte enzyme defect

HMP shunt defect

Glycolytic enzyme defect

Other enzyme defect (adenylate kinase)

2. ACQUIRED

A. Immune mediated

a. Warm reacting Ab (IgG)

Primary (idiopathic)

Secondary (collagen vascular disease, lympho proliferative disorders)

Drug induced

b. Cold agglutinin disease (IgM)

Acute (mycoplasma pneumonia, infectious mononucleosis)

Chronic (lymphoid neoplasms,

c. Paroxysmal nocturnal hemoglobinuria

d. Transfusions reactions

e. Hemolytic disease of newborns

B. Microangiopathic & traumatic

Disseminated intravascular coagulation

Hemolytic uremic syndrome

Thrombotic thrombocytopenic purpura

Prosthetic or diseased heart valves

C. Infection

D. Exogenous substances

E. Others

Liver disease

Hypophosphatemia

PATHOPHYSIOLOGY:

It involves hemolysis of RBC within the circulation (intravascular haemolysis) or taken up by the RES & destroyed (extravascular hemolysis).

Intravascular hemolysis may be caused by trauma to the RBC, complement fixation to the RBC (immune mediated), or exposure to exogenous substances.

During hemolysis, if haptoglobin binding capacity is exceeded, unbound Hb levels , resulting in hemoglobinemia.

Free Hb is filtered through the glomerulus & usually is reabsorbed by the proximal tubules.

In severe intravascular hemolysis, the reabsorptive capacity is exceeded, causing hemoglobinuria.

Some Hb molecules are transferred from hemopexin to albumin forming methemalbumin.

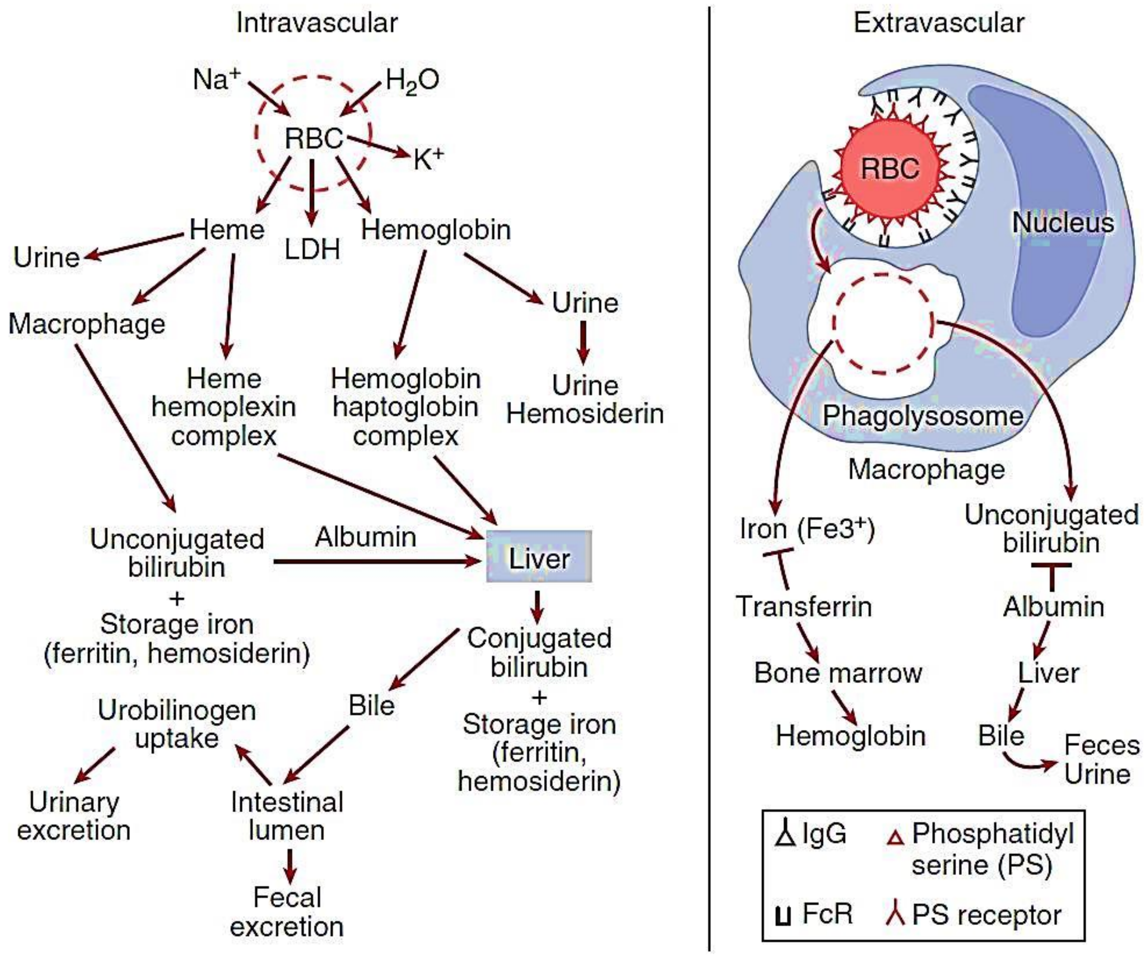
CLINICAL PRESENTATION & DIAGNOSIS:

I Inherited hemolytic anemia : G6PD deficiency :

It is the most prevalent inherited RBC enzyme defect, a sex linked (X chromosome) disorder.

The G6PD enzyme, with glutathione & NADP acts as a protective antioxidant for RBCs against external oxidative stresses.

In G6PD deficiency, oxidative stresses on the RBC viz drugs, infection or acidosis can lead to denaturation of the globin chains which ppts intracellularly onto the cell membrane as Heinz bodies & premature hemolysis occurs oxidative hemolysis.



II Several factors affecting patient's susceptibility for deficiency:

The type of G6PD genetic variant present (i.e. type A- or mediterranean type).

Patient age

Other sources of oxidant stress

Dosage of an offending drugs (nalidixic acid, cephalosporin, nitrofurantoin, etc.)

Patient metabolism & excretion of offending drugs.

III Acquired hemolytic anemia: Autoimmune hemolysis

Autoimmune hemolytic anemia results from the binding of complement or anti-RBC antibodies to the red cell membrane in affected patients.

These disorders are classified according to the temperature at which the antibodies have the greatest affinity for & interaction with red cells.

1. Cold agglutinin hemolytic anemia Here, IgM antibodies bind to RBCs at low temperatures

This agglutination process is reversed quickly during warming.

Most don’t appreciably shorten RBC survival.

It is associated with mycoplasma pneumonia or infectious mononucleosis.

Chronic disease occurs with lymphoproliferative disorders & results in poor peripheral circulation.

It involves preventing exposure to cold environments.

Folic acid supplementation

Blood transfusions (if necessary)Treating any underlying diseases.

Occasssionaly patients may respond to plasmapheresis or cytotoxic agents such as cyclophosphamide or chlorambucil

2. Warm autoimmune hemolytic anemia:

IgG or occasionally IgA have greatest affinity for red cells at room temperature (37□C).

Hemolysis involves the attachment & subsequent destruction of IgG coated erythrocytes to receptors on macrophages in the RES.

It may be idiopathic, secondary to an underlying disease that affects immune system (chronic lymphocytic leukemia, non Hodgkins lymphoma, or systemic lupus erythematosus), or secondary to certain drugs.

When hemolysis is clinically significant, corticosteroid therapy is effective & blood transfusions may be needed.

Splenectomy

Alternative therapies include immunosuppressive agents, danazol, IVIG & cyclosporin

ENDOCRINE SYSTEM
(DIABETES, THYROID DISEASES, DISORDERS OF SEX HORMONES)

DIABETES MELLITUS

- As per the WHO, diabetes mellitus (DM) is defined as a heterogeneous metabolic disorder. DM is a leading cause of morbidity and mortality world over. Top 5 countries with highest prevalence of DM are India, China, US, Indonesia and Japan.
- Diabetes mellitus (DM), commonly known as just diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time
- Diabetes is a group of metabolic disorders characterized by abnormal metabolism, which results most notably in hyperglycemia, due to defects in insulin secretion, insulin action, or both. Diabetes is a serious chronic disease without a cure, and it is associated with significant morbidity and mortality.
- Diabetes is a serious disease associated with acute (due to hyperglycemia) and chronic (due to vascular damage) complications.
- "Diabetes" comes from the Greek word for "*siphon*", and implies that a lot of urine is made. The second term, "mellitus" comes from the Latin word, "*mel*" which means "honey", and was used because the urine was sweet.
- Diabetes mellitus is caused by two pathogenic factors mainly.
    - Insulin Resistance- Increase Blood Sugar Level
    - Insulin deficiency- Lack of Insulin production

DIABETES IN INDIA

- According to the Indian Council of Medical Research- Indian Diabetes study (ICMR-INDIA-B), a national diabetes study, India currently has 63 million people with diabetes.
- India represents the world’s second largest diabetes population after China.
- This is set to increase to over 100 million by 2030.
- The majority of people with diabetes (>90%) have Type 2 diabetes (T2DM).

TYPES OF DIABETES MELLITUS

TYPE - I Diabetes Mellitus

TYPE -II Diabetes Mellitus

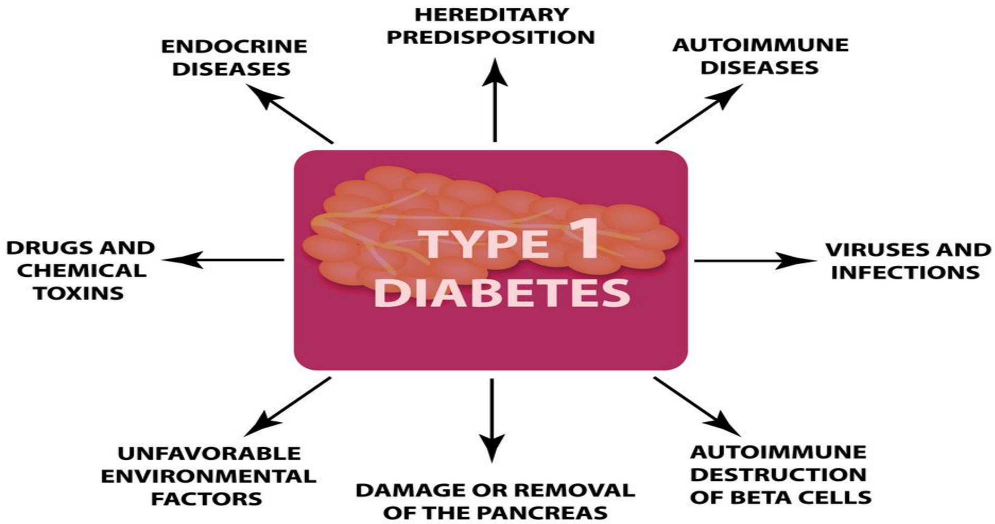
Gestational Diabetes Mellitus (GDM)

Secondary DM: Hormonal problems, pancreatic disorders, drugs

TYPE - I DIABETES MELLITUS

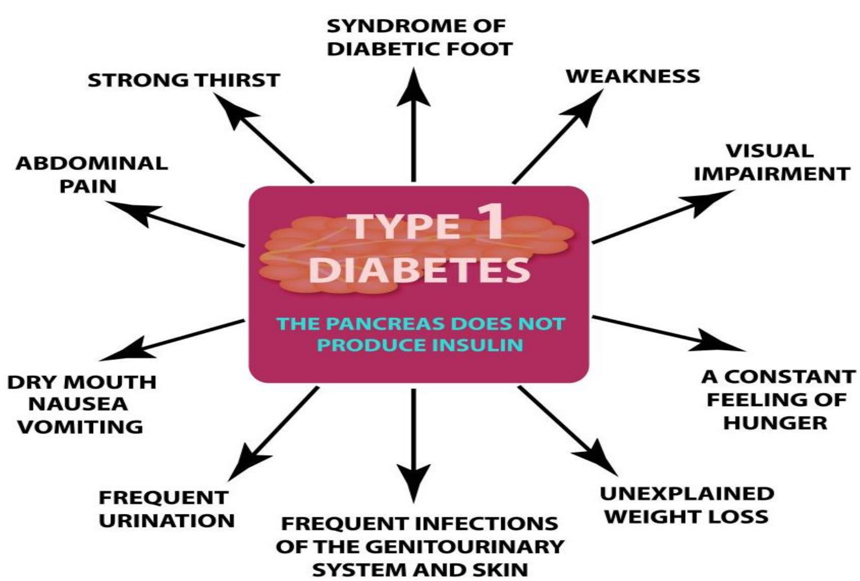
- Juvenile / Insulin Dependent Diabetes Mellitus (IDDM) (5 to 10%)
- Autoimmune destruction of pancreatic beta cells.
- Individual has an absolute insulin deficiency and no longer produces insulin.
- Such patients are absolutely dependent on exogenously administered insulin for survival.
- Beta cell destruction completely leading to absolute insulin deficiency.

ETIOLOGY TYPE-I DM



SIGNS AND SYMPTOMS

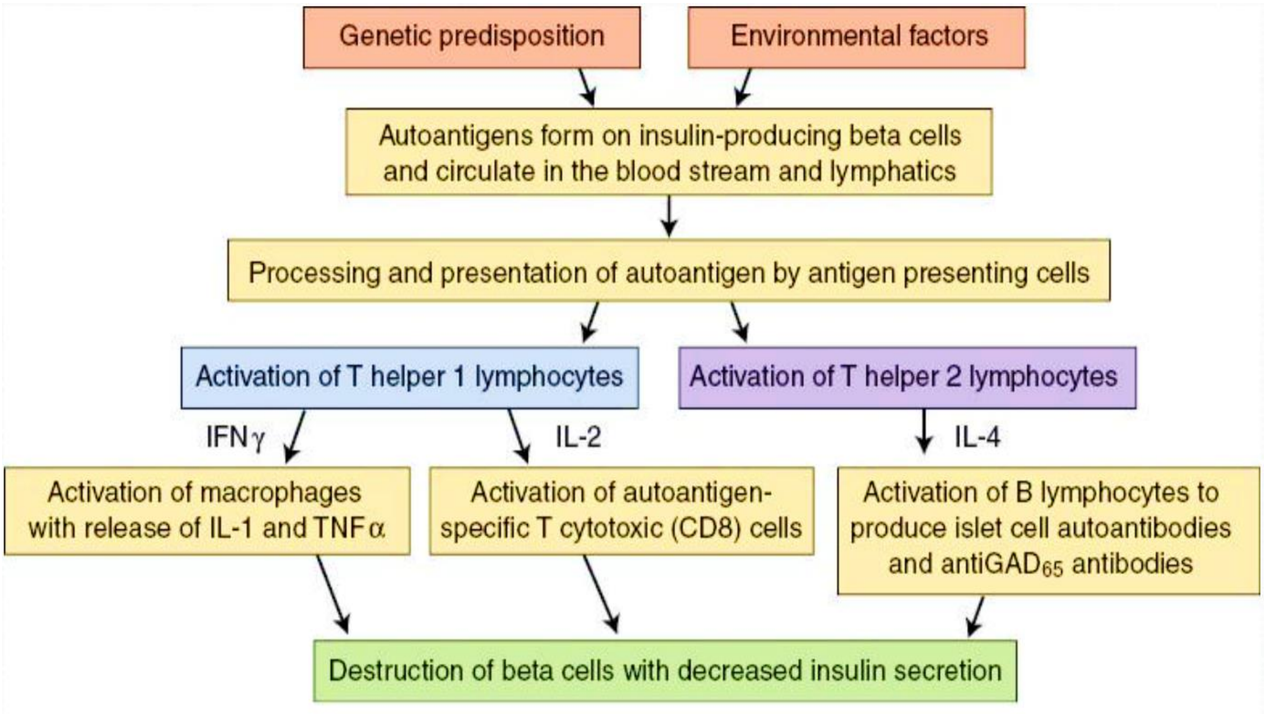
Polyuria (Increase urination), Polydypsia (increase thrist), Polyphagia-Increase Hunger,Weight loss, Fatigue, Increase frequency of infections



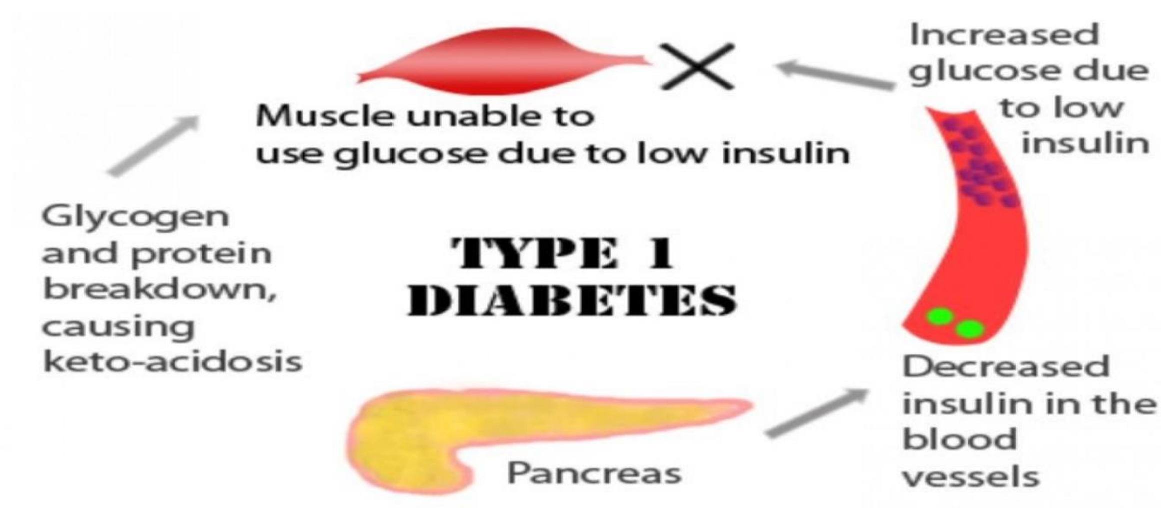
PATHOPHYSIOLOGY OF TYPE-I DM

Type 1 diabetes is characterized by destruction of the pancreatic beta cells. Most likely cause of these conditions is combined genetic, immunologic and possibly environmental (e.g. viral) factors contribute to cell destruction.

This is abnormal response of the body in which the antibodies are direct against the normal tissues as if they were foreign and eventually can damage, specific area of the pancreas that produce insulin, reducing the production of insulin or totally no production of insulin.



Pathophysiology of Type-I DM



TYPE -II DIABETES MELLITUS

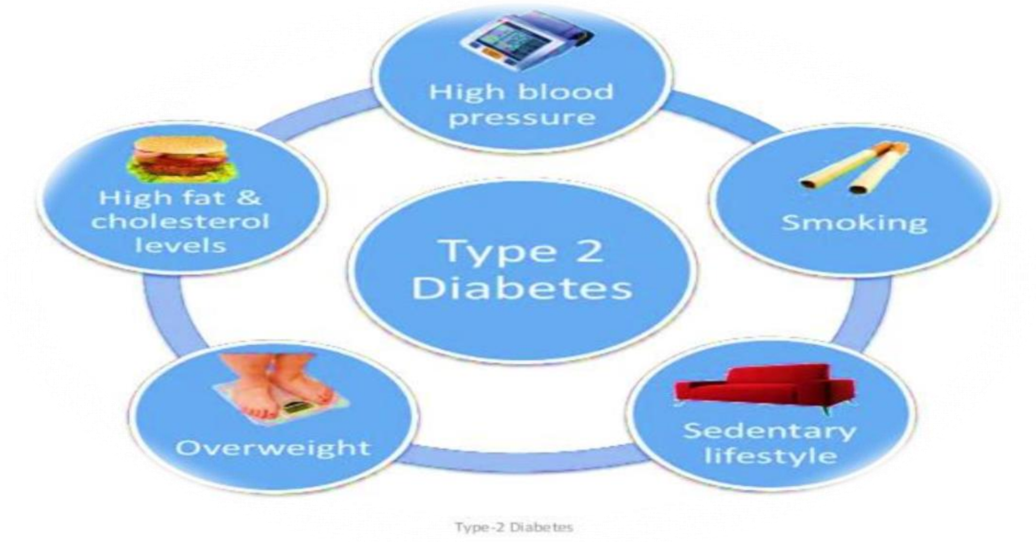
- Most common type. Also called Non-Insulin Dependent Diabetes Mellitus (NIDDM)
- Comprises 90 to 95% of DM cases.
- Most type 2 DM patients are overweight, and most are diagnosed as adults.
- Approximately half of the patients are unaware of their disease.
- combination of insulin resistance and Beta cell dysfunction
- Type 2DM is characterized by following three disorders:

    Peripheral resistance to insulin especially in muscle cells

    Increased production of glucose by the liver

    Insulin secretary defect of the beta cells

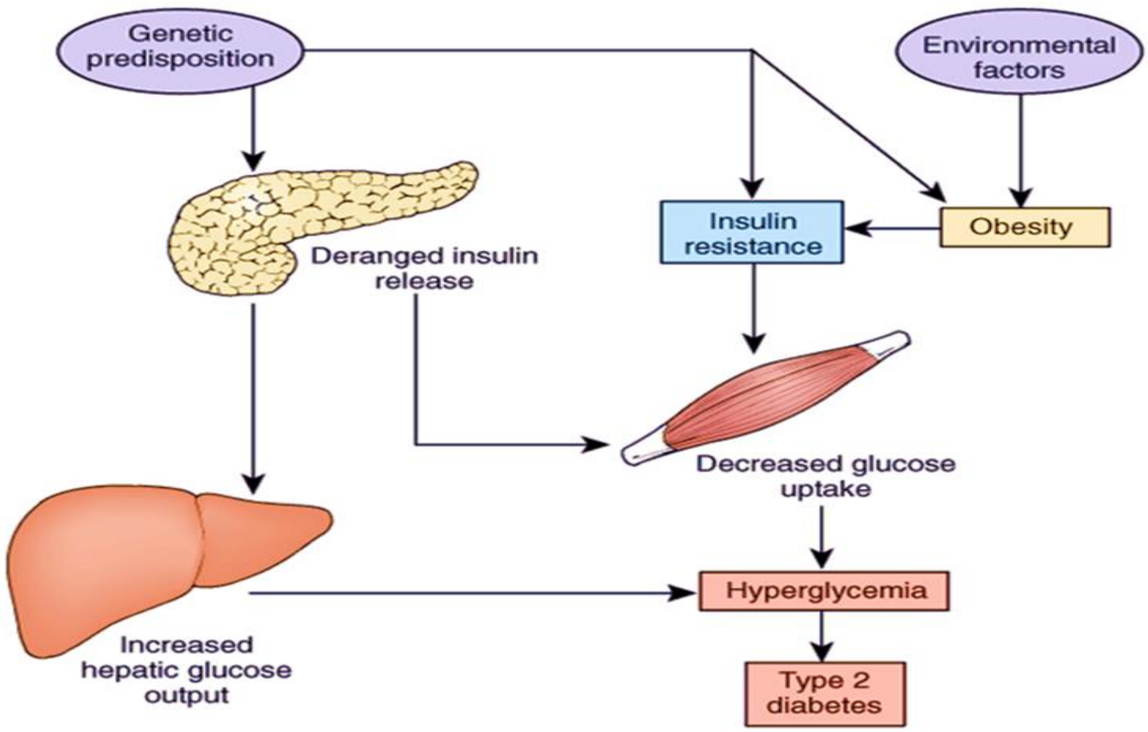
ETIOLOGY OF TYPE-II DM

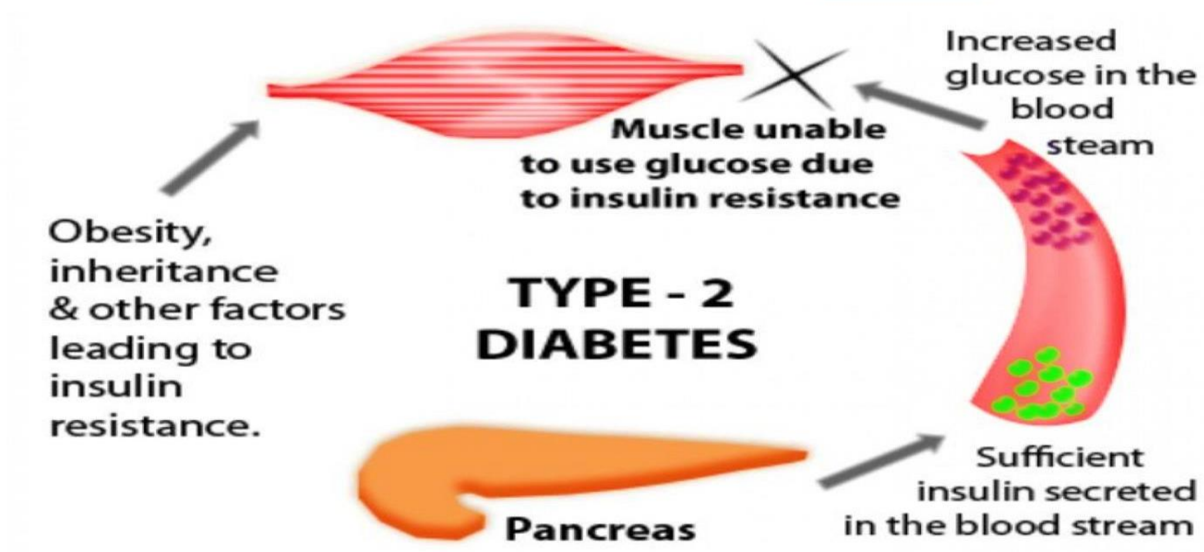


SIGNS AND SYMPTOMS

PATHOPHYSIOLOGY OF TYPE-II DM

Type-II Diabetes Mellitus is a adult onset, and non-insulin dependent. There are 2 main problems related to insulin in type-II diabetes, first one is "insulin resistance " (insulin do not bind with the special receptor on cell surface) and impaired insulin secretion (insulin secreting glands release irregular amount of insulin).





DIFFERENCES BETWEEN TYPE-I AND TYPE-II DIABETES MELLITUS

Type-I Diabetes Mellitus	Type-II Diabetes Mellitus
Young age	Middle aged, elderly
Normal BMI, not obese	Usually overweight/obese
No immediate family history	Family history usual
Short duration of symptoms (weeks)	Symptoms may be present for months/years
Can present with diabetic coma (diabetic ketoacidosis)	Do not present with diabetic coma
Insulin required	Insulin not necessarily required
Previous diabetes not in pregnancy	Previous diabetes in pregnancy

COMMON SYMPTOMS OF DIABETES

Symptoms of new onset Polyurea, Polydipsia, Polyphagia, Weight loss, Fatigue

Symptoms Hypoglycemia Tremor, Headache, Pallor, Dizziness, Paresthesia. Loss of coordination, Anxiety, Mood confusion, seizure

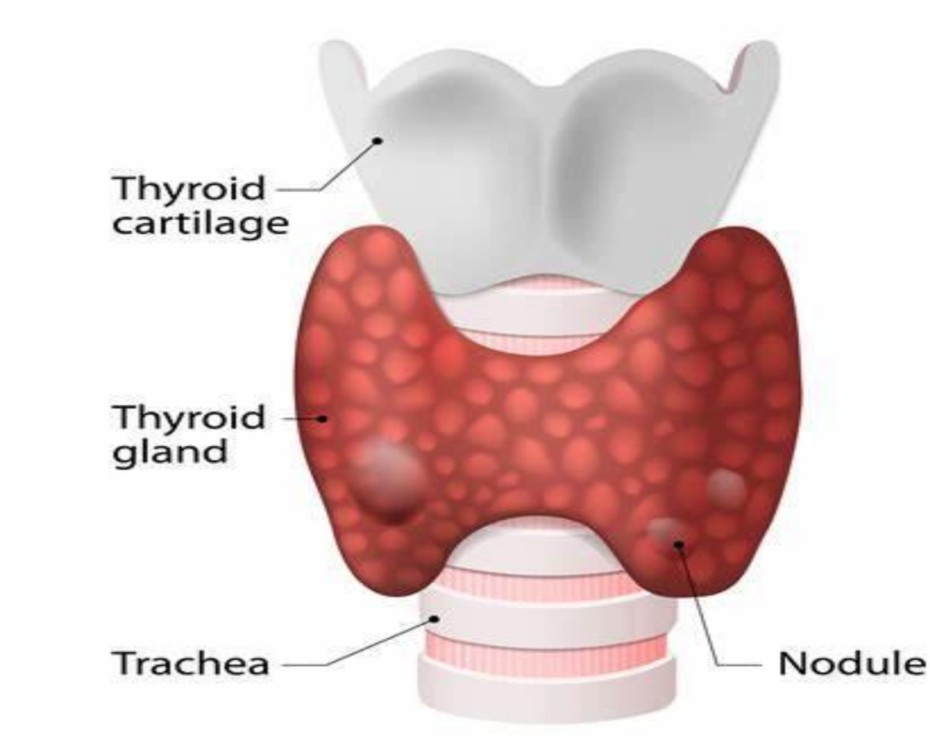
Hyperglycemia Polyurea, Polydipsi, Dry mouth, Ketoacidosis (shortness of breath), Hyperosmolar hyperglycemic non ketotic syndrome(fever,confusion, weakness)

DIAGNOSIS

1. **Glycated haemoglobin test:** Also known as HbA1c test, provides average blood sugar level of past 2-3 months.
2. **Fasting blood sugar (FBS):** Usually performed after overnight fasting. Result of this test can confirm diabetes based on the level of glucose in blood.
3. **Random blood sugar (RBS):** Performed any time of the day and it may be repeated to confirm high blood sugar

THYROID GLAND

- The thyroid, or thyroid gland, is an endocrine gland in vertebrates. In humans it is in the neck and consists of two connected lobes. The lower two thirds of the lobes are connected by a thin band of tissue called the thyroid isthmus. The thyroid is located at the front of the neck, below the Adam's apple.
- It is a butterfly-shaped gland which is located just inferior to the larynx (voice box). It is composed of right and left lateral lobes that are connected by isthmus (a narrow passage). It is highly vascularized and receives 80–120 mL of blood per minute.
- Thyroid gland is made up of microscopic spherical sacs called thyroid follicles. The wall of each follicle consists of follicular cells which produce two hormones: thyroxine (tetraiodothyronine or T4 because it contains four atoms of iodine) and triiodothyronine (T3, which contains three atoms of iodine). T3 and T4 together are also known as thyroid hormones.
- A few cells called parafollicular cells or C cells lie between follicles. They produce the hormone calcitonin which helps regulate calcium balance.



THYROID HORMONES

The thyroid hormones are secreted by the thyroid gland, which is located in front of the neck. These hormones are integral in the regulation of many functions and aspects of the human body, such as temperature regulation, energy levels, weight, hair, nail growth and more.

There are two thyroid hormones:

T_4: Thyroxine (Tetraiodothyronine)

Thyroxine is a hormone secreted by the thyroid gland in the bloodstream. It then travels to the organs such as kidneys and liver where it gets converted into and gets converted into its active form triiodothyronine.

T_3: Triiodothyronine

It is a thyroid hormone that affects physiological processes such as growth, development, metabolism, etc

FORMATION, STORAGE, AND RELEASE OF THYROID HORMONES: SYNTHESIS AND SECRETION OF T_3 AND T_4 OCCURS AS FOLLOWS:

1 Iodide trapping: Thyroid follicular cells trap iodide ions (I-) from the blood into the cytosol. As a result, the thyroid gland normally contains most of the iodide in the body.

2 Synthesis of thyroglobulin: While the follicular cells are trapping I-, they are also synthesizing a glycoprotein thyroglobulin (TGB). The TGB is stored into vesicles which releases it into the lumen of the follicle.

3 Oxidation of iodide: The iodide ions trapped inside the follicular cell are converted into iodine molecules (I_2) by oxidation by peroxidase enzymes. As the iodide ions are being oxidized, they pass into the lumen of the follicle.

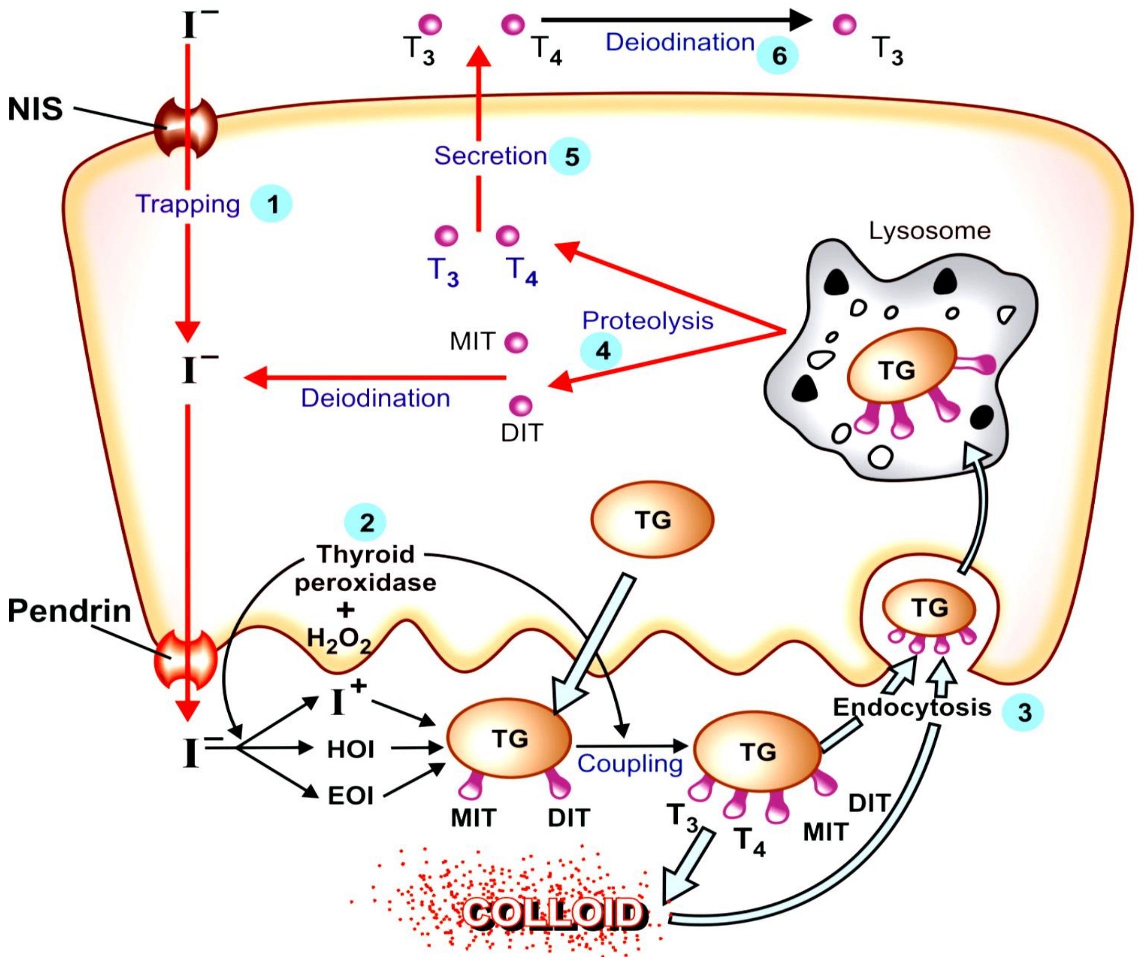
4 Iodination of tyrosine: As iodine molecules (I_2) form, they react with tyrosines (amino acids present in thyroglobulin molecules). Binding of one iodine atom yields monoiodotyrosine (T_1) and binding of two iodine molecules produces diiodotyrosine (T_2). The TGB with attached iodine atoms forms a sticky material called colloid which is stored lumen of the thyroid follicle.

5 Coupling of T_1 and T_2: During the last step in the synthesis of thyroid hormone, two T_2 molecules join to form T_4 or one T_1 and one T_2 join to form T_3.

6 Pinocytosis and digestion of colloid: Droplets of colloid reenter follicular cells by pinocytosis and merge with lysosomes. Digestive enzymes in the lysosomes break down TGB and separates molecules of T3 and T4.

7 Secretion of thyroid hormones: Because T_3 and T_4 are lipid soluble, they diffuse through the plasma membrane into interstitial fluid and then into the blood.

8 Transport in the blood: More than 99% of both the T_3 and the T_4 combine with transport proteins in the blood, mainly thyroxine-binding globulin (TBG) for transportation.



Synthesis, storage and secretion of thyroid hormone

TG—Thyroglobulin; MIT—Monoiodotyrosine; DIT—Diiodotyrosine; T3—Triiodothyronine; T4 Thyroxine (Tetraiodothyronine); HOI—Hypoiodous acid; EOI—Enzyme linked hypoiodate; NIS—Na+-iodide symporter; Thyroid-stimulating hormone (TSH) activates steps 1, 2, 3, 4, and 5; Ionic inhibitors block step 1; Excess iodide interferes with steps 1, 2, 3 and 5 with primary action on step 3 and 5; Propylthiouracil inhibits steps 2 and 6; Carbimazole inhibits step 2 only

FUNCTIONAL DISORDERS

Two significant functional disorders characterised by distinct clinical syndromes are described. These are: hyperthyroidism (thyrotoxicosis) and hypothyroidism.

Hyperthyroidism	**Hypothyroidism.**
Increase T3 and T4	Decrease T3 and T4
Increase T3 as compared toT4	Decrease TSH (Thyroid Stimulating Hormones)
Graves' disease a swelling of the neck and protrusion of the eyes resulting from an overactive thyroid gland ***Goiter*** An abnormal enlargement of the thyroid gland that causes coughing, difficulty breating, hoarseness, and difficulty swallowing	***Cretinism or congenital hypothyroidism*** is the development of severe hypothyroidism during infancy and childhood. ***Myxoedema*** is the adulthood hypothyroidism.

HYPERTHYROIDISM (THYROTOXICOSIS)

Hyperthyroidism is hyperactivity of the thyroid gland with sustained increase in synthesis and release of thyroid hormones.

Hyperthyroidism is a set of disorders that involve excess synthesis and secretion of thyroid hormones (T_3 and T_4) by the thyroid gland, which leads to the hypermetabolic condition of thyrotoxicosis.

The term thyrotoxicosis refers to the physiological effects or clinical syndrome of hypermetabolism that results from excess circulating levels of $T_3$and T_4 or both.

Incidence occurs in women more than men with highest frequency in persons 20 to 40 years old.

GRAVES

Immune system disorder resulting in the over production of thyroid hormone. This causes swelling of thyroid gland, puffy eyes and rapid heartbeat. A swelling of the neck and protrusion of the eyes resulting from an overactive thyroid gland. Also called ***exophthalmic goiter.***

SYMPTOMS

Enlarged thyroid associated with Graves' disease

Enlarged thyroid Open pop-up dialog box

Common signs and symptoms of Graves' disease include:

Anxiety and irritability

A fine tremor of the hands or fingers

Heat sensitivity and an increase in perspiration or warm, moist skin

Weight loss, despite normal eating habits

Enlargement of the thyroid gland (goiter)

Change in menstrual cycles

Erectile dysfunction or reduced libido

Frequent bowel movements

Bulging eyes (Graves' ophthalmopathy)

Fatigue

Thick, red skin usually on the shins or tops of the feet (Graves' dermopathy)

Rapid or irregular heartbeat (palpitations)

Sleep disturbance

CAUSES

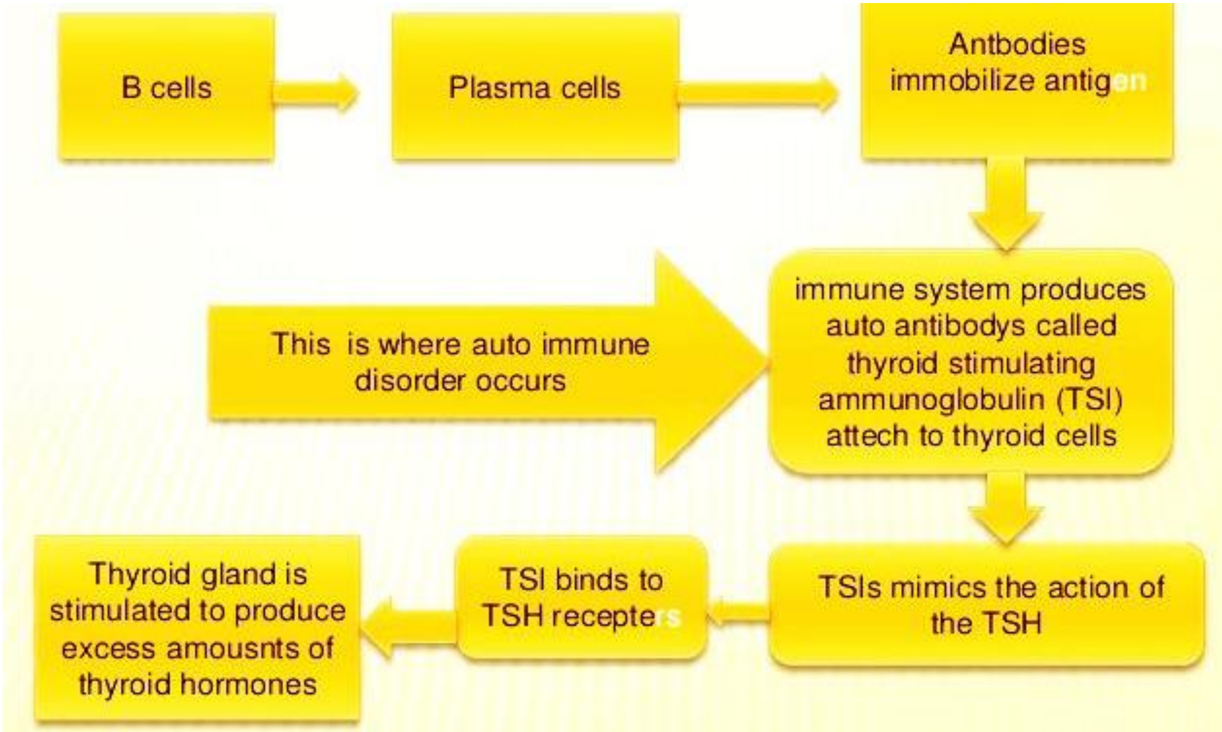
Abnormal immune system response that causes thyroid gland to produce too much thyroid hormone (hyperthyroidism)

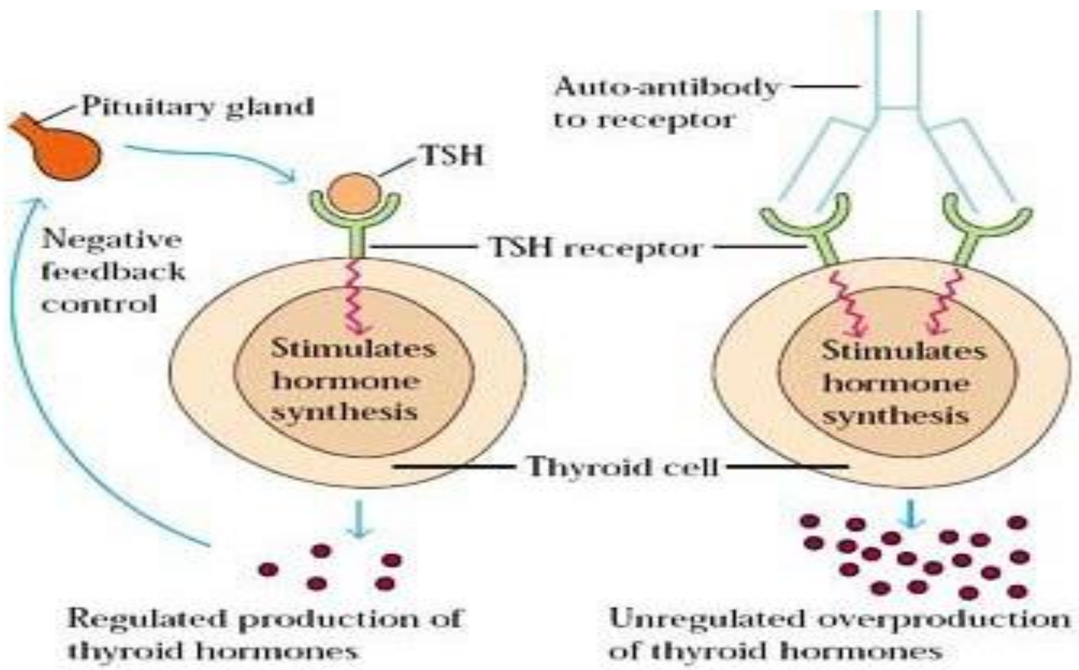
Normally, thyroid gets production orders through TSH (thyroid-stimulating chemical) released by the pituitary gland, but in Graves Disease, a malfunction in the body’s immune system releases abnormal antibodies that mimic TSH

PATHOPHYDIOLOGY GRAVES

- Graves’ disease results from the production of thyroid-stimulating immunoglobulins (TSI) by stimulated B lymphocytes.
- These immunoglobulins bind to the thyroid- stimulating hormone (TSH) receptor to mimic the action of TSH, resulting in follicular cell growth, an increase in vascularity and the excessive synthesis and secretion of thyroid hormone.
- An imbalance between pathogenic and regulatory T cells is thought to be involved in both the development of Graves’s diseases and its severity .leading to production of autoantibodies.

- Patient with GD may have an increased frequency of other autoimmune endocrine diseases (eg, diabetes mellitus, celiac disease and primary adrenal insufficiency) and nonendocrine autoimmune disorders (eg, vitiligo, SLE, rheumatoid arthritis, myasthenia gravis.





DIAGNOSIS

Blood tests. Blood tests can help your doctor determine your levels of thyroid-stimulating hormone (TSH) — the pituitary hormone that normally stimulates the thyroid gland — and your levels of thyroid hormones. People with Graves' disease usually have lower than normal levels of TSH and higher levels of thyroid hormones.

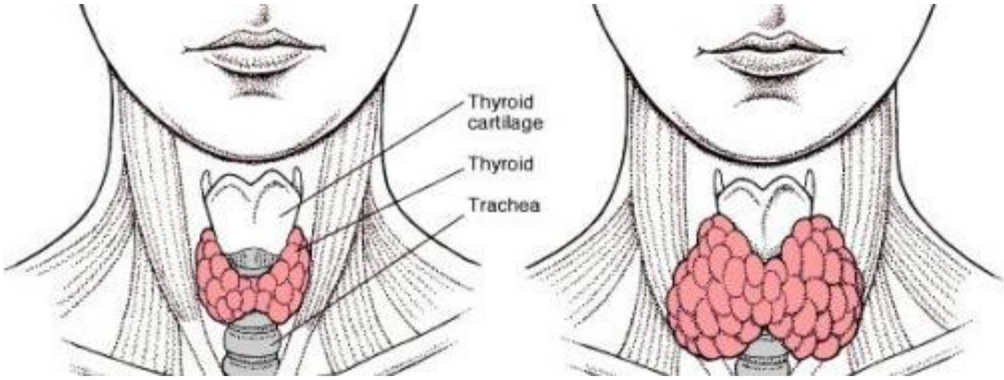
Radioactive iodine uptake. Your body needs iodine to make thyroid hormones. By giving you a small amount of radioactive iodine and later measuring the amount of it in your thyroid gland with a specialized scanning camera, your doctor can determine the rate at which your thyroid gland takes up iodine. The amount of radioactive iodine taken up by the thyroid gland helps determine if Graves' disease or another condition is the cause of the hyperthyroidism. This test may be combined with a radioactive iodine scan to show a visual image of the uptake pattern.

Ultrasound. Ultrasound uses high-frequency sound waves to produce images of structures inside the body. It can show if the thyroid gland is enlarged. It's most useful in people who can't undergo radioactive iodine uptake, such as pregnant women.

Imaging tests. If the diagnosis of Graves' disease isn't clear from a clinical assessment, your doctor may order special imaging tests, such as a CT scan or MRI.

GOITRE

Goiter is a swelling of the neck resulting from enlargement of the thyroid gland. A goiter is an enlarged thyroid gland. The thyroid is the gland in front of the neck. Goiter is the name given to a neck swelling produced by an abnormally enlarged thyroid gland. The thyroid gland is situated in front of the windpipe and is responsible for producing and secreting hormones that regulate growth and metabolism.



Goiters can be any one of several types of growths in the thyroid gland, located at the base of the front side of the neck just below the Adam's apple.

CAUSES OF GOITER

Goiters can also occur when the thyroid gland produces either too much thyroid hormone or not enough hyperthyroidism and hypothyroidism respectively. The problem may arise when the pituitary gland stimulates thyroid growth to boost production of the hormone. Enlargement could also occur with normal production of thyroid hormone, such as a nontoxic multinodular gland. As for developed countries the main cause of goiter is autoimmune disease. Women over the age of 40 are at greater risk of goiter.

The major cause of goiter is Iodine deficiency. Goiter is rare in economically developed countries that add iodine to salt.

Rarely conditions that causes goiter are:

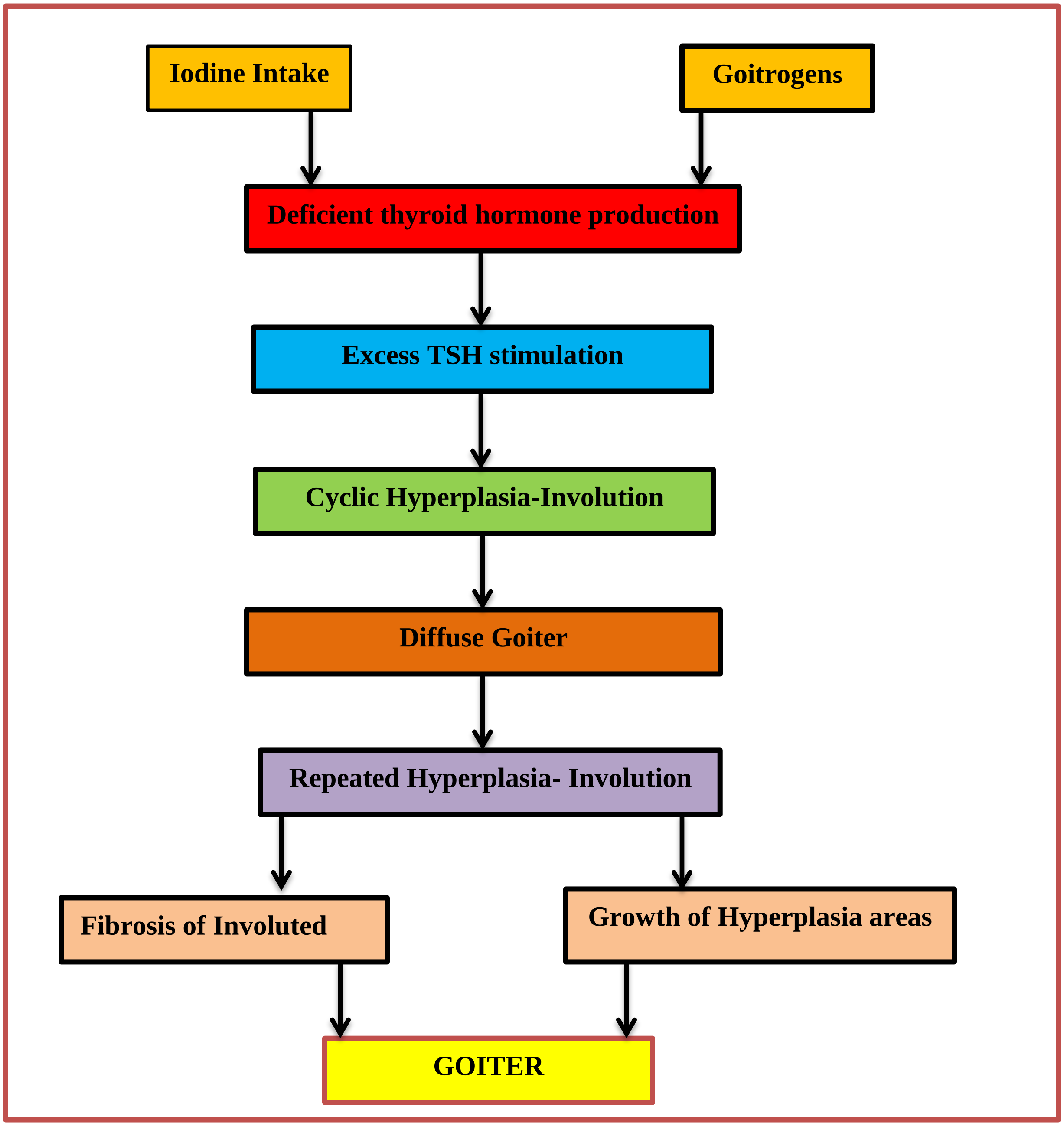
1. Hormonal changes - pregnancy, puberty and the menopause can affect thyroid function
2. Nodules - benign lumps, single or multiple
3. Thyroiditis - inflammation caused by infection, for example
4. Lithium - the psychiatric drug can interfere with thyroid function
5. Overconsumption of iodine - Excess iodine can cause goiter
6. Smoking - The content of tobacco called thiocyanate interferes with iodine absorption
7. Radiation therapy - most especially if it is in the neck.

SYMPTOMS OF GOITER

- Difficulty breathing
- Difficulty concentrating
- Difficulty swallowing(dysphagia)
- Dry cough and hoarseness
- Dry skin, nails and hair
- Drowsiness
- Fatigue
- Increased menstrual flow
- Throat tightness
- Visible swelling at the base of your neck

PATHOPHYSIOLOGY OF GOITER

Goiters may occur as a result of either hypothyroidism, hyperthyroidism, or even with normal levels of thyroid hormone. Thyroid enlargement (goiter) and hypothyroidism may occur due to compensatory responses as a result of a severe underlying disorder. When the thyroid gland cannot secrete enough thyroid hormone to cater to the metabolic requirements, it may lead to simple goiter (smooth enlargement)..



In order to compensate for inadequate hormone synthesis, the thyroid gland enlarges, this type of compensation overcomes mild to moderate hormonal impairment. When the TRH-TSH thyroid hormone axis is interfered, it results in the structural and functional changes of the thyroid gland. Increased TSH production is triggered by a deficiency in thyroid hormone synthesis or intake. In order to normalize thyroid hormone levels, the increase in TSH leads to increased cellularity and hyperplasia of the thyroid gland and when this process is continuous, it leads to goiter. Thyroid hormone deficiency may occur secondary to to iodine deficiency, inborn errors of thyroid hormone synthesis and goitrogens

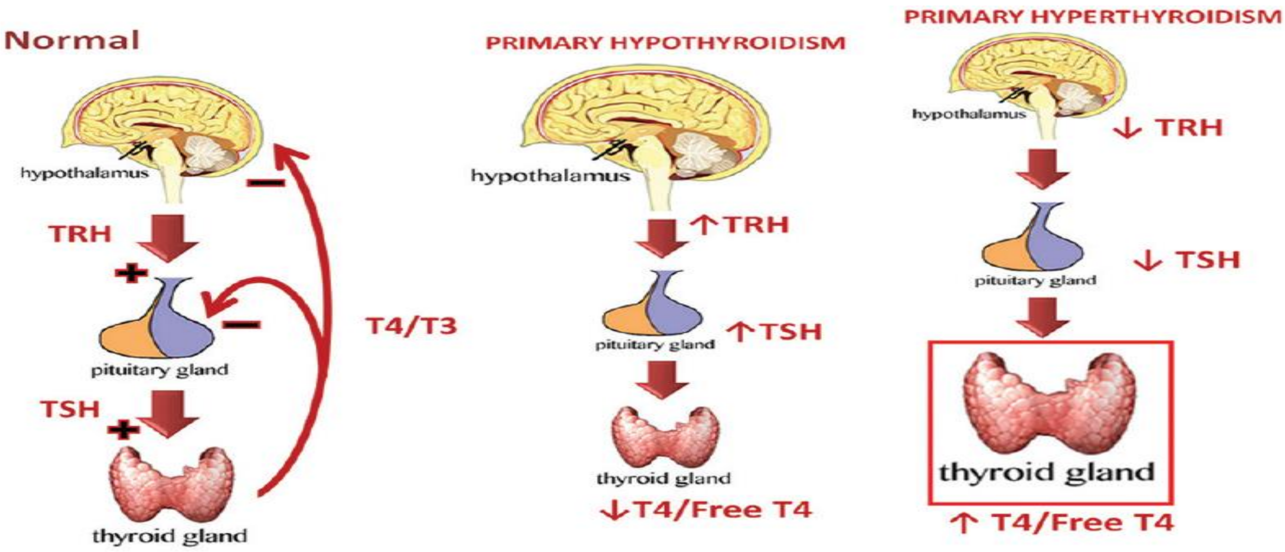
DIAGNOSIS

Blood Test: Measurement of the levels of thyroid stimulating hormone (TSH) and T4 in the blood stream are important because they help the doctor determine whether or not the goiter is making a normal amount of thyroid hormone. If the gland has a lump in it, the doctor may order a thyroid scan or an ultrasound to see if there are any masses in the thyroid that might be suspicious for a thyroid cancer.

Thyroid Scan: A thyroid scan is performed by having the patient take oral capsules that contain a harmless radioactive tracer (which is a tiny quantity of radioactive iodine). After four, six, or twenty-four hours (depending on the institution) a detector is placed over the thyroid gland. The amount of radioactive iodine that wound up in the thyroid gland is measured and a picture is taken of the distribution of radioactive iodine in the thyroid.

Ultrasound

Ultrasound is a way of taking a picture of the inside of the thyroid. Ultrasound bounces sound waves off the thyroid and makes a picture out of the returning echoes. If the ultrasound shows a large mass that is suspicious for cancer, then the ultrasonographer can use the ultrasound to guide a needle into the mass to perform a fine needle aspiration biopsy. If there are no large lumps in the thyroid gland that are suspicious for cancer, then no biopsy needs to be done.



HYPOTHYROIDISM

Hypothyroidism – also called underactive thyroid – is the most common thyroid disorder. It happens when your thyroid gland doesn't produce enough thyroid hormone, which is essential because thyroid hormone helps regulate important body processes, such as your metabolism. But with low thyroid function, these body processes slow down.

Inadequate production of thyroid hormone for prolonged periods or form the resistance of the peripheral tissues to the effects of thyroids hormones in the two ways

- ***Cretinism or congenital hypothyroidism*** is the development of severe hypothyroidism during infancy and childhood.
- ***Myxoedema*** is the adulthood hypothyroidism.

CAUSES:

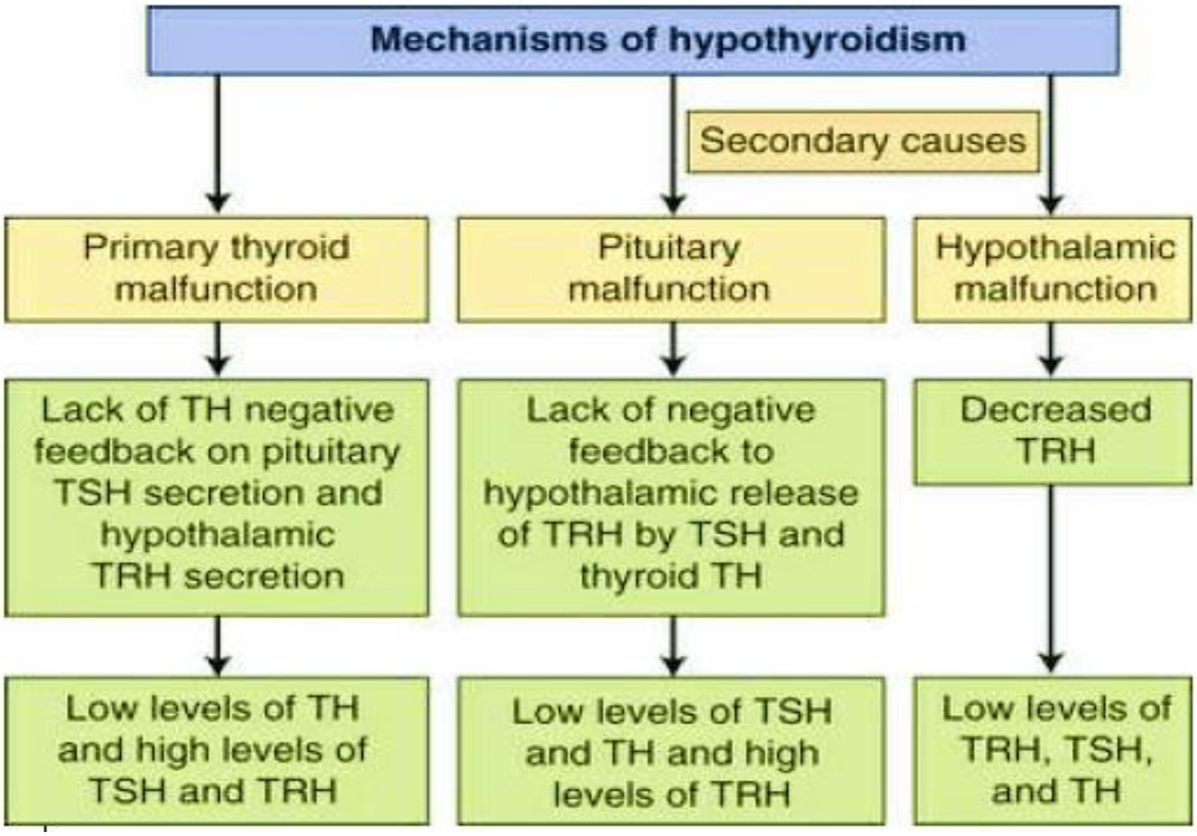
- Autoimmune distruction of thyroid gland (hashimoto's thyroiditis) –most common
- Iodine deficiency – leading cause
- Radio ablation of the thyroid for Grave's disease or thyroid nodule
- Thyroidectomy – partial or near complete for treatment of benign or malignant neoplasm, Graves's disease)
- Medications – Lithium, amioderone

SIGNS AND SYMPTOMS:

- Fatigue, constipation, cold intolerance, weight gain.
- Voice changes, reduced memory, muscle cramps, dry skin.
- Carpel tunnel syndrome, hair loss.

PATHOPHYSIOLOGY OF HYPOTHYROIDISM

- The hormones produced by the thyroid gland are T3 and T4. These hormones have an action on almost all parts of the body.
- The secretion of these hormones is regulated by TSH or thyroid stimulating hormone that is secreted by the pituitary gland.
- The secretion of thyroid hormone occurs only from this particular gland. The presence of iodine and amino acid tyrosine are a must for the production of thyroid hormones.



- Hypothyroidism and low levels of the thyroid hormones can occur if there is a deficiency of iodine for thyroid or thyroid stimulating hormone (TSH).

- The hypothalamus of the brain secretes TRH thyroid releasing hormone which acts on the pituitary gland and initiates the release of TSH or thyroid stimulating hormone.
- TSH then acts directly on the thyroid gland to release thyroid hormones T3 and T4.
- The normal functioning of the thyroid (healthy thyroid) is regulated by negative feedback mechanism where the levels of thyroid hormones increase or decrease under the influence of TSH

DIAGNOSIS

Blood test:

There are several types of blood tests – the most definitive one is called the TSH test (thyroid-stimulating hormone). However, in some cases, physicians may refer to the free thyroxine or T4, free T4 index, or total T4 to aid in the diagnosis.

TSH Test:

A thyroid-stimulating hormone or TSH is a blood test that measures the amount of T4 (thyroxine) that the thyroid is being signaled to make. If you have an abnormally high level of TSH, it could mean you have hypothyroidism. 0.4 mU/L to 4.0 mU/L is considered the reference range (there may be a slight variation depending on the laboratory), TSH >4.0/mU/L with a low T4 level indicates hypothyroidism.

T4 (thyroxine) Test:

The thyroid gland produces T4 (thyroxine). The free T4 and the free T4 index are blood tests that, in combination with a TSH test, can let your physician know how your thyroid is functioning.

Anti-thyroid Microsomal Antibodies Testing:

A third hypothyroid test is for anti-thyroid microsomal antibodies—anti-thyroid peroxidase (anti-TPO). These antibodies, which are produced by the immune system, may attack thyroid cells. If a blood test determines their presence, it shows that there has been thyroid damage which could potentially lead to hypothyroidism.

DISORDER OF SEX HORMONES

- The sex hormones are a group of hormones responsible for controlling puberty, reproduction, birth, and lactation. Sex hormone disorders, also referred to as reproductive hormone disorders, are medical conditions that affect the different glands and organs of the body responsible for the production of the sex hormones.
- The sex hormones, which include testosterone (male) and estrogen (female) are substances that essential in almost every body function, but more so in sexual functions and reproduction.
- Both testosterone and estrogen are present in males and females, but the levels differ according to sex. Males have higher levels of testosterone and females have higher levels of estrogen.
- Sex hormone disorders disrupt the normal production of hormones, which would then result in a variety of medical problems, such as a reduced sex drive (libido), vaginal dryness, infertility, or excessive body hair.

CAUSE OF CONDITION

- Women are more prone to sex hormone disorders than men are. This is mostly because women undergo normal changes in their bodies that affect the production of sex hormones. Such changes include menstruation and menopause.
- Sex hormone disorders are can be caused by injuries or diseases to the primary and supporting glands and organs responsible for the production and regulation of the hormones.
- In men, testosterone is primarily produced in the testicles, but other glands and organs in the endocrine system, such as the adrenal glands and pituitary gland, are also involved.
- In women, the ovaries produce estrogen, but the adrenal glands and pituitary gland also help in the production and/or regulation of the hormone.
- In addition to the endocrine glands, the heart, liver, kidney, and gonad also help to produce sex hormones. Therefore, sex hormone disorders can be caused by problems in the endocrine glands or the other organs.

The primary causes of sex hormone disorders include:

- Infections in the glands or organs
- Diseases

- Excessive alcohol consumption or drug use
- Injury to the testicles
- Surgical removal of the testicles
- Medications, which include steroids
- Hereditary factors

Sex hormone disorders can also be caused by:

- Obesity
- Low body fat
- Other health problems
- Hormone supplements
- Thyroid problems
- Ovarian cysts
- Ovarian tumors

It's important to understand that several glands and organs are involved in the production of sex hormones. Problems with any one of these glands and organs will display different symptoms, and will also need to be diagnosed and treated accordingly.

KEY SYMPTOMS

Sex hormone disorders lead to a variety of medical conditions, which would then display different symptoms. Some of the most common are

1. ***Polycystic ovarian syndrome,***
2. ***Hirsutism,***
3. ***Menopause***
4. ***Hypogonadism.***
5. ***Erectile dysfunction***
6. ***Gynecomastia***

1. POLYCYSTIC OVARIAN SYNDROME

Also called polycystic ovary syndrome, occurs when a woman experiences hormonal imbalance. As a result, women can experience menstruation difficulties or problems in conceiving a child. The condition can also result in unwanted changes in her appearance.

SYMPTOMS

PCOS signs and symptoms are typically more severe in obese females. Common symptoms include:

➢ Amenorrhea (missed periods) or irregular periods	➢ Mood changes
➢ Unwanted hair growth (excessive facial hair)	➢ Sleep problems
➢ Thinning hair on the head	➢ Infertility
➢ Acne	➢ Depression
➢ Fatigue	➢ Weight gain

CAUSES

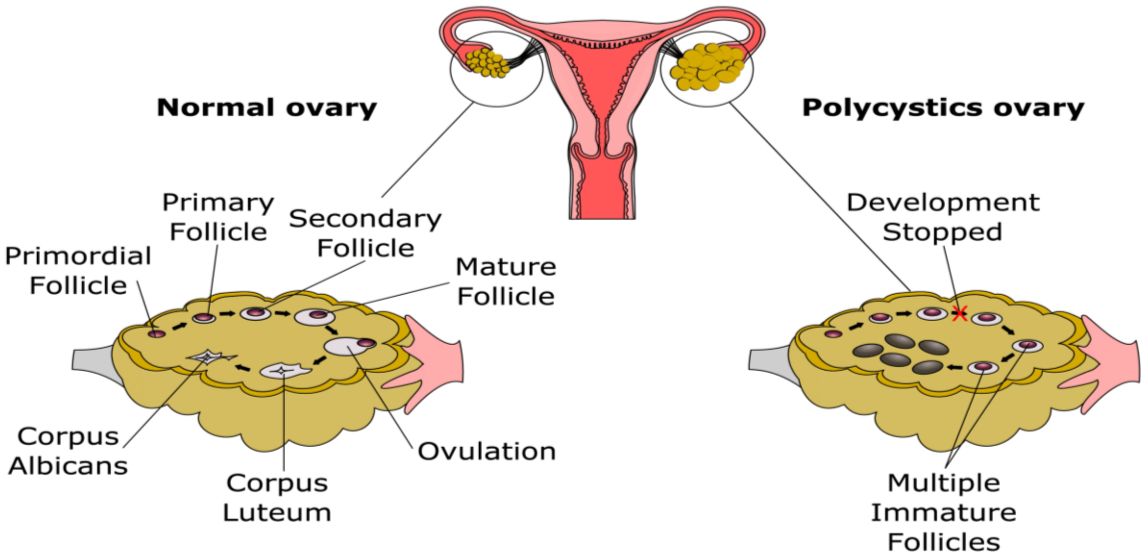
- The exact cause of PCOS is unknown.
- Factors that might play a role include:

Excess androgen: the ovaries produce abnormally high levels of androgen (male hormone), resulting in hirsutism (excessive facial hair) and acne.

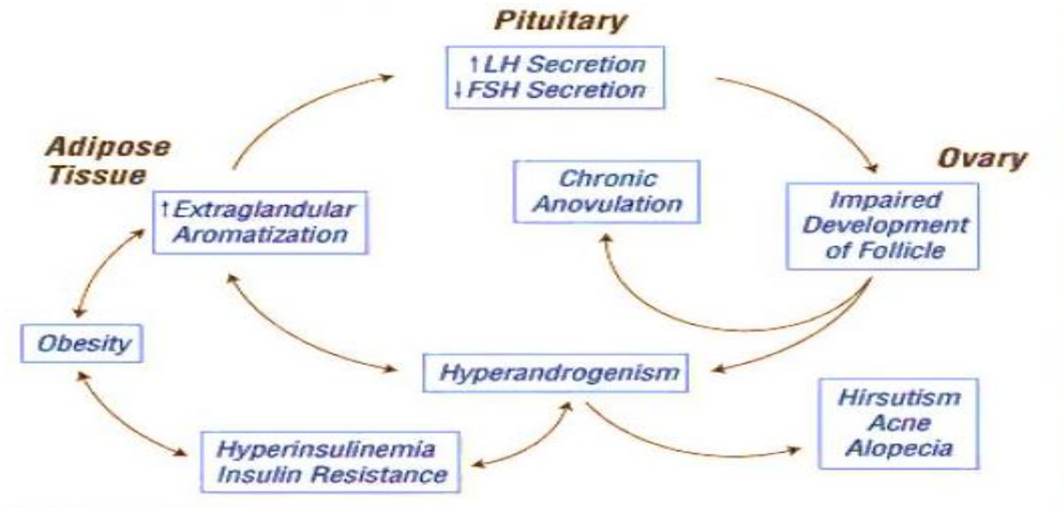
Heredity: Research suggests that certain genes might be linked to PCOS.

Excess insulin: Insulin is the hormone produced in the pancreas that allows cells to use glucose - body's primary energy supply. If cells become resistant to the action of insulin, then blood sugar levels can rise and body might produce more insulin.

Low-grade inflammation: Research has shown that women with PCOS have a type of low-grade inflammation that stimulates polycystic ovaries to produce androgens, which can lead to heart and blood vessel problems.



PATHOPHYSIOLOGY



DIAGNOSIS

Pelvic examination: Examination of the reproductive organs for masses, growths or other abnormalities.

Hormone test: A blood test to measure levels of hormones such as testosterone, prolactin, thyroid stimulating hormone (TSH) and adrenal gland hormones.

Ultrasound: Physician checks the appearance of ovaries and the thickness of the lining of uterus

2. HIRSUTISM

Hirsutism is characterized by excessive male pattern hair growth caused by increased levels of the male hormone testosterone and other androgens.

Hirsutism is excessive body hair on parts of the body where hair is normally absent or minimal. It may refer to a "male" pattern of hair growth that may be a sign of a more serious medical condition, especially if it develops well after puberty.

Cultural stigma against hirsutism can cause much psychological distress and social difficulty. Discrimination based on facial hirsutism often leads to the avoidance of social situations and to symptoms of anxiety and depression.

Hirsutism is usually the result of an underlying endocrine imbalance, which may be adrenal, ovarian, or central.

It can be caused by increased levels of androgen hormones. The amount and location of the hair is measured by a Ferriman-Gallwey score. It is different from hypertrichosis, which is excessive hair growth anywhere on the body

SYMPTOMS

Hirsutism affects members of either sex, since rising androgen levels can cause excessive body hair, particularly in locations where women normally do not develop terminal hair during puberty (chest, abdomen, back, and face).

CAUSE

- Hirsutism can be caused by an increased level of androgens, the male hormones, or an oversensitivity of hair follicles to androgens.
- Male hormones such as testosterone stimulate hair growth, increase size and intensify the growth and pigmentation of hair.
- Symptoms associated with a high level of male hormones include acne, deepening of the voice, and increased muscle mass. The condition is called hyperandrogenism.
- Growing evidence connects high circulating levels of insulin in women to the development of hirsutism. Women are at high risk of becoming hirsute. Further, treatments that lower insulin levels will lead to a reduction in hirsutism.

3. MENOPAUSE

Menopause is the end of a woman's menstrual cycles. The term can describe any of the changes you go through just before or after you stop having your period, marking the end of your reproductive years.

Causes

Women are born with all of their eggs, which are stored in their ovaries. Their ovaries also make the hormones estrogen and progesterone, which control their period (menstruation) and the release of eggs (ovulation). Menopause happens when the ovaries no longer release an egg every month and menstruation stops.

Menopause is a regular part of aging when it happens after the age of 40. But some women can go through menopause early. It can be the result of surgery, like if their ovaries are removed in a hysterectomy, or damage to their ovaries, such as from chemotherapy. If it happens before age 40, for any reason, it's called premature menopause.

Menopause Symptoms

First signs of menopause

Most women nearing menopause will have hot flashes, sudden feelings of warmth that spread over the upper body, often with blushing and sweating. These flashes can range from mild in most women to severe in others.

- Uneven or missed periods
- Vaginal dryness
- Sore breasts
- Trouble sleeping
- Emotional changes
- Dry skin, eyes, or mouth

Symptoms of menopause

Later symptoms often include:

Fatigue, Depression, Crankiness, Racing heart, Changes in libido (sex drive)

Headaches, Joint and muscle aches and pains, Weight gain, Hair loss.

STAGES OF MENOPAUSE

Natural menopause isn't caused by any type of medical or surgical treatment. It's slow and has three stages:

Perimenopause:

This phase usually begins several years before menopause, when your ovaries slowly make less estrogen. Perimenopause lasts until menopause, the point at which your ovaries stop releasing eggs. In the last 1 to 2 years of this stage, estrogen levels fall faster. Many women have menopause symptoms.

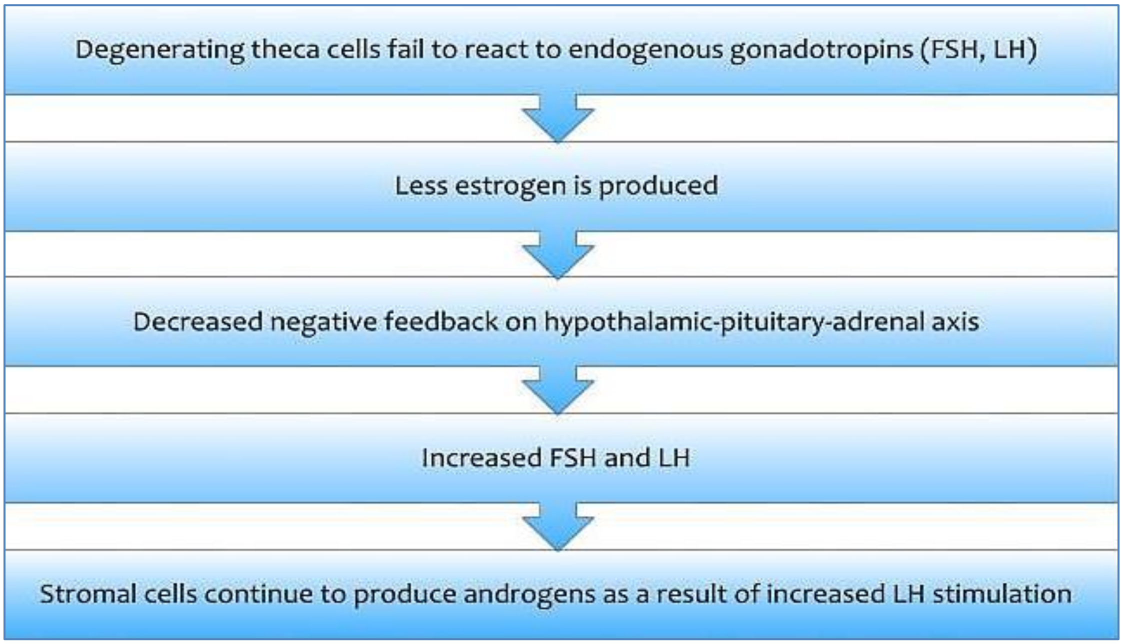
Menopause:

This is when it's been a year since women had a period. Women ovaries have stopped releasing eggs and making most of their estrogen.

Postmenopause:

These are the years after menopause. Menopausal symptoms such as hot flashes usually ease. But health risks related to the loss of estrogen increase as you get older.

PATHOPHYSIOLOGY



DIAGNOSIS

Follicle-stimulating hormone (FSH) This usually goes up as you near menopause.

Estradiol This tells your doctor how much estrogen your ovaries are making.

Thyroid hormones. This shows problems with your thyroid gland, which can affect your period and cause symptoms that look like menopause.

Anti-Mullerian hormone (AMH). Your body makes this in its reproductive tissues. It can help your doctor learn about the reserve of eggs in your ovaries.

4. ERECTILE DYSFUNCTION

- The inability of men to get and maintain an erection throughout the sexual activity
- Erectile dysfunction results due to reduced blood flow to the penis or inability of the penile muscles to relax during sexual activity. There could be various underlying causes for erection problems, including diabetes and heart problems.
- Inability to get and maintain erection is the primary symptom noted. The choice of treatment is based on the underlying cause, and includes medications, therapies such as self-injections and exercises, and surgical implants

Symptoms

Erectile dysfunction symptoms might include persistent:

- Trouble getting an erection
- Trouble keeping an erection
- Reduced sexual desire

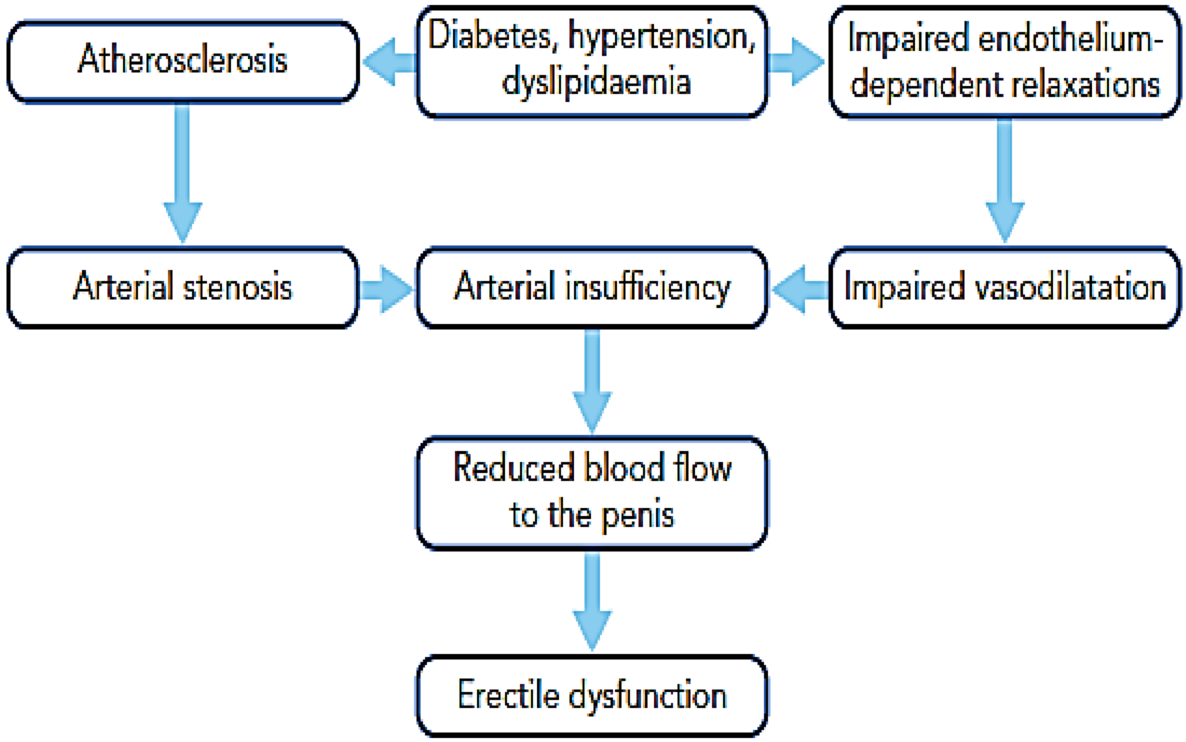
CAUSES

Physical causes of erectile dysfunction

In many cases, erectile dysfunction is caused by something physical. Common causes include:

- Heart disease, atherosclerosis, High cholesterol, Diabetes, Tobacco use.
- High blood pressure, Obesity Multiple sclerosis, Certain prescription medications.
- Metabolic syndrome — a condition involving increased blood pressure, high insulin levels, body fat around the waist and high cholesterol
- Peyronie's disease — development of scar tissue inside the penis
- Alcoholism and other forms of substance abuse
- Treatments for prostate cancer or enlarged prostate
- Surgeries or injuries that affect the pelvic area or spinal cord
- Low testosterone

PATHOPHYSIOLOGY



Psychological causes of erectile dysfunction

The brain plays a key role in triggering the series of physical events that cause an erection, starting with feelings of sexual excitement. A number of things can interfere with sexual feelings and cause or worsen erectile dysfunction. These include:

- Depression, Stress, Anxiety or other mental health conditions
- Relationship problems due to stress, poor communication or other concerns

DIAGNOSIS

Physical exam: This might include careful examination of your penis and testicles and checking your nerves for sensation.

Blood tests: A sample of your blood might be sent to a lab to check for signs of heart disease, diabetes, low testosterone levels and other health conditions.

Urine tests (urinalysis). Like blood tests, urine tests are used to look for signs of diabetes and other underlying health conditions.

Ultrasound: This test is usually performed by a specialist in an office. It involves using a wandlike device (transducer) held over the blood vessels that supply the penis. It creates a video image to let your doctor see if you have blood flow problems.

Psychological exam: Your doctor might ask questions to screen for depression and other possible psychological causes of erectile dysfunction.

5. GYNECOMASTIA

- Gynecomastia is the abnormal non-cancerous enlargement of one or both breasts in men due to the growth of breast tissue as a result of a hormone imbalance between estrogen and androgen.
- Gynecomastia is different from "pseudogynecomastia", which is defined as an excess of skin and adipose tissue in the male breasts without the development of true breast glandular tissue; pseudogynecomastia is commonly present in men with obesity.

CAUSES OF GYNECOMASTIA

- The chief cause of gynecomastia is a much lower level of the male sex hormone testosterone compared with the female reproductive hormone estrogen, within the system of a boy or man.
- This occurs due to mechanisms that trigger blocking testosterone activity, lowering the amount of male hormone synthesized, or elevated secretion of estrogen.
- Various circumstances can lead to the abnormal testosterone-estrogen hormone balance in the male body, such as:
  - Natural hormonal modifications during puberty or adulthood
  - Medications for other illnesses that interfere with hormonal production
  - Alcohol or drug addictions
  - Underlying health anomalies and phenomena, like thyroid malfunctions and Graves' disease, hyperthyroidism, the ageing process and liver problems

SIGNS AND SYMPTOMS

- Swelling and pain in the breast glands, in either one or both breasts
- Increase in diameter of the areola i.e the area surrounding the nipple
- Irregular discharge from either one or both nipples
- Difference between both the chest tissues in size
- Anxiety, depression and low self-esteem due to the abnormal appearance of breasts
- Decline in general health and eating disorders
- Limited social interactions with friends and colleagues

PATHOPHYSIOLOGY

Hormones involved in breast development

- Estrogen and progesterone act in a coordinated manner to support breast development. Estrogen helps duct growth and progesterone promotes alveolar development which only occurs in female as gynecomastia doesn't have alveolar development.
- Growth hormone which acts through IGF-1 acts as a mediator in the presence of estrogen and progesterone for ductal breast duct development.

- The IGF-1 levels have been found higher in boys with pubertal gynecomastia which shows the role of GH and IGF-1 in the pathogenesis of gynecomastia.
- Prolactin in the presence of estrogen and progesterone also supports breast development. It also plays an indirect role as it causes central hypogonadism which alters the androgen/estrogen balance.
- Aromatase catalyzes the conversion of androgens to estrogen and promotes the breast development. So, gynecomastia can also result from overexpression of aromatase.

DIGNOSIS

Physical examination: Examines the signs and symptoms and will inspect the breast development.

Blood test: To determine the cause of gynaecomastia.

CT scan: To identify any abnormalities in the breast.

Mammogram: A technique which uses X-rays to diagnose and locate abnormalities in breasts.

Biopsy: Done to rule out the possibility of breast cancer.

NERVOUS SYSTEM

EPILEPSY, PARKINSON'S DISEASE, STROKE

EPILEPSY

- The word epilepsy derived from the Greek word ***Epilepsia***
- Epilepsy is the fourth most common neurological disorder and affects people of all ages Epilepsy means the same thing as "seizure disorders"
- Epilepsy is characterized by unpredictable seizures and can cause other health problems
- Epilepsy is a spectrum condition with a wide range of seizure types and control varying from person-to-person
- It affects approximately 60 million people worldwide.
- It is usually controlled, but not cured.
- Epilepsies have been classified variously; major types are described below.
- Epilepsy is a chronic disorder, the hallmark of which is recurrent, unprovoked seizures. Many people with epilepsy have more than one type of seizure and may have other symptoms of neurological problems as well.
- Having seizures and epilepsy can also affect one's safety, relationships, work, driving and so much more. How epilepsy is perceived or how people are treated (stigma) often is a bigger problem than the seizures.

EPILEPSY: A new definition: Seizures and epilepsy are not the same. An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is a disease characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition. A seizure is an event and epilepsy is the disease involving recurrent unprovoked seizures.

SEIZURE

- A seizure is a sudden flow of electrical activity in the brain
- A seizure usually affects how a person appears or acts for a short time
- Many different things can occur during a seizure.

What happens in the brain during a seizure?

The electrical activity is caused by complex chemical changes that occur in nerve cells.

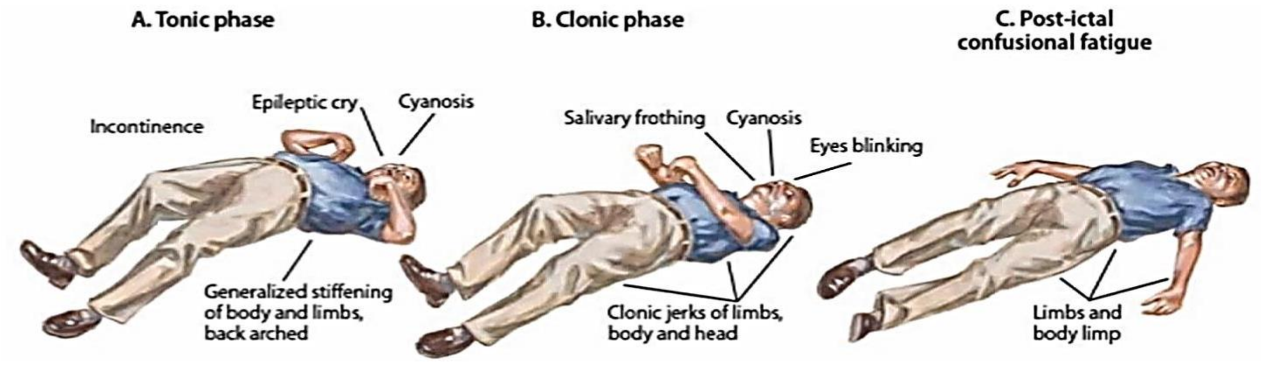
Brain cells either excite or inhibit (stop) other brain cells from sending messages. Usually there is a balance of cells that excite and those that can stop these messages. However, when a seizure occurs, there may be too much or too little activity, causing an imbalance between exciting and stopping activity. The chemical changes can lead to surges of electrical activity that cause seizures. Seizures are not a disease in themselves. Instead, they are a symptom of many different disorders that can affect the brain. Some seizures can hardly be noticed, while others are totally disabling.

TYPES OF SEIZURES

I. Generalized seizures

1. *Generalized tonic-clonic seizures* (major epilepsy, grand mal): commonest, lasts 1–2 min.

- This is the type of seizure most people associate with epilepsy.
- A generalized tonic-clonic seizure often begins without warning.
- It involves a sudden stiffness of the body, followed by muscle contractions or jerking motions.
- There may also be changes in blood pressure, an increase in saliva, and loss of bladder control.
- This type of seizure has a high risk of injury due to the potential for falling to the ground and the sometimes violent jerking movements



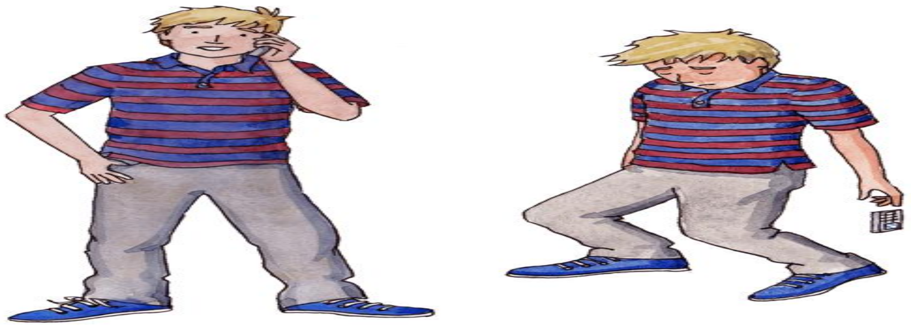
2. *Absence seizures* (minor epilepsy, petit mal): prevalent in children, lasts about 1/2 min.

- Momentary loss of consciousness, patient apparently freezes and stares in one direction, no muscular component or little bilateral jerking.

- Absence seizures often occur in young children and are commonly mistaken for daydreaming. An absence seizure involves a brief disruption of consciousness— lasting from a few seconds to about half a minute.
- Typically, this seizure starts suddenly: the student stops what he or she is doing and stares blankly.
- This student's eyes may roll upwards briefly before this event and then the episode disappears as quickly as it came.
- There is usually a loss of awareness for a few seconds. For example, you may call the student's name, and he or she won't respond. Absence seizures can happen many times a day.

3. *Atonic seizures* (A kinetic epilepsy)

- Unconsciousness with relaxation of all muscles due to excessive inhibitory discharges.
- Atonic seizures sometimes known as a "drop attack," atonic seizures cause a sudden loss of muscle tone.
- This may result in the dropping of the head or a limb, or lead a student to fall to the ground.
- There also may be a brief loss of consciousness. Because the student may fall to the ground, there is a risk of injury.



4. *Myoclonic seizures*

- Shock-like momentary contraction of muscles of a limb or the whole body.
- Myoclonic seizures are one of the most common types of seizures, typically affecting children and young adults.
- A myoclonic seizure involves a sudden contraction of muscles and can appear as a jerk of one or both arms or sometimes the head.
- Myoclonic seizures may cause just a single jerk or several jerking movements. Generally, the seizure is so brief that although the student loses consciousness, he or she may appear conscious.
- While myoclonic seizures are common, you may be less likely to see them in the classroom as they often happen while falling asleep or within a short time of waking up.

5. *Infantile spasms (Hypsarrhythmia)*

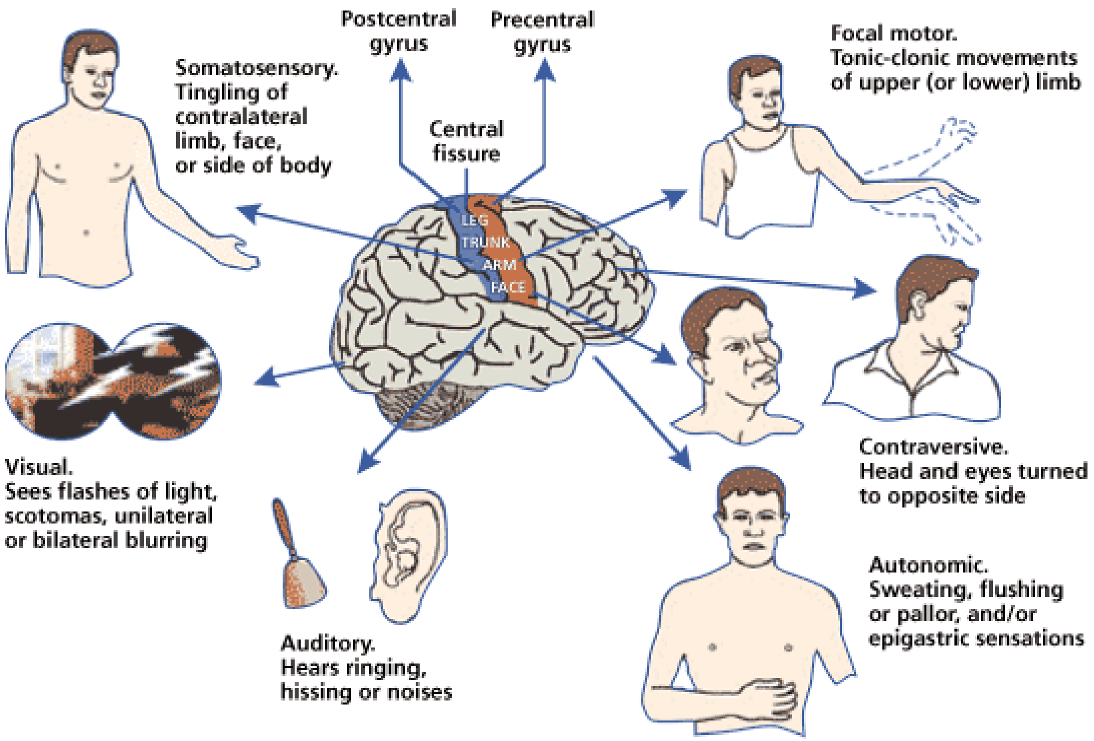
- Seen in infants.
- Probably not a form of epilepsy.
- Intermittent muscle spasm and progressive mental deterioration. Diffuse changes in the interseizure EEG are noted.

II. Partial seizures

1. *Simple partial seizures* (SPS, cortical focal epilepsy): lasts 1/2–1 min. Often secondary.

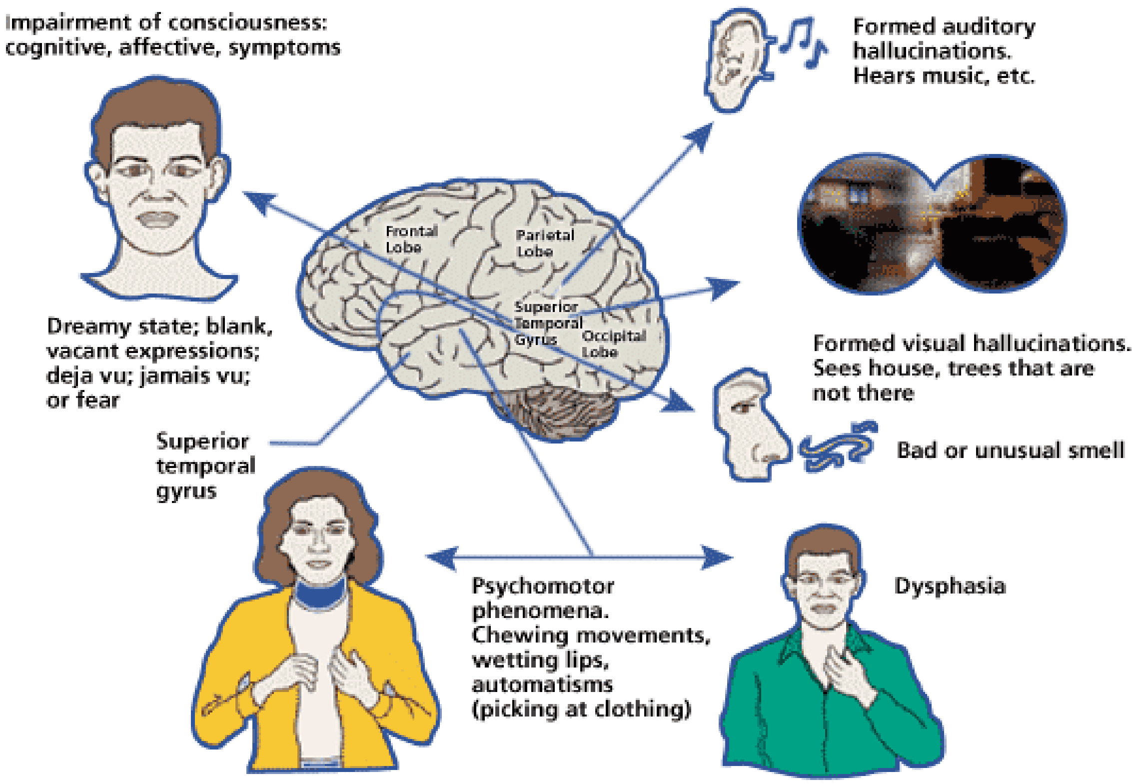
- Convulsions are confined to a group of muscles or localized sensory disturbance depending on the area of cortex involved in the seizure, without loss of consciousness.

- In this type of seizure, an electrical disturbance starts in one half (or hemisphere) of the brain, so the student may experience symptoms like twitching, numbness, dizziness, or disturbances to their senses.
- In a simple partial seizure, the student will remain conscious. Be aware that partial seizures can spread to involve both hemispheres of the brain.
- The resulting seizure would be categorized as "secondarily generalized."



2. *Complex partial seizures* (CPS, temporal lobe epilepsy, psychomotor):

- Attacks of bizarre and confused behavior and purposeless movements, emotional changes lasting 1–2 min along with impairment of consciousness. An aura often proceeds.
- The seizure focus is located in the temporal lobe.
- A complex partial seizure starts in one hemisphere of the brain, and can spread to areas that involve consciousness.
- When there is an altered state of consciousness at the onset of the event, the student may experience a change in awareness and may seem confused.
- A common symptom is tugging at clothing; the student may seem conscious but it is important to remember that he or she is completely unaware of their actions.



3. *Secondarily generalized*

- The partial seizure occurs first and evolves into generalized tonic-clonic seizures with loss of consciousness.
- The antiepileptic drugs are drugs which prevent the seizures are known as epilepsy.

SYMPTOMS

Common symptoms include muscle jerking and contractions, brief loss of consciousness or awareness, weakness, anxiety, and staring. Seizures are the main symptom of epilepsy. Symptoms differ from person to person and according to the type of seizure.

Generalized seizures involve the whole brain. There are six types:

Tonic-clonic seizures used to be called “grand mal seizures.” Symptoms include:

- Stiffening of the body
- Shaking
- Loss of bladder or bowel control
- Biting of the tongue
- Loss of consciousness

Tonic seizures cause muscle stiffness.

Clonic seizures are characterized by repeated, jerky muscle movements of the face, neck, and arms.

Absence seizures, which used to be called “petit mal seizures,” cause a blank stare. This type of seizure may also cause repetitive movements like lip smacking or blinking. There’s also usually a short loss of awareness.

Atonic seizures lead to loss of muscle control and can make you fall down suddenly.

Myoclonic seizures cause spontaneous quick twitching of the arms and legs.

Simple partial seizure doesn’t involve loss of consciousness. Symptoms include:

- Alterations to sense of taste, smell, sight, hearing, or touch
- Dizziness, Tingling and twitching of limbs

Complex partial seizures involve loss of awareness or consciousness. Other symptoms include:

- Staring blankly
- Unresponsiveness
- Performing repetitive movements

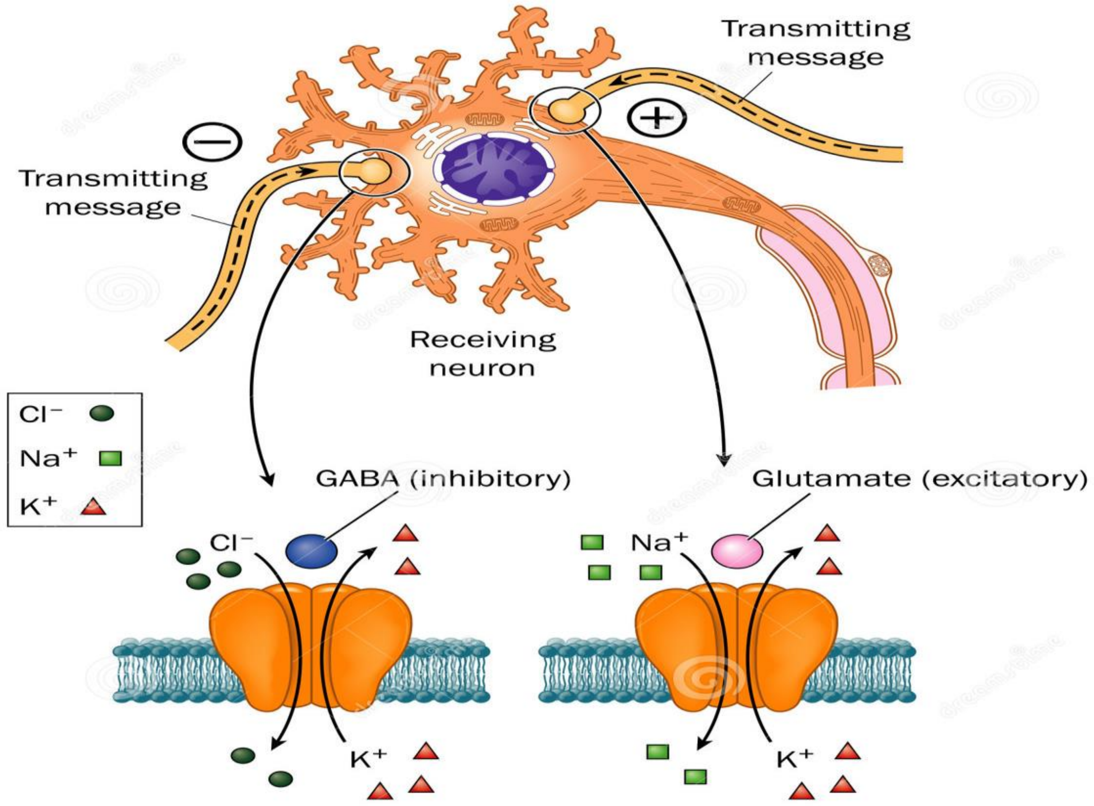
ETIOLOGY

- Brain abnormalities that occur in utero (before birth)
- Low oxygen during birth
- Brain injury, such as after a traumatic head injury
- Brain infection, such as meningitis or encephalitis
- Stroke, which can lead to scarring of the brain
- Brain tumour, either benign or malignant
- Neurodegenerative diseases, such as Alzheimer’s disease

PATHOPHYSIOLOGY

- A seizure occurs when a portion of the brain becomes overly excited or when nerves in the brain begin to fire together in an abnormal fashion.
- Seizure activity can arise in areas of the brain that are malformed from birth defects or genetic disorders or disrupted from infection, injuries, tumors, strokes, or inadequate oxygenation.

- The pathophysiology of seizures results from an abrupt imbalance between the forces that excite and inhibit the nerve cells such that the excitatory forces take precedence.
- This electrical signal then spreads to the surrounding normal brain cells, which begin to fire in concert with the abnormal cells.
- With prolonged or recurrent seizures over a short period, the risk of future seizures increases as nerve cell death, scar tissue formation, and sprouting of new axons occur.
- Nerve cells between discharges normally have a negative charge internally due to the active pumping of positively charged sodium ions out of the cell.
- Discharge or firing of the nerve cell involves a sudden fluctuation of the negative charge to a positive charge as ions channels into the cell open and positive ions, such as sodium, potassium, and calcium, flow into the cell.
- Both excitatory and inhibitory control mechanisms act to allow appropriate firing and prevent inappropriate excitation of the cell.
- The pathophysiology of seizures can occur due to increased excitation of the nerve cell, decreased inhibition of the nerve cell, or a combination of both influences.



DIAGNOSIS

Complete blood count (CBC): To determine the number of blood cells, check for infections or other conditions causing the symptoms.

Neurological examination: To assess motor, mental functions and determine the type of epilepsy.

Electroencephalogram (EEG): Electrodes are attached to the scalp to record the brain's electrical activity.

Neuropsychological examination: To assess the thinking, memory, and speech skills.

CT scan: To check for abnormalities in the brain.

Functional MRI (fMRI): To examine the brain activities.

Positron emission tomography (PET): To observe the oxygen utility by the brain.

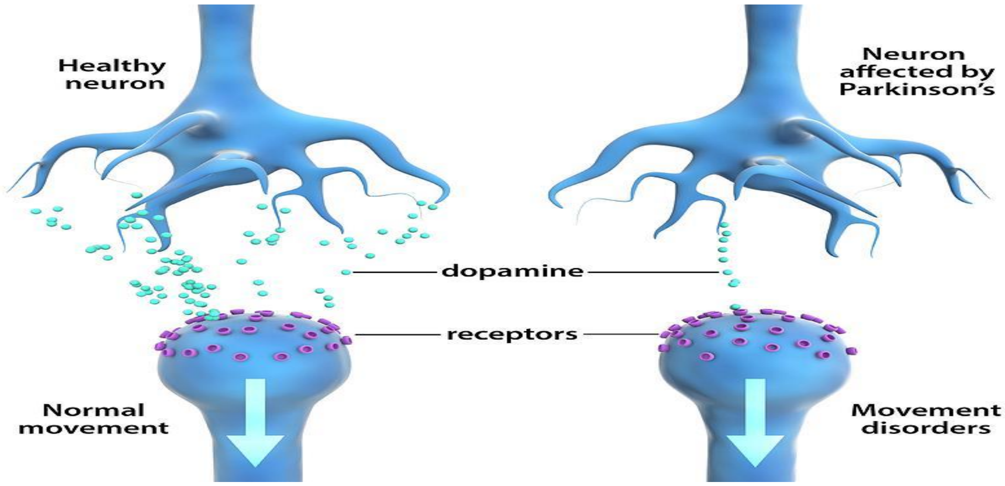
Single photon emission computed tomography (SPECT): A small amount of radioactive material is injected into the brain to assess blood flow.

Magnetoencephalography (MEG): Measures the magnetic field produced by brain activity

PARKINSON'S DISEASE

Parkinson disease is a slowly progressive, chronic neurological disease that affects a small area of nerve cells in an area of the brain known as the substantia nigra.

This cell normally produces dopamine, a chemical (neurotransmission) that transmits signal between areas in the brain that when working normally coordinates smooth and balanced muscle movement. Parkinson's disease cause this nerve cells to die and as a result body movement are effected



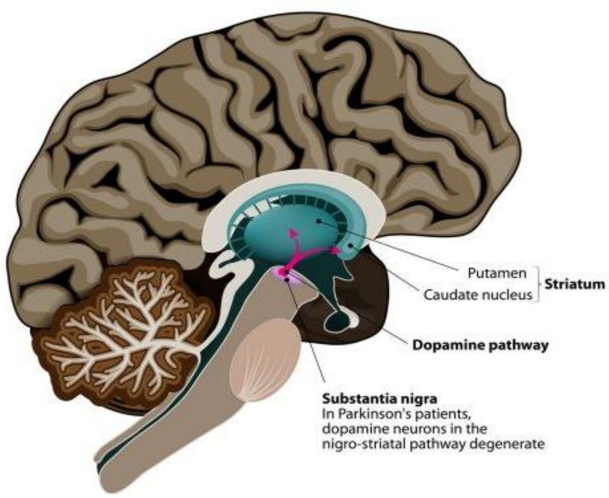
DEFINITION:

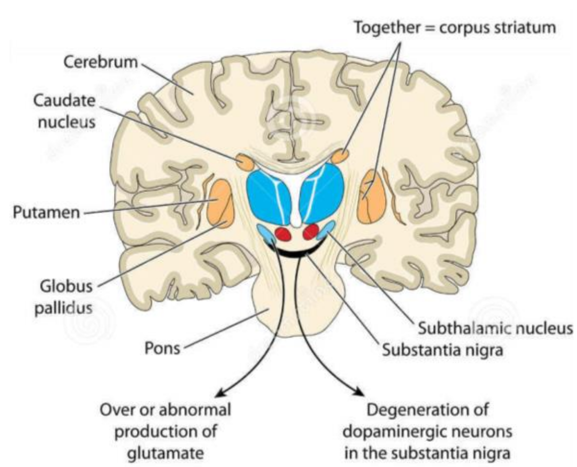
Parkinson disease is characterized by tremor at rest, rigidity and slowness or difficulty in initiating and executing movement (Akinesis or Bradykinesis). This combination of clinical features is collectively known as Parkinsonism.

Parkinsonism is a syndrome with numerous causes of which Parkinson disease is the most common

ANATOMY

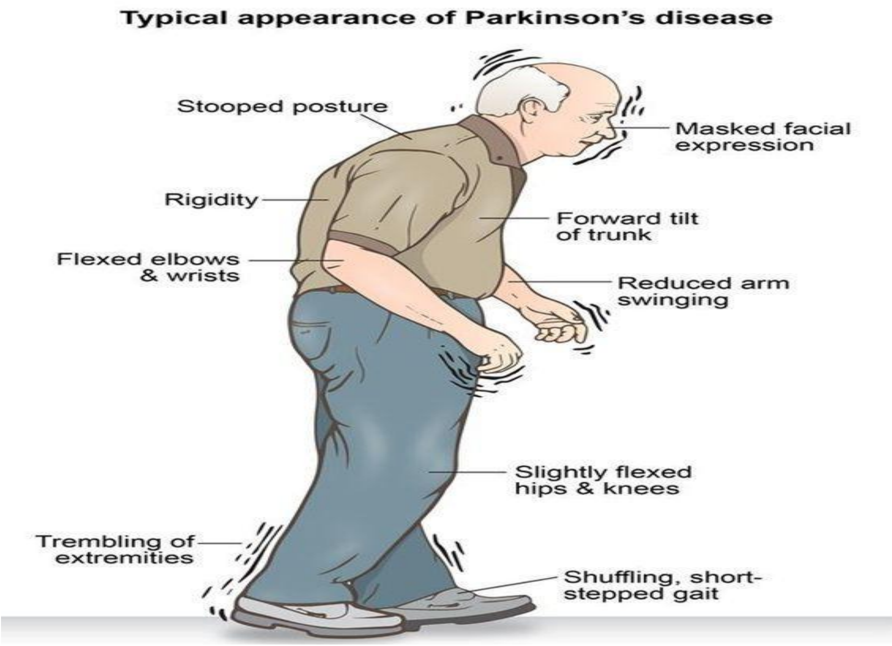
- The substantia nirga is a nucleus in the mid brain which is part of the Basal Ganglia.
- The substantia nigra is made up of two automatically and functionally distinct portion:
- Substantia nigra pars compacta –more darkened
- Substantia Nigra pars reticulata –less darken.
- Most of the dopamine neuron of the brain originate in the midbrain and are found in either the substantia Nigra.
- The Dopamine neurons in the substantia Nigra express high level of pigment called Neuromelanin which accounts for thin dark colour .
- The substantia Nigra par compacta contain more dopamine neurons while pars Reticulate contains more GABA neurons





CLINICAL SIGNIFICANCE:

Parkinson disease is associated with the death of dopamine Neuron in the substantia Nigra pars compacta which is due to neuro-degeneration . When a significant number of this neuron have died, the individual will likely to start to experienced movement –related problems like tremors, rigidity, slowness of movement and postural instability – which are the hall mark symptoms of Parkinson disease.



ETIOLOGY/RISK FACTORS:

Advancing age : Above 60 years mostly seen while young onset Parkinson disease is called a patients develop Parkinson disease between 21-40 years.

Sex: male are more likely to get than female.

Family History: Having one or more close relatives with the disease increase the rise of getting.

Low Estrogen Level: most menopausal women who don't use hormone replacement therapy are more risk of getting the disease.

Agricultural work: exposure to environmental toxin such as pesticide ,herbicides ,inhabits dopamine production and promote free radical damage. these involved in farming and are exposed to such toxins have a greater risk of getting the disease.

Low level of vitamins: researchers de was found that people with low level of vitamin B develop severe Parkinson symptoms.

Head Trauma: Trauma to the head ,neck and upper cervical spine increase the chance of getting Parkinson's.

Genetic Mutation: people who have both young onset Parkinson's disease and a strong family history of the disease are more likely carry genes linked to Parkinson's disease which includes;

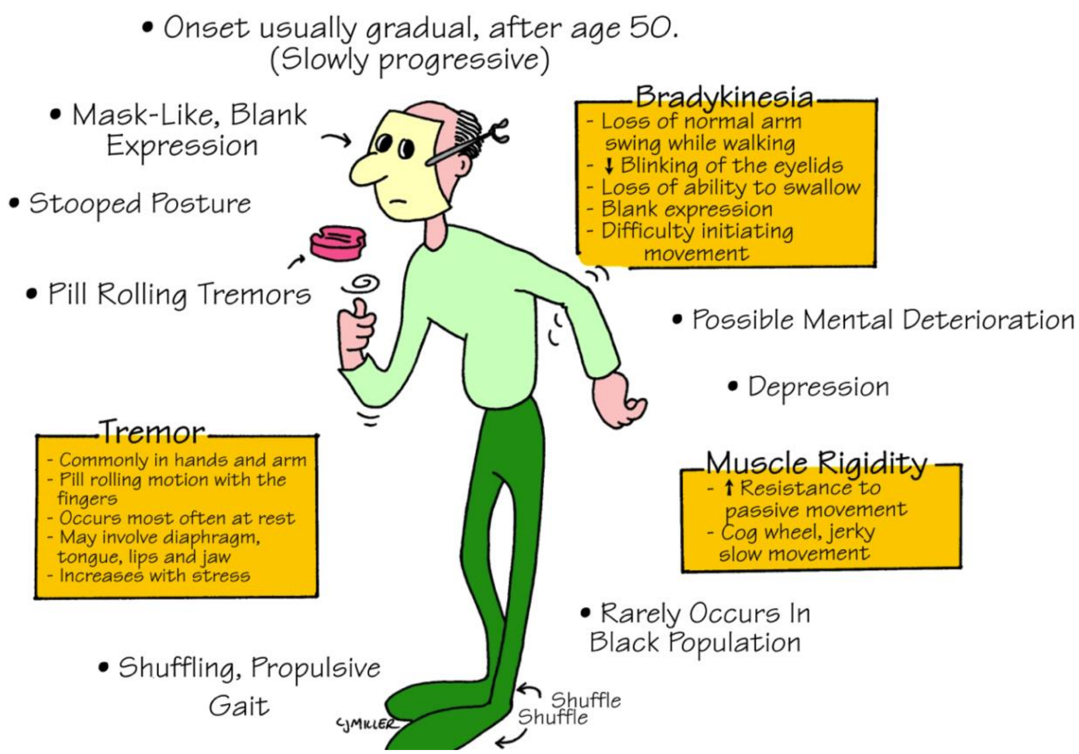
Alpha Synuclein: Autosomal dominant, LRRK2(leucine rich repeat kinesis2): Autosomal. PINK1/PARKIN/DJ-1: Autosomal recessive, GBA(Glucocerebrocidase): Autosomal recessive, Alpha synuclein and LRRK2 gene mutation is linked with Young onset Parkinson Disease.

SIGNS AND SYMPTOMS: Four cardinal sign: ¬ Resting tremor ¬ Rigidity ¬ Akinesia ¬ Postural instability Cog-wheeling

Tremors – hands and head develop involuntary movements when at rest; pin-rolling sign (finger and thumb)

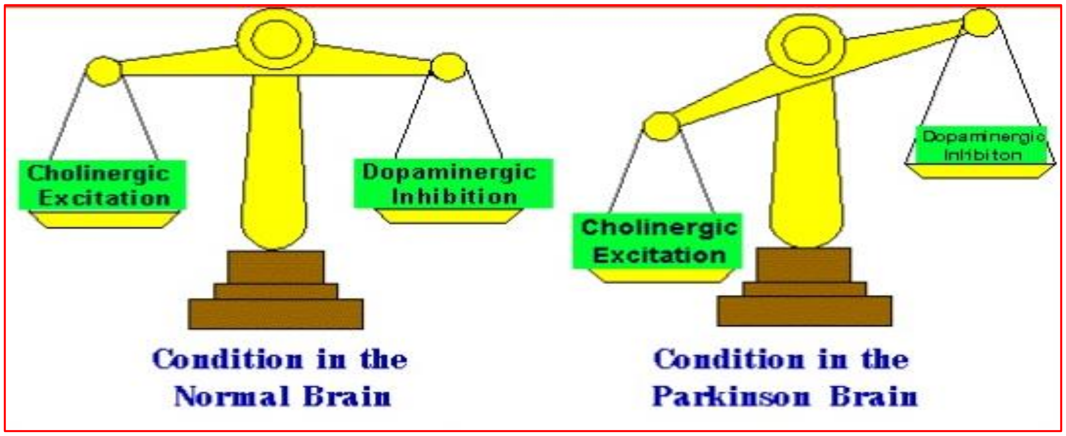
Muscle rigidity – arthritis-like stiffness, difficulty in bending or moving limbs; poker face. Brandykinesia – problems chewing, swallowing or speaking; difficulty in initiating movements and controlling fine movements; walking becomes difficult.

Postural instability – humped over appearance, prone to falls



PATHOPHYSIOLOGY:

Etiological Factors: ¬ Environmental factors ¬ Gene mutation ¬ Degenerative disease Destruction of Dopaminergic neuronal cells in the substantia nigra in the basal Ganglia Neuronal cells loss and depigmentation Degeneration of dopaminergic activity particularly in the nigro-striatal pathway Depletion of dopamine store Imbalance between excitatory (Acetylcholine) and inhibiting (dopamine) neurotransmitter in the corpus striation Impairment of extrapyramidal tract controlling complex body movement Tremors Rigidity Akinesis Postural instability



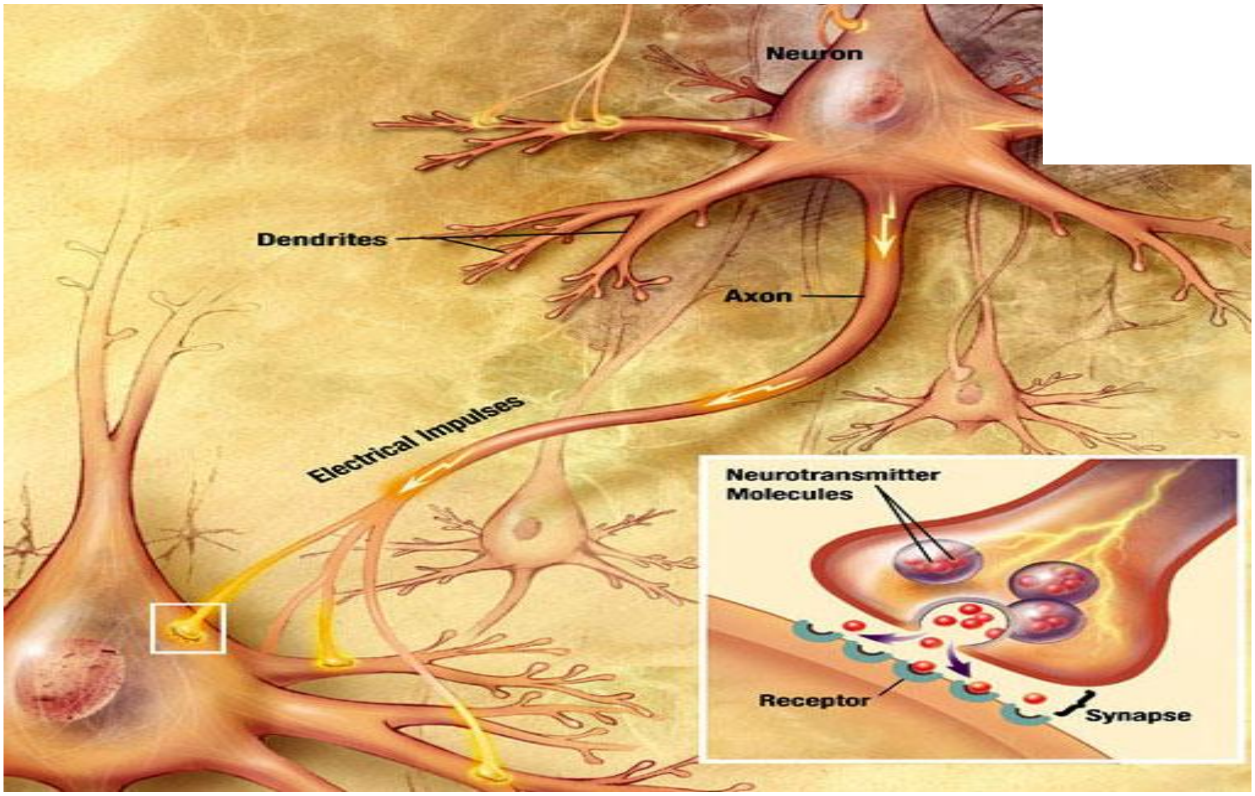
ROLE OF DOPAMINE

Brain cells, called neurons, communicate using specific chemicals called neurotransmitters. One type of neurotransmitter, called dopamine, is produced by neurons in the brain, including in the substantia nigra (SN). Dopamine helps to facilitate movement and is also involved in reward-based behaviors and hormone release. There is an area of the substantia nigra called the substantia nigra pars compacta (SNpc) that is made up specifically of these dopamine-producing neurons. When those neurons die, less dopamine is produced. A characteristic symptom of Parkinson's is below-average levels of dopamine due to the death of those dopaminergic neurons in the SNpc, which is why dopamine agonists are regularly prescribed for people with Parkinson's.

When those dopamine-producing neurons die and your body can no longer produce adequate levels of dopamine, motor control is impaired. Thus, the hallmark motor symptoms of Parkinson's – tremors, bradykinesia, poor balance, involuntary movements, etc. – are clearly correlated with a lack of dopamine. However, motor symptoms usually do not begin to appear until there has already been about 60% dopamine neuron loss, and most people with Parkinson's eventually lose 80% or more of their dopamine-producing neurons.

LEWY BODIES AND ALPHA-SYNUCLEIN

Lewy bodies are abnormal aggregates and inclusions of protein that develop inside nerve cells in people with Parkinson's disease. The aggregations usually consist of insoluble fibrillary aggregates containing misfolded proteins.

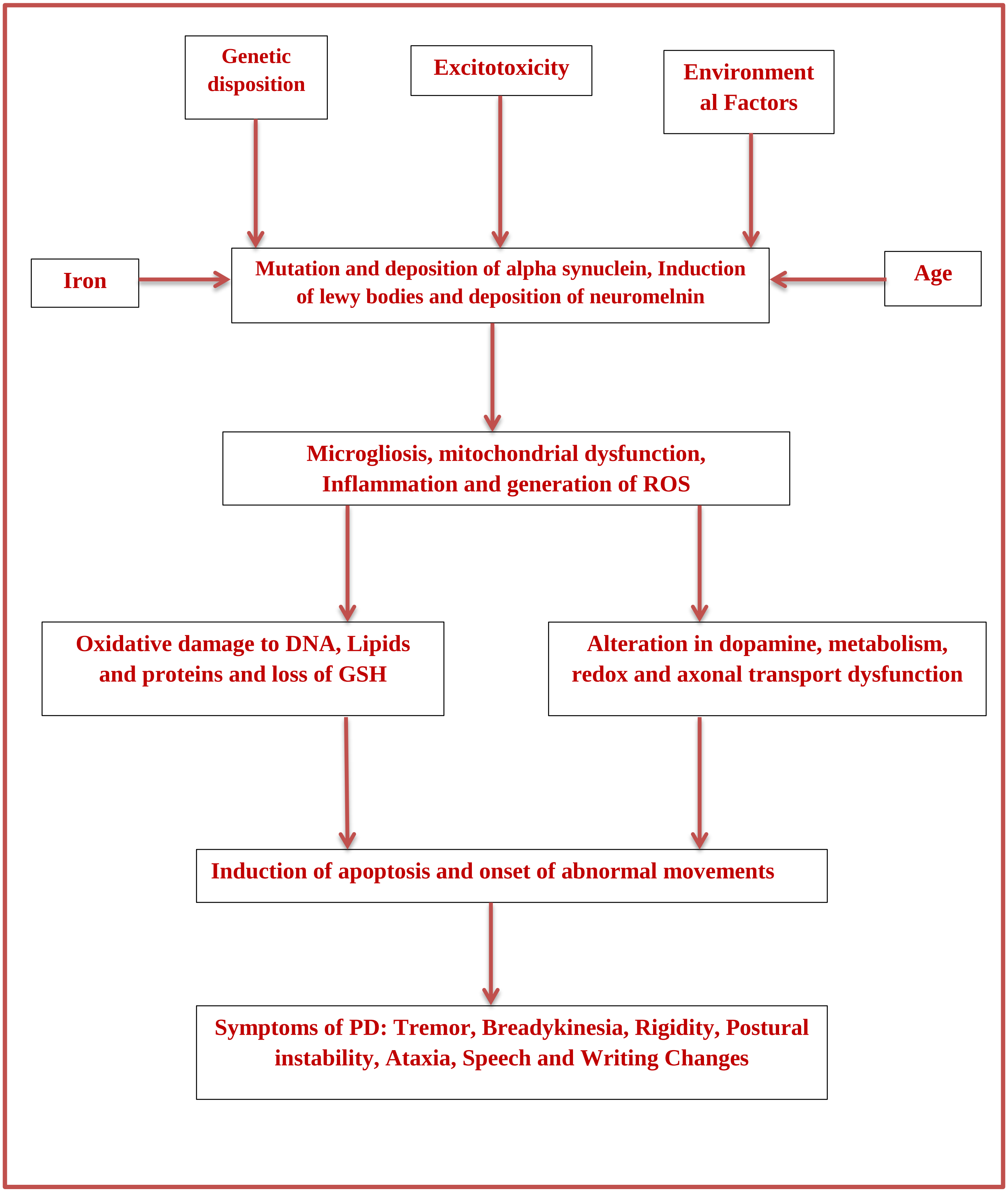


DIAGNOSTIC EVALUATION:

Laboratory test and imaging studies are not helpful in the diagnosis of Parkinson's disease. Criteria for making diagnosis of Parkinson's disease include the following

1. Through patients' history and performed complete neurological examination.
2. CT scan or MRI of head to rule out secondary cause.
3. PET-scan to evaluate levodopa uptake and conversion to Dopamine in the corpus Striatum.
4. Present of two or more cardinal features (resting tremors, rigidity, Akinesia, postural instability).

5.Final diagnosis usually made by the pressure of heavy bodies in the brain during Autopsy

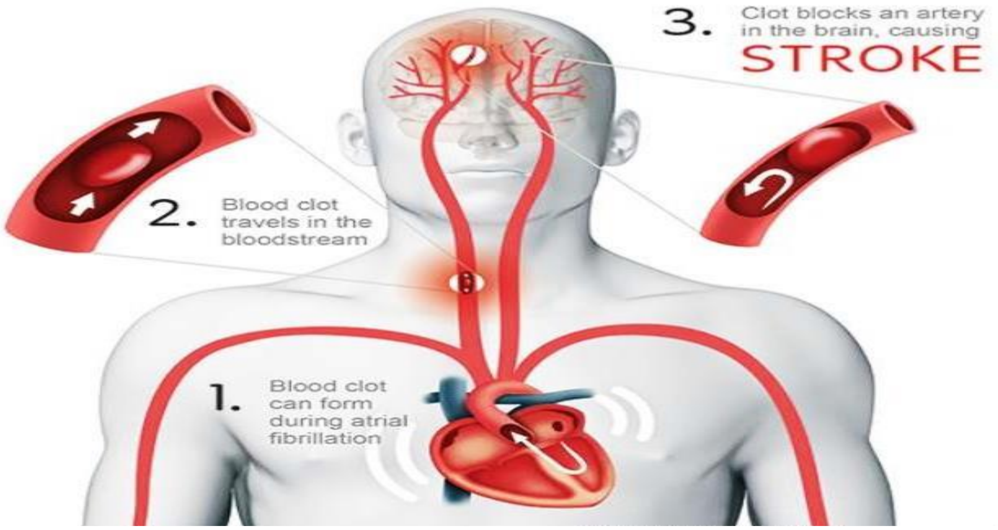


Pathophysiology of PD

STROKE

A stroke is defined as the clinical syndrome of rapid onset of cerebral deficit lasting more than 24 hours or leading to death with no apparent cause other than a vascular one.

A stroke is a rapid loss of brain function due to the disturbance in the blood supply to brain. A stroke happens when blood flow to a part of the brain stops and it is sometimes called a “brain attack”



There are three main kinds of stroke:

- Ischemic strokes
- Hemorrhagic strokes
- Transient ischemic attacks (TIAs), also referred to as mini-strokes

ISCHEMIC STROKE

Ischemic stroke is the most common form of stroke, accounting for around 85% of strokes.

This type of stroke is caused by blockages or narrowing of the arteries that provide blood to the brain, resulting in ischemia - severely reduced blood flow.

These blockages are often caused by blood clots. Clots can be caused by fatty deposits within the arteries called plaque.

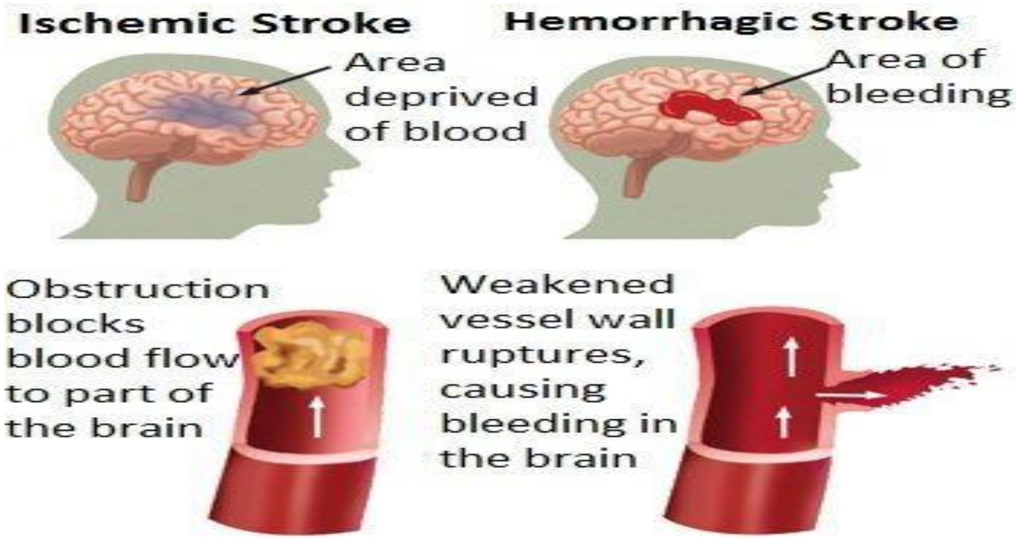
HEMORRHAGIC STROKE

Hemorrhagic stroke are caused by arteries in the brain either leaking blood or bursting open.

The ruptures can be caused by conditions such as hypertension, trauma, blood-thinning medications and aneurysms (weaknesses in blood vessel walls).

Intra cerebral hemorrhage is the most common type of hemorrhagic stroke and occurs when brain tissue is flooded with blood after an artery in the brain bursts.

Subarachnoid hemorrhage is the second type of hemorrhagic stroke and is less common. In this type of stroke, bleeding occurs in the subarachnoid space - the area between the brain and the thin tissues that cover it.

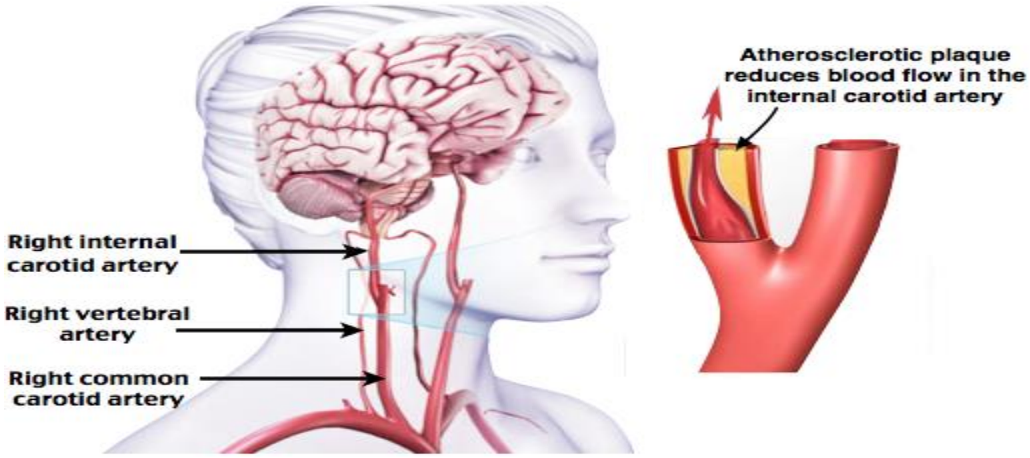


TRANSCIENT ISCHEMIC ATTACK (TIA)

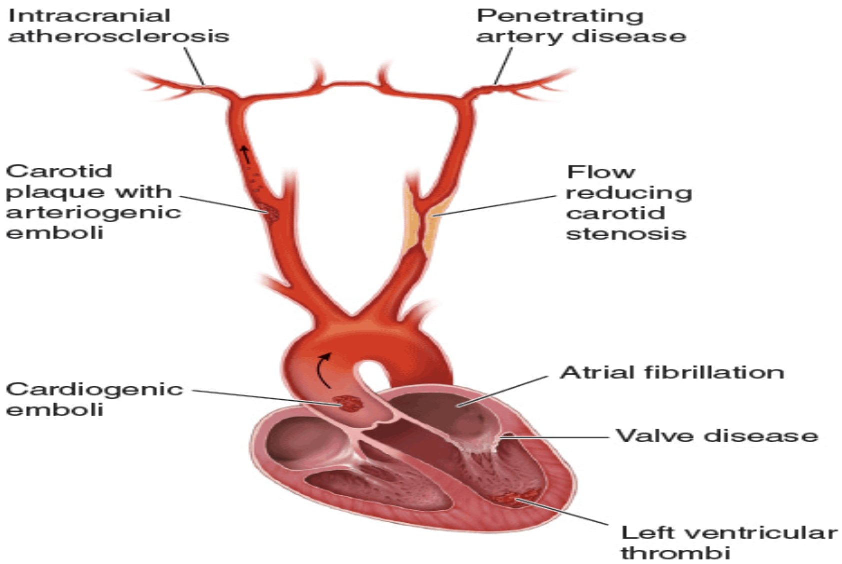
TIAs are different from the aforementioned kinds of stroke because the flow of blood to the brain is only briefly interrupted. TIAs are similar to ischemic strokes in that they are often caused by blood clots or other debris.

TIAs should be regarded as medical emergencies.

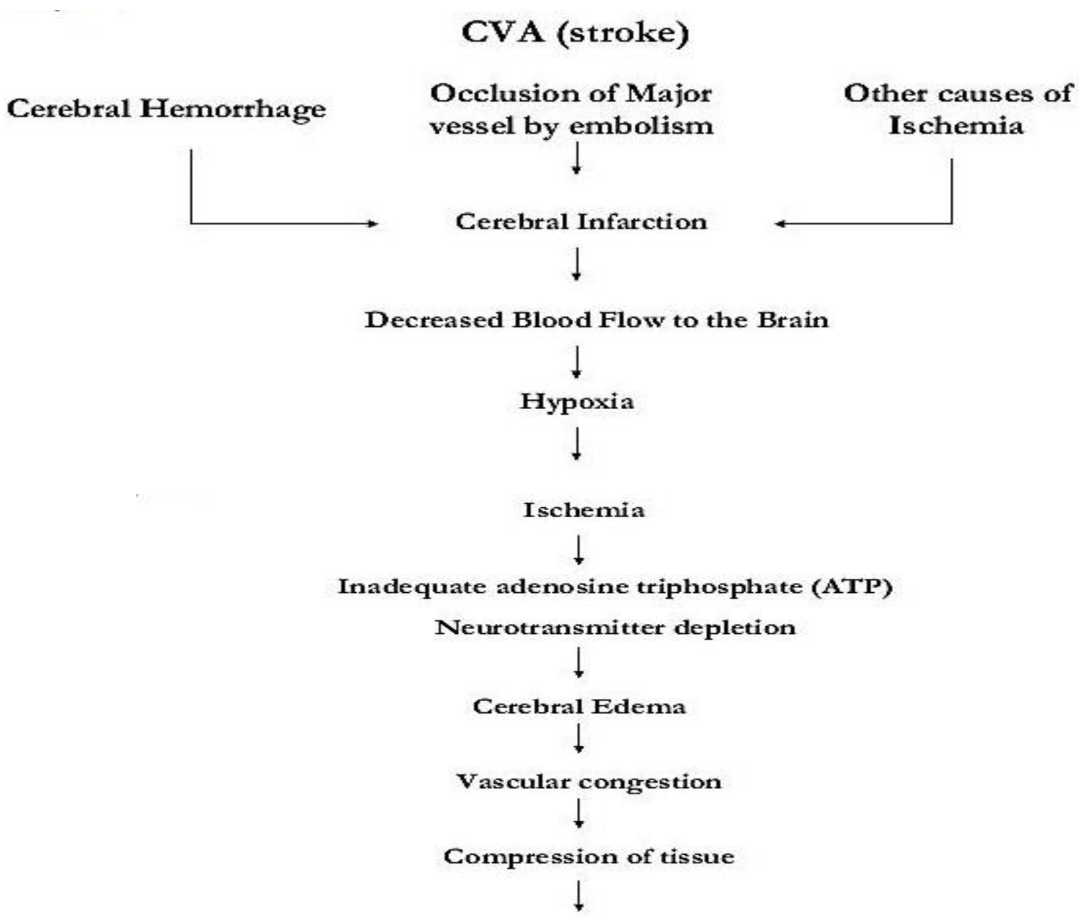
They serve as warning signs for future strokes and indicate that there is a partially blocked artery or clot source in the heart.

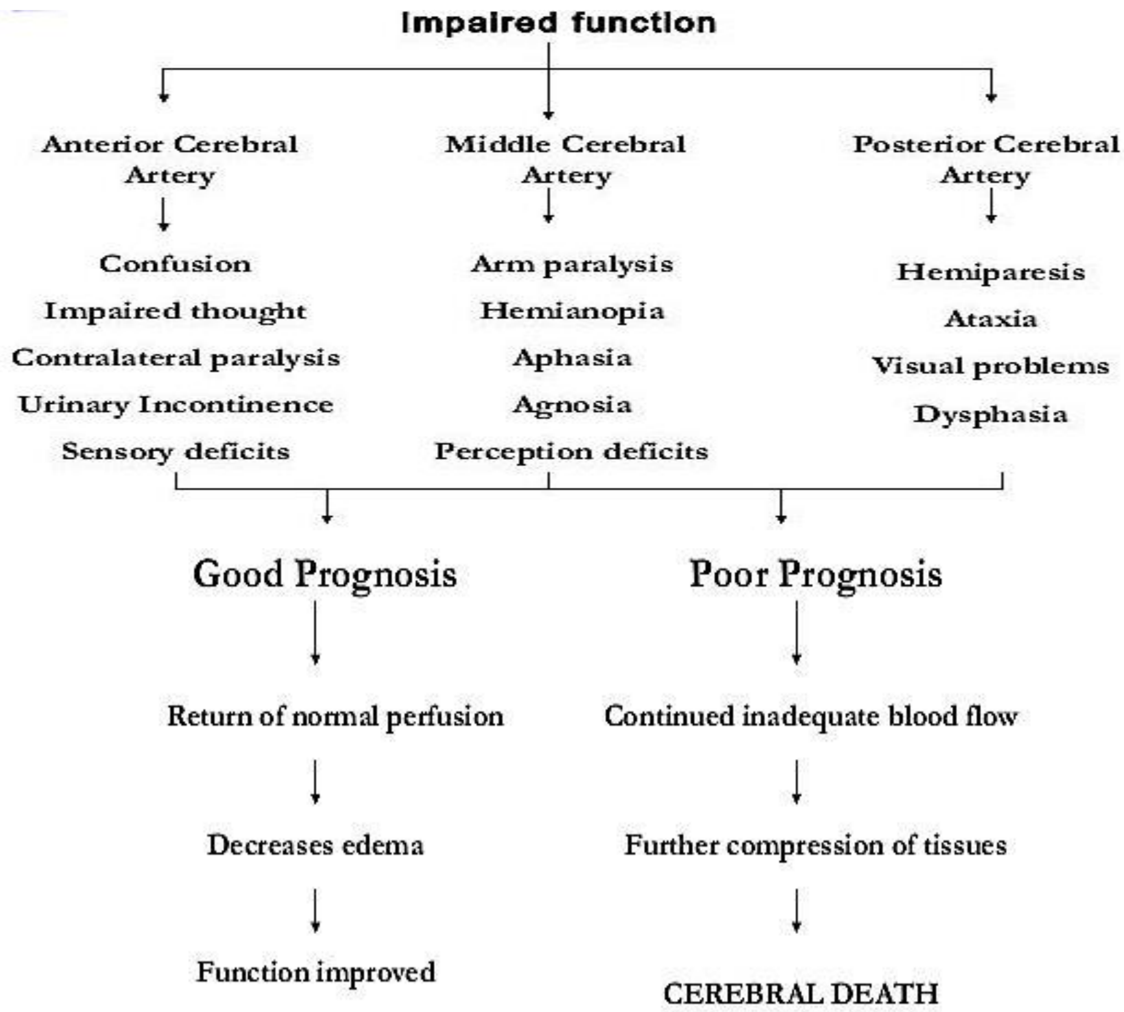


According to the Centers for Disease Control and Prevention (CDC), over a third of people who experience a TIA go on to have a major stroke within a year if they have not received any treatment. Between 10-15% will have a major stroke within 3 months of a TIA.



PATHOPHYSIOLOGY





SYMPTOMS

- Strokes occur quickly and, as such, symptoms of stroke often appear suddenly without warning.
- The main symptoms of stroke are as follows: Confusion, including trouble with speaking and understanding, Headache, possibly with altered consciousness or vomiting, Numbness of the face, arm or leg, particularly on one side of the body, Trouble with seeing, in one or both eyes, Trouble with walking, including dizziness and lack of co-ordination.
- In addition to the persistence of the problems listed previously, patients may also experience the following:
- Bladder or bowel control problems
- Depression
- Pain in the hands and feet that gets worse with movement and temperature changes

- Paralysis or weakness on one or both sides of the body
- Trouble controlling or expressing emotions.

DIAGNOSIS

There are several different types of diagnostic tests that doctors can use in order to determine which type of stroke has occurred:

Physical examination: a doctor will ask about the patient's symptoms and medical history. They may check blood pressure, listen to the carotid arteries in the neck and examine the blood vessels at the back of the eyes, all to check for indications of clotting

Blood tests: a doctor may perform blood tests in order to find out how quickly the patient's blood clots, the levels of particular substances (including clotting factors) in the blood, and whether or not the patient has an infection

CT scan: a series of X-rays that can show hemorrhages, strokes, tumors and other conditions within the brain

MRI scan: radio waves and magnets create an image of the brain to detect damaged brain tissue

Carotid ultrasound: an ultrasound scan to check the blood flow of the carotid arteries and to see if there is any plaque present

Cerebral angiogram: dyes are injected into the brain's blood vessels to make them visible under X-ray, in order to give a detailed view of the brain and neck arteries

Echocardiogram: a detailed image of the heart is created to check for any sources of clots that could have traveled to the brain to cause a stroke

PSYCHIATRIC DISORDERS
(Depression, Schizophrenia and Alzheimer disease)

DEPRESSION

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. Also called major depressive disorder or clinical depression, it affects how you feel, think and behave and can lead to a variety of emotional and physical problems.

A very common, highly treatable, medical illness.

Affects physical, mental and emotional well-being.

Affects basic, everyday activities like eating and sleeping.

Affects how people think about things and feel about themselves.

In contrast to the normal emotional experiences of sadness, loss, or passing mood states, clinical depression is persistent and can interfere significantly with an individual's ability to function. Give up like tendency

Symptoms can last months or even years.

SYMPTOMS OF DEPRESSION

- People with Major Depression experience at least five of these symptoms all day, nearly every day, for at least 2 weeks.
- The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- Feeling sad, blue, or down in the dumps
- Loss of interest in things you usually enjoy
- Feeling slowed down or restless
- Having trouble sleeping or sleeping too much
- Loss of energy or feeling tired all the time
- Having an increase or decrease in appetite or weight
- Having problems concentrating, thinking, remembering or making decisions
- Feeling worthless or guilty
- Having thoughts of death or suicide

CAUSES OF DEPRESSION

Causes not known, but current theories include:

- **Genetic** Runs in families. However, depression can also occur in people who have no family history.
- **Environmental** A serious loss, difficult relationship, financial problem, or any stressful change in life patterns can trigger a depressive episode.
- **Physical Illness** Serious complications such as cancer, some disorders eg Cushing's syndrome etc
- **Drug induced** eg betablockers and corticosteroids
- **Hormonal changes:** postmenopausal depression, post-partum depression
- **Personality Characteristics** low self-esteem, pessimistic world view, low stress tolerance
- **Biological** Current thinking explores problems in brain functioning in the following areas: Limbic system, neurotransmitters and neurons, hormones and the endocrine system combination of genetic, psychological, environmental, and/ or biological factors may contribute to the onset of a depressive disorder.

TYPES OF DEPRESSION

Major Depression (Clinical Depression)

Major depressive disorder, also known as unipolar or clinical depression, is characterized by a persistent feeling of sadness or a lack of interest in outside stimuli. You might have this type of depression if you have five or more of the following symptoms on most days for 2 weeks of longer. At least one of the symptoms must be a depressed mood or loss of interest in activities.

Dysthymia (Persistent Depressive Disorder)

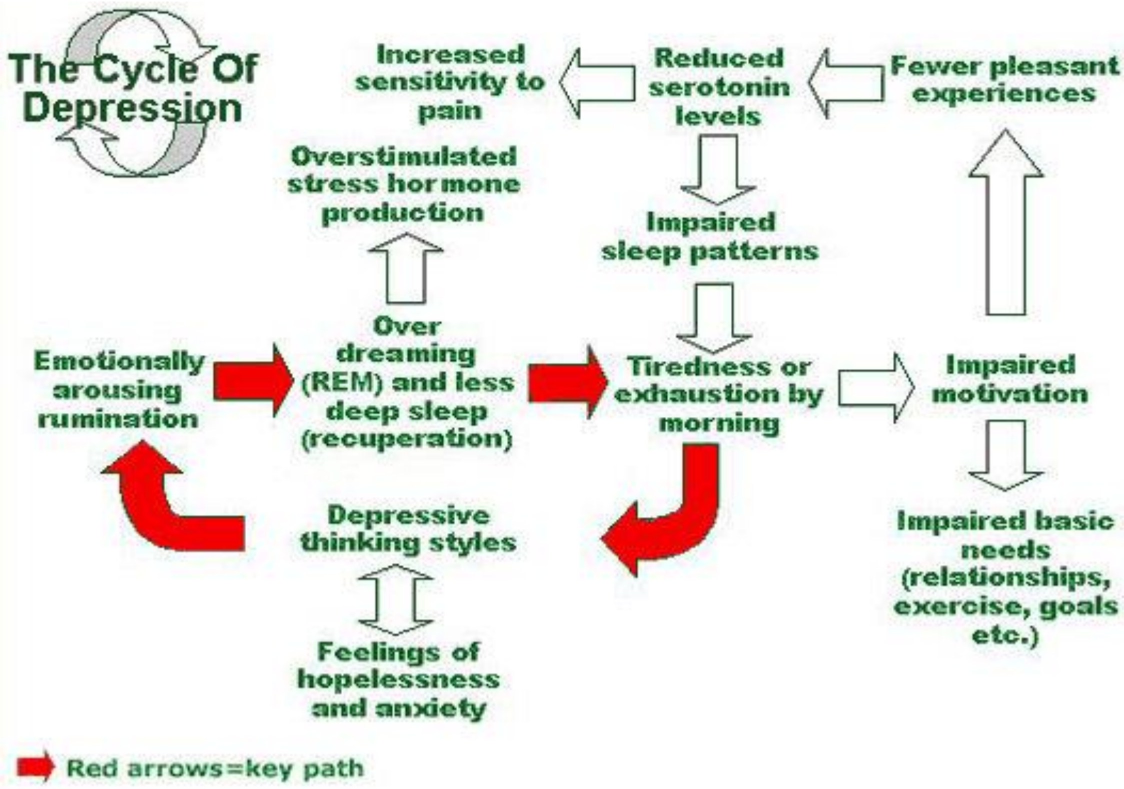
Dysthymia, also known as persistent depressive disorder, is a long-term form of depression that lasts for years and can interfere with daily life, work, and relationships. People with dysthymia often find it difficult to be happy even on typically joyous occasions. They may be perceived as gloomy, pessimistic, or a complainer, when in reality they are dealing with a chronic mental illness. Symptoms of dysthymia can come and go over time, and the intensity of the symptoms can change, but symptoms generally don't disappear for more than two months at a time.

Manic Depression (Bipolar Disorder)

Bipolar disorder, sometimes referred to as manic depression, is a mental health condition that causes extreme fluctuations in mood and changes in energy, thinking, behavior, and sleep. With manic depression, you don't just feel "down in the dumps;" your depressive state may lead to suicidal thoughts that change over to feelings of euphoria and endless energy. These extreme mood swings can occur more frequently–such as every week–or show up sporadically–maybe just twice a year.

Seasonal Affective Disorder (SAD)

Seasonal affective disorder (SAD) is a type of depression related to the change of season. People who suffer from SAD notice symptoms beginning and ending at about the same times each year. For many, symptoms start in the fall and continue into the winter months, though it is possible for SAD to occur in the spring or summer. In either case, symptoms of depression, such as hopelessness, fatigue, and loss of interest or pleasure in activities, start out mild and progress to be more severe as the weeks go on.

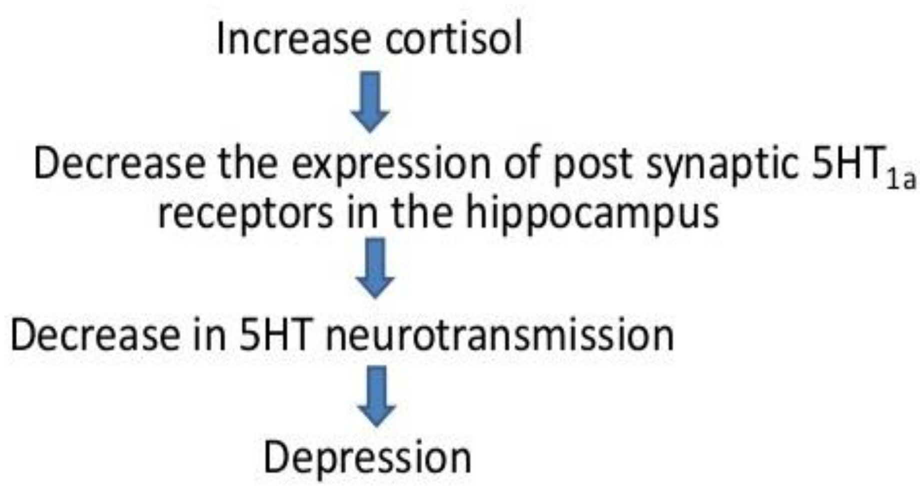


Postpartum Depression (Peripartum Depression)

Sad feelings and crying bouts that follow childbirth are known as the "baby blues." The baby blues are common and tend to decrease within a week or two. This type of sadness is often attributed to the dramatic hormonal changes that follow childbirth. Around one in seven women will experience something more extreme than the typical baby blues. However, women that give birth and struggle with sadness, anxiety or worry for several weeks or more may have postpartum depression (PPD).

PATHOPHYSIOLOGY

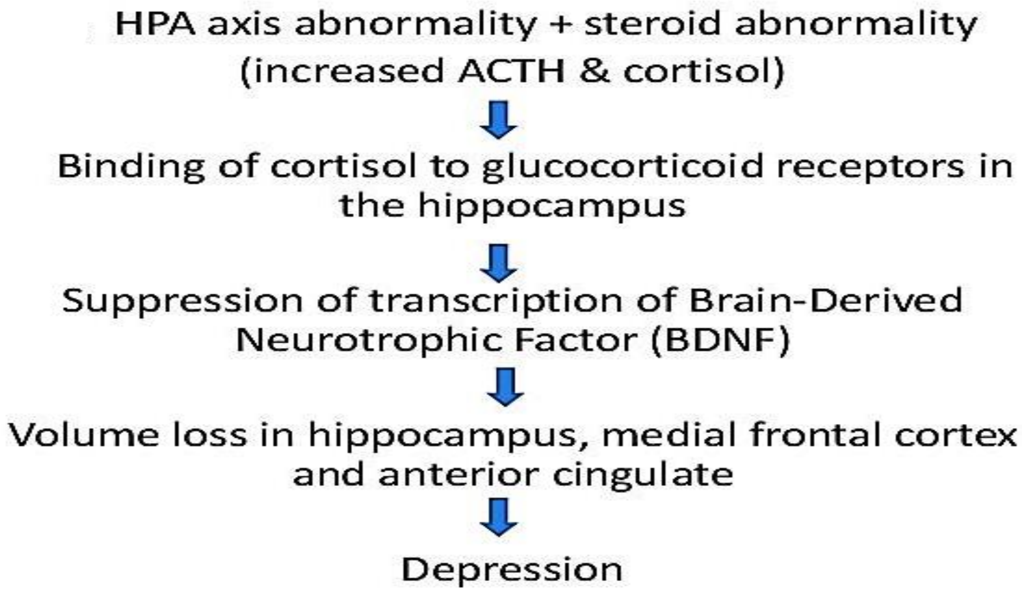
Monoamine Hypothesis: depression is related to a deficiency in the amount or function of cortical and limbic serotonin (5- HT), norepinephrine (NE), and dopamine (DA).



Neurotrophic hypothesis: Brain Derived growth factor (BNDF) promotes the growth and development of immature neurons including mono-aminergic neurons, enhances the survival and function of adult neurons. Low BNDF level may be responsible for loss of mono- aminergic neurons and loss of function or atrophy of hippocampus and other brain areas. Hippocampi lose its ability to inhibit CRF release by hypothalamus leading to increased release of glucocorticoids.

Neuroendocrine hypothesis:

Dexamethasone supression test doesn't reduce cortisol level in 50% of depression patient; indicates imbalance in stress HPA axis (hypothalamus-pituitory- adrenal gland axis). Dysregulation in HPA axis results in increased corticotropinc releasing factor (CRF) from hypothalamus (result of hippocampus atrophy), Enlarged adrenal gland and increased secretion of cortisol (glucocorticoids). Dysregulation in HPT axis (hypothalamus-pituitary- thyroid) creates thyroid hormone defiency, which may be seen in depression



DIAGNOSIS

Physical examination. Your doctor may do a physical exam and ask questions about your health. In some cases, depression may be linked to an underlying physical health problem.

Lab tests. For example, your doctor may do a blood test called a complete blood count or test your thyroid to make sure it's functioning properly.

Psychiatric evaluation. Your mental health professional asks about your symptoms, thoughts, feelings and behavior patterns. You may be asked to fill out a questionnaire to help answer these questions.

DSM-5. Your mental health professional may use the criteria for depression listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), published by the American Psychiatric Association.

SCHIZOPHRENIA

Schizophrenia is a serious mental disorder in which people interpret reality abnormally. Schizophrenia may result in some combination of hallucinations, delusions, and extremely disordered thinking and behavior that impairs daily functioning, and can be disabling.

Schizophrenia literally means "Fragmented Mind".

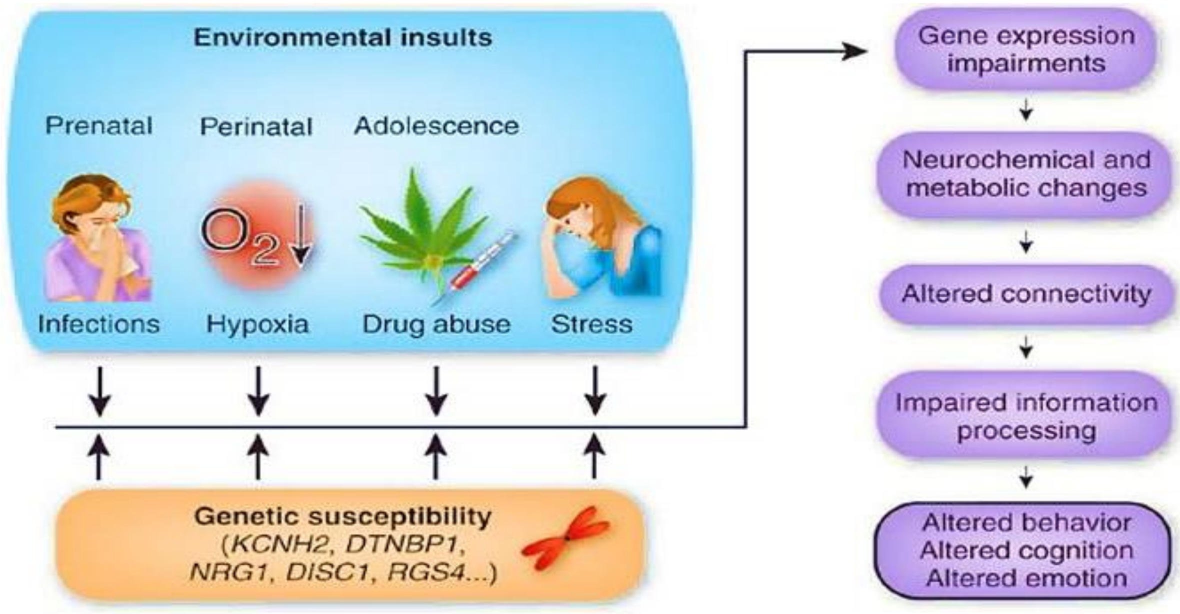
Schizophrenia is one of the most complex, chronic and challenging of psychiatric disorders that affects how a person thinks, feels, behaves.

It represents a heterogeneous syndrome of disorganized thoughts, delusions, hallucinations, and impaired psychosocial functioning.

People with schizophrenia require lifelong treatment. Early treatment may help get symptoms under control before serious complications develop and may help improve the long-term outlook

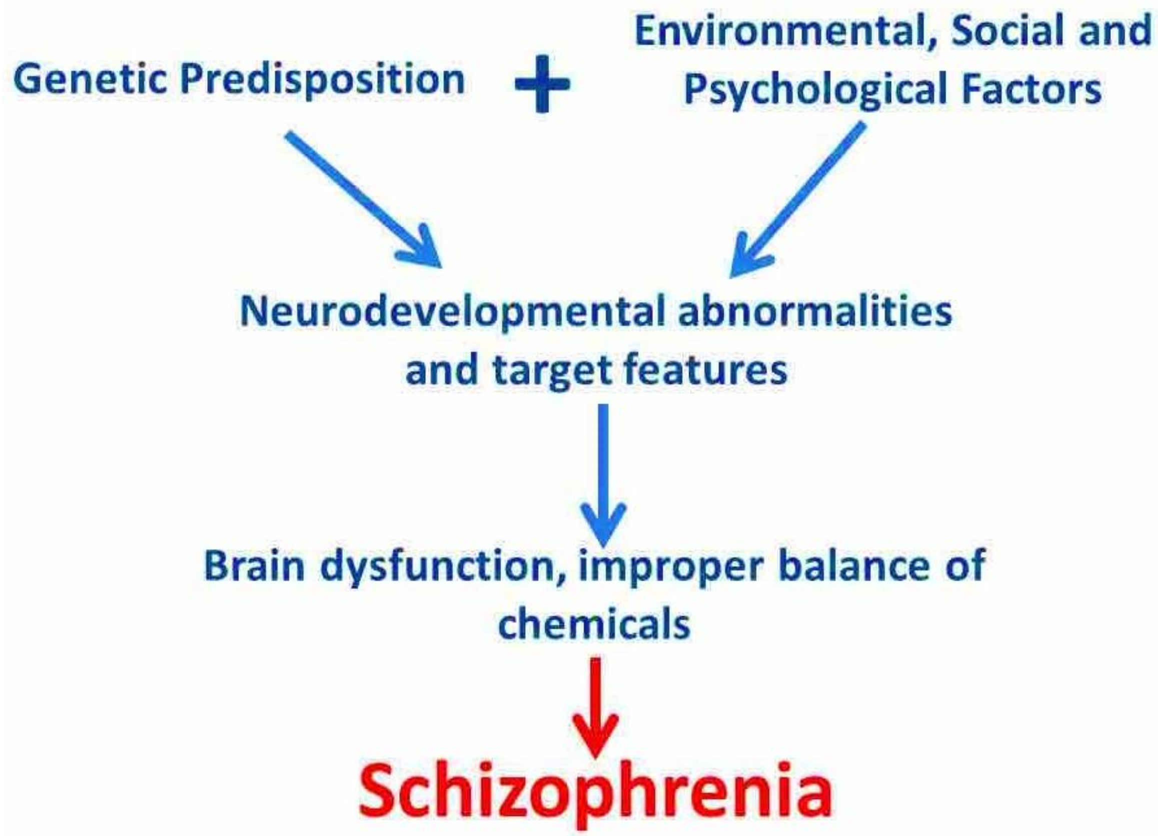
ETIOLOGY While many factors have been associated with developing schizophrenia—including genetics, early environment, neurobiology, and psychological and social processes—the exact cause of the disease is unknown.

Viral Infections and Immune Disorders: Schizophrenia may be triggered by environmental events, such as viral infections or immune disorders. For instance, babies whose mothers get the flu while they are pregnant are at higher risk of developing schizophrenia later in life. People who are hospitalized for severe infections are also at higher risk.



Genetics (Heredity): Scientists recognize that the disorder tends to run in families and that a person inherits a tendency to develop the disease. Similar to some other genetically-related illnesses, schizophrenia may appear when the body undergoes hormonal and physical changes.

The risk of developing schizophrenia is increases to approximately 10% if a first-degree relative has the illness and to 3% if a second-degree relative has the illness. If both parents have schizophrenia, the risk of producing a schizophrenic offspring increases to approx 40%



SIGNS & SYMPTOMS

Positive Symptoms

Delusion : False beliefs that are not based in reality

Hallucination: Involving seeing or hearing things that don't exist

Disorganized speech & thinking : Effective communication can be impaired and answers to questions may be partially or completely unrelated

Catatonia: Purposeless abnormal motor activity or aggressive behavior

Negative Symptoms

Flat effect: Reduced expression of emotions via facial expression or voice tone

Alogia: reduced speech

Avolition: Inability to begin & sustain activities

Anhedonia: Inability to experience pleasure

Asociality: Withdrawal from social contacts • Reluctance to perform everyday tasks

Cognitive Symptoms

Poor Executive Functioning: Unability to understand information to make decisions

Poor Working Memory: Unability to use information immediately after learning

TYPES

Paranoid schizophrenia: Suspicion of others; grand schemes of persecution at the root of their behaviour. Hallucinations, and more frequently delusions, are a prominent and common part of the illness.

Hebephrenic Schizophrenia: In this case the person is verbally incoherent and may have moods and emotions that are not appropriate to the situation. Hallucinations are not usually present.

Catatonic schizophrenia - In this case, the person is extremely withdrawn, negative and isolated, and has marked psychomotor disturbances. Rarer than other types. At risk for malnutrition, exhaustion or self-injury. Unusual movements, often switching between extremes of over- activity and stillness

Residual schizophrenia- In this case the person is not currently suffering from delusions, hallucinations, or disorganised speech and behaviour, but lacks motivation and interest in day-to-day living.

Schizoaffective disorder - symptoms of schizophrenia as well as mood disorder such as major depression, bipolar mania, or mixed mania.

Undifferentiated Schizophrenia- Conditions meeting the general diagnostic criteria for schizophrenia but not conforming to any of the above subtypes, or exhibiting the features of more than one of them without a clear predominance of a particular set of diagnostic characteristics

PATHOPHYSIOLOGY

Dopamine Hypothesis

Numerous **Positron Emission Tomography (PET)** studies have shown dopaminergic hyperactivity in the nucleus accumbens and dopaminergic hypofunction in the fronto temporal regions.

PET studies using D2-specific ligands provide data suggesting increased densities of D2 receptors in the nucleus accumbens.

PET studies assessing D1 function suggest that subpopulations of schizophrenics may have decreased densities of D1 receptors in the prefrontal cortex.

Thus positive symptoms are thought to result from overactivity in the mesolimbic dopaminergic pathway activating D2 receptors whereas negative symptoms may result from a decreased activity in the mesocortical dopaminergic pathway where D1 receptors predominate.

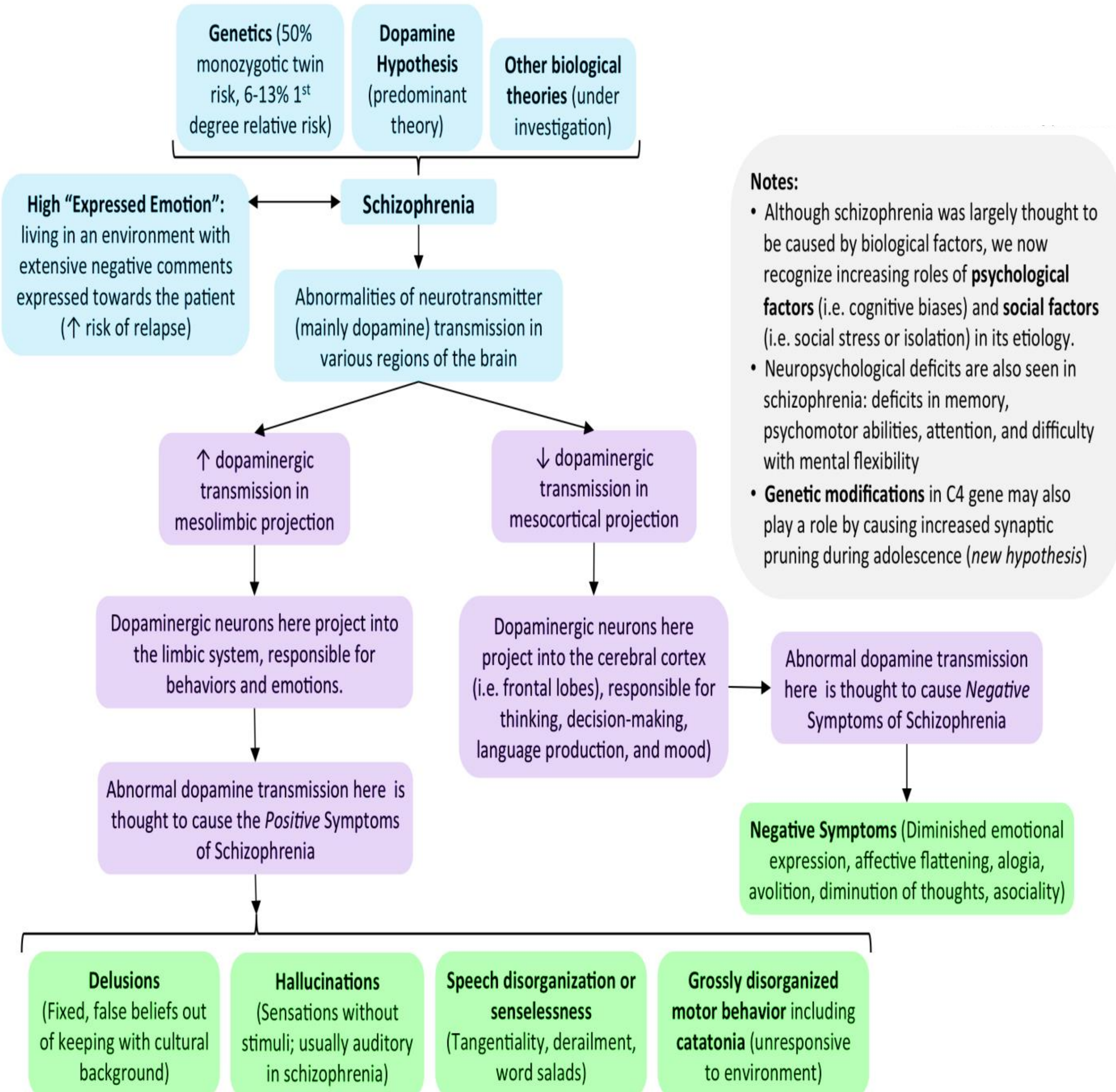
DIAGNOSIS

Medical History: A thorough medical history is the first step in the diagnosis of schizophrenia. This may be done to find other problems that could be causing symptoms and to check for any related complications.

Blood Tests & Imaging: A Complete Blood Count (CBC) test is helpful to monitor general health and rule out other conditions that may have been responsible for the symptoms. A blood test can provide accurate information about the involvement of recreational drugs. In some cases, certain imaging techniques such as Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) scan may aid in the diagnosis.

Psychiatric Evaluation : A doctor or mental health professional checks mental status by observing appearance, demeanor and asking about thoughts, moods and awareness. A person may be diagnosed if they have at least 2 of the following symptoms usually over a month :

Delusions, Hallucinations, Disorganised behaviour , Disorganised speech and thought processes, Negative symptoms, impaired normal function


Genetics (50% monozygotic twin risk, 6-13% 1st degree relative risk)
Dopamine Hypothesis (predominant theory)
Other biological theories (under investigation)
High "Expressed Emotion": living in an environment with extensive negative comments expressed towards the patient (↑ risk of relapse)
Schizophrenia
Abnormalities of neurotransmitter (mainly dopamine) transmission in various regions of the brain
↑ dopaminergic transmission in mesolimbic projection
↓ dopaminergic transmission in mesocortical projection
Dopaminergic neurons here project into the limbic system, responsible for behaviors and emotions.
Dopaminergic neurons here project into the cerebral cortex (i.e. frontal lobes), responsible for thinking, decision-making, language production, and mood)
Abnormal dopamine transmission here is thought to cause Negative Symptoms of Schizophrenia
Abnormal dopamine transmission here is thought to cause the Positive Symptoms of Schizophrenia
Negative Symptoms (Diminished emotional expression, affective flattening, alogia, avolition, diminution of thoughts, asociality)
Delusions (Fixed, false beliefs out of keeping with cultural background)
Hallucinations (Sensations without stimuli; usually auditory in schizophrenia)
Speech disorganization or senselessness (Tangentiality, derailment, word salads)
Grossly disorganized motor behavior including catatonia (unresponsive to environment)
Notes:
Although schizophrenia was largely thought to be caused by biological factors, we now recognize increasing roles of psychological factors (i.e. cognitive biases) and social factors (i.e. social stress or isolation) in its etiology.
Neuropsychological deficits are also seen in schizophrenia: deficits in memory, psychomotor abilities, attention, and difficulty with mental flexibility
Genetic modifications in C4 gene may also play a role by causing increased synaptic pruning during adolescence (new hypothesis)

GIT Disorder

PEPTIC ULCERS

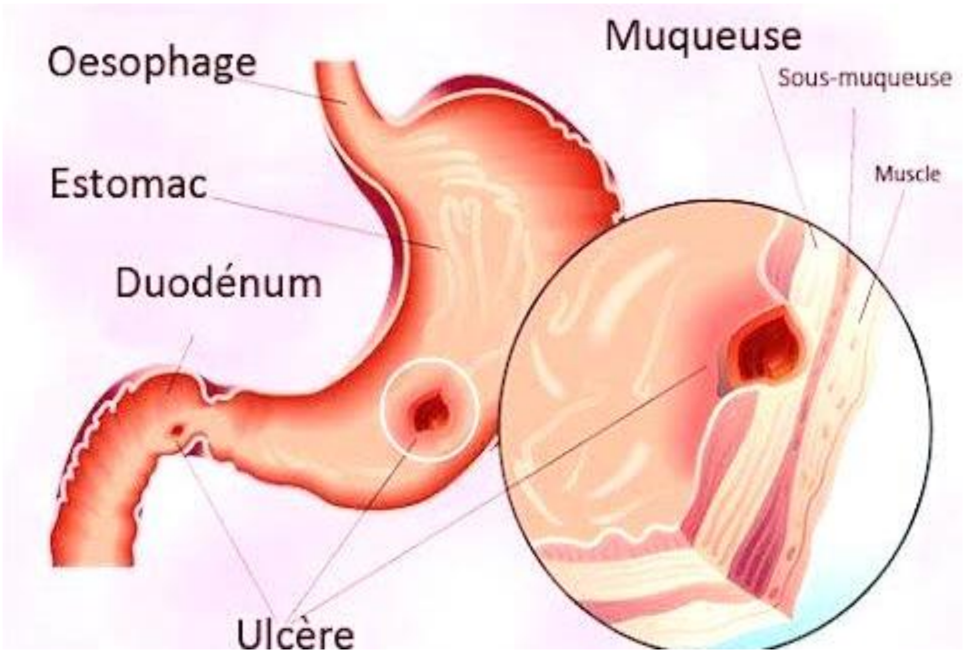
Peptic ulcer is a chronic lesion that occurs in any portion of the GIT (usually stomach) exposed to the aggressive action of acid-peptic juices.

At least 98 % of peptic ulcers are in the upper portion of the duodenum Peptic ulcer disease mainly comprises of painful sores or ulcers in the lining of the stomach or first part of the small intestine, called the duodenum

A peptic ulcer in the stomach is called a gastric ulcer. An ulcer in the duodenum is called a duodenal ulcer

It causes disruption of the mucosal integrity of the stomach, duodenum, or both caused by local inflammation, which leads to a well-defined mucosal defect Peptic ulcers are relapsing lesions that most often diagnosed in middle-aged to older adults

Duodenal ulcers are more frequent in patients with alcoholic cirrhosis, COPD and chronic renal failure.



Normally, the lining of the stomach and small intestines is protected against the irritating acids produced in the stomach. If this protective lining stops working correctly and the lining breaks down, it results in inflammation (gastritis) or an ulcer.

The imbalance between defensive mechanism and aggressive factors (gastric acid and pepsin and H. pylori)

Defensive mechanism include:

- Secretion of mucus by epithelial cells
- Secretion of bicarbonate which act as buffer
- Rapid gastric epithelial regeneration
- Mucosal blood flow to sweep away hydrogen ion

Aggressive factors:

- Secretion of gastric HCl from the parietal cells
- Secretion of pepsin
- Presence of H.pylori which survives in the gastric mucosal layer

Agents that increase the complications-

- NSAIDs drug therapy
- Cigarette smoking
- Alcohol
- Corticosteroids therapy

TYPES OF PEPTIC ULCER

1. **Acute Peptic Ulcers**
2. **Chronic Peptic Ulcers**

1. ACUTE PEPTIC ULCERS

There are multiple small mucosal erosions and is seen mostly in the stomach but occasionally involved duodenum.

CAUSES The causes of Acute peptic ulcers are:

- Psychological stress
- Physiological stress
- Drugs, such as aspirin, indomethacin and steroids
- Local irritants such as alcohol, coffee.

Pathogenesis

The mechanism of mucosal erosions in stress ulcers is not known clearly because actual hypersecretion of gastric acid is demonstrated in only cushing's ulcers occurring from intracranial conditions such as due to brain trauma and brain tumours

The gastric acid secretion in this case is normal or below normal. So, the possible hypothesis for genesis of stress ulcers are:-

»Depletion of the gastric mucous barrier rendering mucosa susceptible to attack by acid-pepsin secretion.

»Ischaemia induced hypoxic injury to the mucosal cell

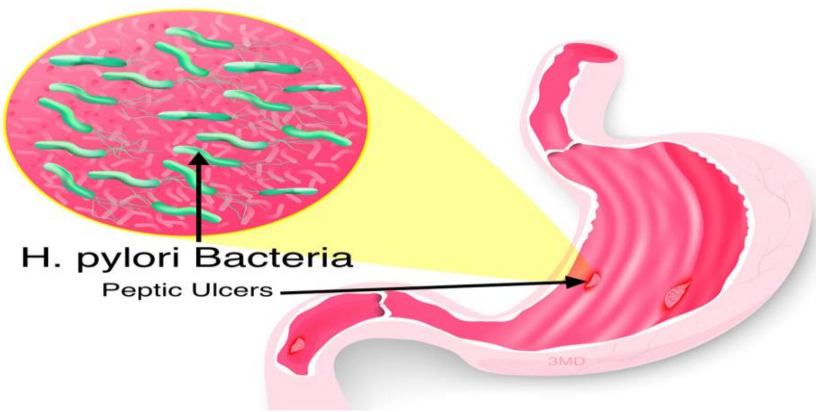
2. CHRONIC PEPTIC ULCERS (GASTRIC OR DUODENAL ULCERS)

Both of the gastric and duodenal ulcers are more common in males than in females. The incidence of duodenal ulcer is four times more than the gastric ulcers

CAUSES

The early cause of peptic ulcer disease is disturbance of normal protective mucosal barrier by acid-pepsin, resulting in digestion of the mucosa. Various causes which are responsible for the development of chronic peptic ulcers are given below

***Helicobacter Pylori*:** Persons infected with H. Pylori, develop duodenal ulcers in their life time, while gastric colonization by H. pylori never develop ulceration and remain asymptomatic.



Mucous secretions: The secretions those decrease the quality and quantity of the mucous protective barrier predisposes to the development of the peptic ulcer

Acid pepsin' seretions: Some levels of acid-pepsin secretions are also responsible for the development of gastric and duodenal ulcers

Dietary factors: Nutritional deficiencies have significant role in the development of peptic ulcers

Psychological factors: Psychological factors like psychological stress, fatigue and anxiety

Genetic factors: People with blood group 0' appear to be more prone to develop peptic ulcer than those with other blood groups

Miscellaneous: Duodenal ulcer occurs in association with various other conditions such as alcoholic cirrhosis chronic renal failure, cold and chronic pancreatitis.

SYMPTOMS

- Epigastric pain
- The pain tends to be worse at night and occurs 1 to 3 hrs after meals
- Nausea, Vomiting, Belching, Significant weight loss.
- Complications of hemorrhage occurs in one-third patients
- Feeling of fullness - unable to drink as much fluid
- Pain or discomfort in the upper abdomen
- Bloody or dark tarry stools

PATHOPHYSIOLOGY

***H.pylori* Induced Ulcer**

Gram negative bacteria produced heat shock proteins →Cytokines, histamine, lipopolysaccharides, certain enzymes Phospholipase Urease, protease, fucosidase etc. →Urease convert in acidic media urea into ammonia and carbon dioxide. →Ammonia itself cause destruction of mucosal lining → Ammonia cause infection of mucosal lining and ultimately inflammatory mediators release→Cytokines →Leukocytes adhesion and inflammatory reactions starts → Damage mucosa of GIT → Ulcer occurs

Drug Induced Ulcer

Drugs for example NSAIDS as aspirin (non selectively inhibit COX1 and COX2 in human body Arachidonic acid COX1,2 Prostaglandins → Controls gastric juice secretions →Damage mucosal lining lead to ulcer

Stress Induced Ulcer

In stress energy consumption increase so increase glycolysis which is usually done by cortisol hormone →This hormone inhibit phospholipase A2 → No arachidonic acid formation no prostaglandin increase gastric juice secretions → Cause ulcer

Steroids Induced Ulcer

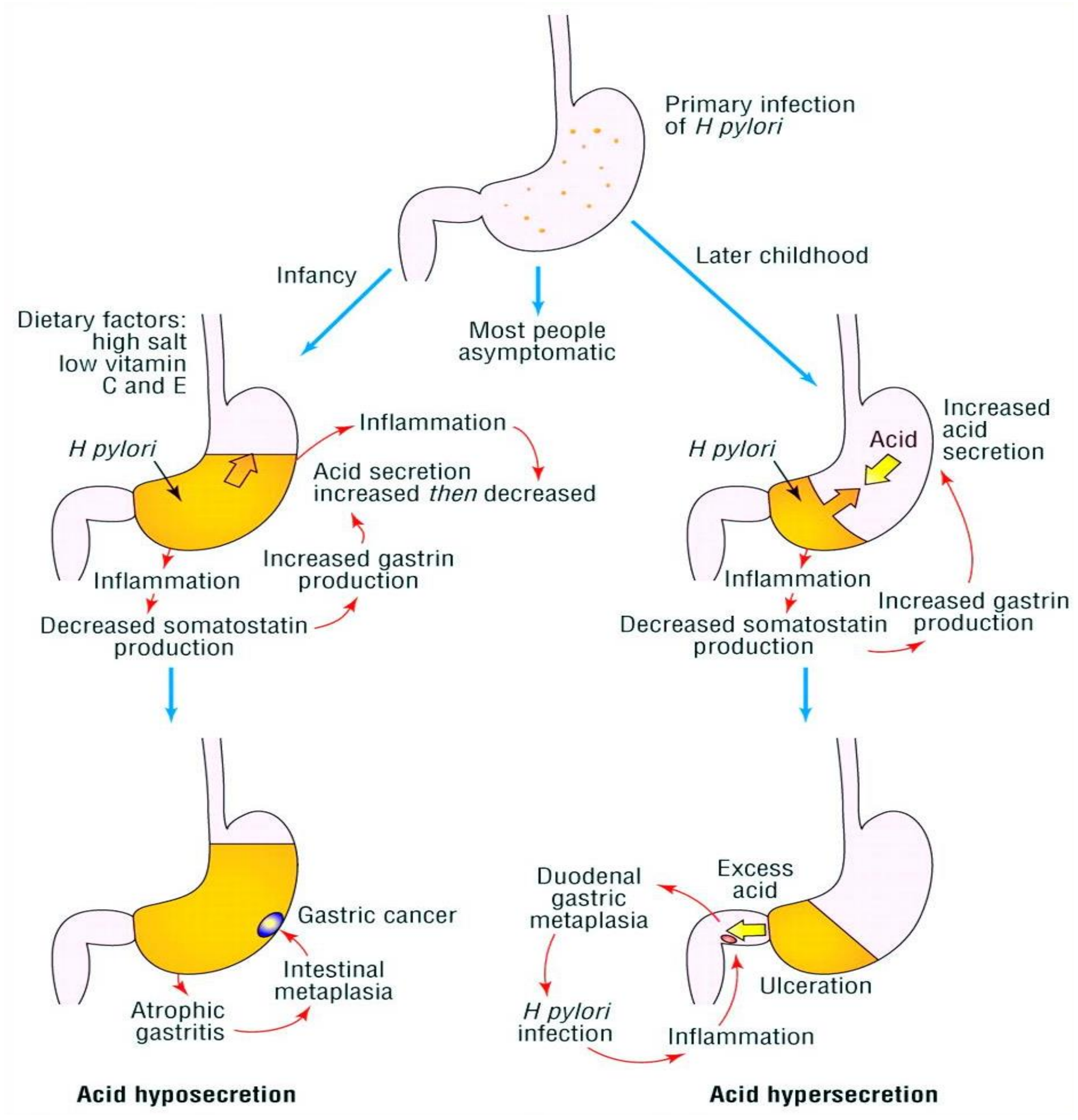
Steroids acts on cell membrane (phospholipid) → Inhibit phospholipase →Inhibits arachidonic acid no prostaglandins and damaging of mucosal lining

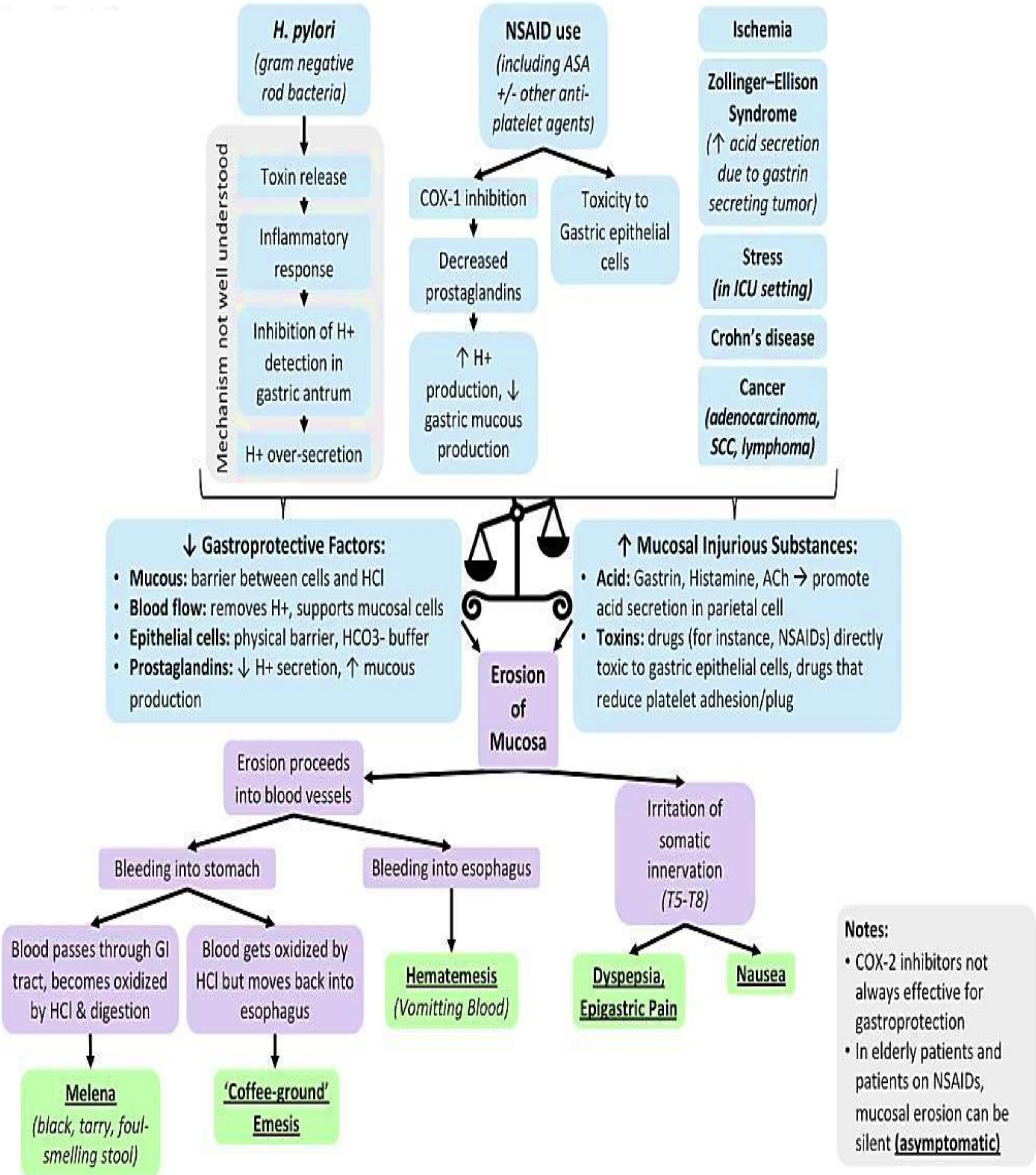
Ulcer Due to Genetic Defect

Rare genetics occurs some time having blood group O positive the size of parietal cell is increase → Increase cell demand as HCL secretions increase → Cause destruction of mucosal lining leading towards ulcer

ZES(Zollinger-Ellison Syndrome)

In this syndrome tumor of goblet cell occurs → Abnormal mucus secretions(gastrin acts on parietal cells) →Increase secretions of gastric juice → Mucosal lining damage





H. pylori (gram negative rod bacteria)
Toxin release
Inflammatory response
Inhibition of H+ detection in gastric antrum
H+ over-secretion
Mechanism not well understood
NSAID use (including ASA +/- other anti-platelet agents)
COX-1 inhibition
Decreased prostaglandins
↑ H+ production, ↓ gastric mucous production
Toxicity to Gastric epithelial cells
Ischemia
Zollinger–Ellison Syndrome (↑ acid secretion due to gastrin secreting tumor)
Stress (in ICU setting)
Crohn's disease
Cancer (adenocarcinoma, SCC, lymphoma)
↓ Gastroprotective Factors:
• Mucous: barrier between cells and HCl
• Blood flow: removes H+, supports mucosal cells
• Epithelial cells: physical barrier, HCO3- buffer
• Prostaglandins: ↓ H+ secretion, ↑ mucous production
↑ Mucosal Injurious Substances:
• Acid: Gastrin, Histamine, ACh → promote acid secretion in parietal cell
• Toxins: drugs (for instance, NSAIDs) directly toxic to gastric epithelial cells, drugs that reduce platelet adhesion/plug
Erosion of Mucosa
Erosion proceeds into blood vessels
Irritation of somatic innervation (T5-T8)
Bleeding into stomach
Bleeding into esophagus
Blood passes through GI tract, becomes oxidized by HCl & digestion
Blood gets oxidized by HCl but moves back into esophagus
Hematemesis (Vomitting Blood)
Dyspepsia, Epigastric Pain
Nausea
Melena (black, tarry, foul-smelling stool)
'Coffee-ground' Emesis
Notes:
• COX-2 inhibitors not always effective for gastroprotection
• In elderly patients and patients on NSAIDs, mucosal erosion can be silent (asymptomatic)

DIAGNOSIS OF PEPTIC ULCER

Radiological Diagnosis: Barium x-ray or upper GI series is a widely used for diagnosis. Barium x-ray is difficult to analysis and less sensitive and accurate.

Laboratory test: – Noninvasive urea breath test. – Patient with refractory or recurrent peptic ulcer may have underlying H. pylori infection, histopathology investigation may req. – Serologic test for detecting H. pylori (levels of IgG and IgA ELISA test) – Stool antigen test for non-invasive detecting the presence of H. pylori.

Blood test: To check for the presence of H pylori.

Breath test: To check H pylori infection (bacterial infection).

Stool test: To check H pylori infection (bacterial infection).

Endoscopy: Endoscopy of the upper stomach is performed to inspect the stomach.

Upper gastroinstestinal series: To check for ulceration in the digestive tract.

Biopsy: Biopsy sample of the intestinal lining is examined to rule out cancer.

Very short answer questions (02 marks)

1. Define anemia.
2. Complications of Diabetes mellitus.
3. What is a peptic ulcer?
4. What is the most common type of anemia?
5. Define sickle cell anemia
6. Explain risk factor involved in aplastic anemia
7. How serious id autoimmune hemolytic anemia
8. What is Diabetes?
9. What is hypothyroidism?
10. Etiology of goiter and graves
11. What is Thyroxin?
12. Define Sex hormones

13. What is Hirsutism?
14. Define menopause/premenopausal
15. Define erectile dysfunction
16. What is Gynecomeastia?
17. What are the causes of epilepsy?
18. Is depression a mental illness?
19. What is Sessional depression?
20. What are the neurotransmitters involved in the pathophysiology of depression.
21. What are the positive and negative symptoms of schizophrenia?
22. What are the causes of PDs?
23. What kind of diseases is Parkinson's?
24. What are the early symptoms of Alzheimer disease?
25. What is dementia?
26. Define Stroke and its type
27. What is the cause of Peptic Ulcer?
28. What are the three type of peptic Ulcer?

Short answer questions (05 marks)

1. Describe the pathogenesis of type 2-diabetes Mellitus.
2. Describe iron deficiency anemia.
3. Discuss about the pathophysiology of sickle cell anemia.
4. Describe the Thalassemia.
5. Write briefly about Aplastic anemia.
6. Enlist thyroid disorders
7. Describe the Type-T DM
8. Explain the pathophysiology and diagnosis of Type-II DM
9. Explain goiter in detail
10. Describe about Graves disorder.
11. Write a Short note on sex hormones disorders.
12. Describe and classify epilepsy.

13. Write a note on:
    a) Parkinson's
    b) Stroke
    c) Alzheimer's
    d) Epilepsy
    e) Depression
14. Discuss about the pathophysiology of Peptic ulcer

Long answer questions (10 marks)

1. What is anemia? Classify various types of anemia. Discuss about symptoms and etiology of various type of anemia.
2. Describe the Iron deficiency anemia and sickle cell anemia.
3. Describe the megaloblastic anemia and folic acid deficiency anemia.
4. Describe Type-I and Type-II DM.
5. Discuss the pathophysiology, etiology and diagnosis of Hyperthyroidism.
6. What are sex hormones? Discuss anyone sex hormones disorders in details.
7. Write a note on erectile dysfunction.
8. Discuss the pathophysiology, etiology and diagnosis Alzheimer's
9. Discuss the pathophysiology, etiology of Parkinson's diseases
10. Discuss the symptoms, pathophysiology and etiology Schizophrenia
11. Write a detail note on epilepsy.
12. Discuss the pathophysiology, etiology and diagnosis of Peptic Ulcer