Unit – III
Haematological Diseases

Presented By

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ANAEMIA

- Anaemia is defined as a decrease in the total amount of red blood cells (RBCs) or haemoglobin concentration in the blood below the lower limit of the normal range.
- In adult lower extreme of the normal haemoglobin is taken as 13.0 - 14.0 g/dl (130-140 g/L) for males and 12.0-13.0 g/dl (120-130 g/L) for females.
- In anaemia , the body does not get enough oxygen rich blood. As a result, the person may feel tired and have other symptoms.
- With severe or long lasting anemia, the lack of oxygen in the blood can damage the vital tissues of heart, brain & other organ of the body.

Types

- 1. Iron deficiency anemia
- 2. Megaloblastic (Vitamin B12 deficiency anemia Folic acid-deficiency anemia)
- 3. Haemolytic anemia
- Thalassaemia
- Sickle cell anemia
- Hereditary acquired anemia
- 4. Hemophilia

Risk factors

Major Risk factors for Anemia

- A diet that is low in iron, vitamins or minerals.
- Blood loss from surgery or an injury.
- Long term or serious illnesses, such as kidney disease, cancer, diabetes, HIV/AIDS, Inflammatory bowel disease, heart failure and thyroid disease.
- Malfunctions of liver & spleen.

Symptoms

- Pallor- most common sign (paleness or whiteness) which may be seen in mucous membranes, conjunctivae & skin.
- Central nervous system: Faintness(Weakness & tired), headache, drowsiness, numbness (loss of feeling in a part of the body).
- Ocular: Retinal haemorrhages may occur
- Reproductive system: Menstrual disturbances such as amenorrhoea & menorrhagia.
- Renal System: Mild proteinuria and impaired concentrating capacity of the kidney may occur in severe anemia.
- Gastrointestinal systems: Anorexia(Eating disorder), nausea(feeling an urge to vomit), constipation(when waste or stool moves too slowly through the digestive tract) & weight loss may occur.

IRON DEFICIENCY ANEMIA

- IDA is the most common form of anemia occurs when the body does not have adequate iron.
- Also occur as a result of blood as in menstrual blood loss, pregnancy, gastrointestinal bleeding (peptic ulcer, inflammatory bowel disease and cancer).
- Low levels of serum iron and ferritin (iron storing protein) in blood.
- Iron is the central atom present in the haemoglobin in ferrous state and is a crucial element for RBCs formation.
- Normal daily requirement of iron intake in men is about 1-2 mg and 3 mg for women.

SYMPTOMS

- Fatigue
- Chest pain
- Shortness of breath
- Pale colour of skin
- Tachycardia
- Headache
- Brittle nails

Pathophysiology

- Iron deficiency anemia occurs in three stages:

1. Storage iron deficiency
2. Iron deficient erythropoiesis
3. Iron deficiency anemia

1. Storage iron deficiency:- Initially during blood loss, body preferentially utilizes all the iron it has stored in the liver, bone marrow and other organs for accelerated erythropoiesis (red blood cell (erythrocyte) production).

- Once the stored iron is depleted, erythropoiesis and production of myoglobin (iron containing proteins) become limited, leading to an IDA.

2. Iron deficient erythropoiesis:-

- Iron is a constituent of haemoglobin and rate limiting for erythropoiesis. If glycoprotein hormone (erythropoietin) is present without sufficient iron, the RBCs production will be abnormal.
- The morphological changes in erythrocyte with iron deficiency imitate severely hampered haemoglobin synthesis and are characterized by Hypochromasia (increase in central pallor) and Microcytosis (RBCs are unusually).

3. Iron deficiency anemia:-

- Iron is required for the formation of Haem moiety in haemoglobin, myoglobin and haem enzymes (cytochromes).

- In the deficiency, stored iron are used up and the patients becomes iron deficient. Poor iron stores result in impaired haemoglobin synthesis which causes decreased oxygen carrying capacity.

MEGALOBLASTIC ANEMIA

- Megaloblastic anemia is a red blood cell disorder due to the inhibition of DNA synthesis during erythropoiesis.
- This disorder caused by the partial formation of RBC resulting in large number of immature and incompletely developed cells.
- These RBCs do not function like healthy RBCs and crowd out healthy cells, leading to anemia.
- These cells are underdeveloped and they also have a short life expectancy.

Causes for megaloblastic anemia

- Hypovitaminosis especially deficiency of vitamin B12.
- Folic acid deficiency.
- Direct intervention of DNA synthesis by HIV infections.
- Due to myelodysplastic disorder (group of cancers in which immature blood cells in the bone marrow).

Vitamin B12 deficiency anemia

- Also called Hypocobalaminemia.
- Refers to low count of RBCs due to lack of vitamin B12 or cobalamin.
- Cobalamin is a complex molecule homologous to haem with a cobalt atom instead of iron at its centre.
- Cobalamin deficiency is generally attributable to impairment of DNA synthesis in bone marrow.
- Due to lack of vitamin B12, body cannot make enough healthy RBCs.

Folic acid deficiency anemia

- Occurs because of problems with absorbing vitamins or a diet lacking in folic acid.
- Humans are unable to make folate endogenously due to unavailability of PABA(Para-aminobenzoic acid)
- Folic acid is required for the purine synthesis for DNA.
- Thus folic acid deficiency ultimately leads to impaired DNA synthesis.

Symptoms

- Extreme numbness (lack of sensation).
- Tender tongue (inflamed taste buds).
- Diarrhoea
- Loss of appetite
- Muscle weakness
- Fast heart beat

Pathophysiology

- Megaloblastic anemia results from defect/ inhibition in DNA synthesis in rapidly dividing cells during RBCs production.
- RNA and protein synthesis are also impaired but to a lesser extent.
- Due to impairment in DNA synthesis, the cell cycle cannot progress from growth stage G2(The last part of interphase) to mitosis stage M(separation of the chromosomes).
- This impairment leads to continuing unbalanced and immature growth of RBCs.
- These immature and dysfunctional RBCs are known as megaloblasts.

HAEMOLYTIC ANEMIA

- Hemolytic anemia is a form of anemia due to hemolysis (abnormal breakdown of RBCs) either in the blood vessels (intravascular hemolysis).

- Treatment depends on the cause and nature of the breakdown.

- This is a condition in which RBCs are demolished(Destroy) and eliminated from blood stream before their normal life span 120 days.

Symptoms

- Fatigue
- Shortness of breath
- Pallor
- Heart failure
- But in addition, the breakdown of red cells leads to jaundice
- Increases the risk of particular long-term complications, such as gallstones and pulmonary hypertension.

CAUSES

- Defects of red blood cell membrane production.

- Defects in hemoglobin production: (as in thalassemia, sickle-cell disease and congenital dyserythropoietic anemia).

Treatment

- Symptomatic treatment can be given by blood transfusion, if there is marked anemia. In cold hemolytic anemia there is advantage in transfusing warmed blood.
- In severe immune-related hemolytic anemia, steroid therapy is sometimes necessary.
- In steroid resistant cases, consideration can be given to rituximab or addition of an immunosuppressant (azathioprine, cyclophosphamide).
- Association of methylprednisolone and intravenous immunoglobulin can control hemolysis in acute severe cases.
- Sometimes splenectomy can be helpful where extravascular hemolysis (i.e., most of the red blood cells are being removed by the spleen).

Types of Haemolytic Anemia

- Congenital or hereditary anemia
- Sickle cell anemia
- Thalassemia

Sickle cell anemia

- This is a blood disorder inherited from a person's parents in which body produces abnormal haemoglobin. This leads to sickle or crescent shape of RBCs.
- Sickle cell disease occurs when a person inherits two abnormal copies of the haemoglobin gene, one from each parent. This gene occurs in chromosome 11.
- Several subtypes exist, depending on the exact mutation in each haemoglobin gene. An attack can be set off by temperature changes, stress, dehydration.
- It can also harm organs, muscles, and bones.

Treatment

- Treatment might include antibiotics, vitamins, blood transfusions, pain-relieving medicines, other medications and possibly surgery, such as to correct vision problems or to remove a damaged spleen.

PATHOPHYSIOLOGY

- Normal RBCs are quite elastic, which allows the cells to deform to pass through capillaries.
- In sickle cell disease, low oxygen tension promotes red blood cell sickling and decrease the cell's elasticity.
- These cells fail to return to normal shape when normal oxygen tension is restored.
- As a consequence, these rigid blood cells are unable to deform as they pass through narrow capillaries, leading to vessel occlusion and ischemia.
- Healthy RBCs typically function for 90–120 days, but sickled cells only last 10–20 days.

Congenital or hereditary anemia

- Congenital or birth defects.
- Congenital dyserythropoietic anemia (CDA) is a rare blood disorder, similar to the thalassemias.
- CDA is one of many types of anemia, characterized by ineffective erythropoiesis, and resulting from a decrease in the number of red blood cells (RBCs) in the body and a less than normal quantity of hemoglobin in the blood.

THALASSEMIA

- Thalassemia is an inherited (i.e., passed from parents to children through genes) blood disorder caused when the body doesn't make enough hemoglobin.
- It is an inherited autosomal recessive blood disorder, which is caused by missing or variant genes, that interferes with process of formation of normal haemoglobin.
- Abnormal haemoglobin results inappropriate oxygen transport and leads to destruction of RBCs.

SYMPTOMS

- Iron overload: Too much iron can result in damage to the heart, liver.
- Bone deformities: Abnormal bone structure, especially in the face and skull. Bone marrow expansion also makes bones thin, increasing the risk of broken bones.
- Enlarged spleen: The spleen aids in fighting infection and filters unwanted material, such as old or damaged blood cells.
- Slowed growth rates: anemia can cause a child's growth to slow.
- Heart problems: congestive heart failure and abnormal heart rhythms, may be associated with severe thalassemia.

TREATMENT

- Blood Transfusions. Transfusions of red blood cells are the main treatment for people who have moderate or severe thalassemias.
- Iron Chelation Therapy. Doctors use iron chelation therapy to remove excess iron from the body. Two medicines are used for iron chelation therapy: Deferoxamine and Deferasirox.
- Folic Acid Supplements.
- Blood and Marrow Stem Cell Transplant.

Haemophilia (A Royal Disease)

- Haemophilia (A Royal Disease)
- Haemophilia is a mostly inherited genetic disorder that impairs the body's ability to make blood clots, a process needed to stop bleeding.
- This results in people bleeding longer after an injury, easy bruising, and an increased risk of bleeding inside joints or the brain.
- Those with a mild case of the disease may have symptoms only after an accident or during surgery.
- Bleeding into a joint can result in permanent damage while bleeding in the brain can result in long term headaches, seizures, or a decreased level of consciousness.

Types of Haemophilia

- There are two main types of haemophilia:
- Haemophilia A, which occurs due to not enough clotting factor VIII, and

- Haemophilia B, which occurs due to not enough clotting factor IX.

Treatment and Prevention

- There is no long-term cure. Treatment and prevention of bleeding episodes is done primarily by replacing the missing blood clotting factors.
- Factor VIII is used in haemophilia A and factor IX in haemophilia B. Factor replacement can be either isolated from human blood serum.
- Desmopressin (DDAVP) may be used in those with mild haemophilia A.
- Tranexamic acid or epsilon aminocaproic acid may be given along with clotting factors to prevent breakdown of clots.
- Pain medicines, steroids, and physical therapy may be used to reduce pain and swelling in an affected joint.

UNIT – III
DIABETES MELLITUS

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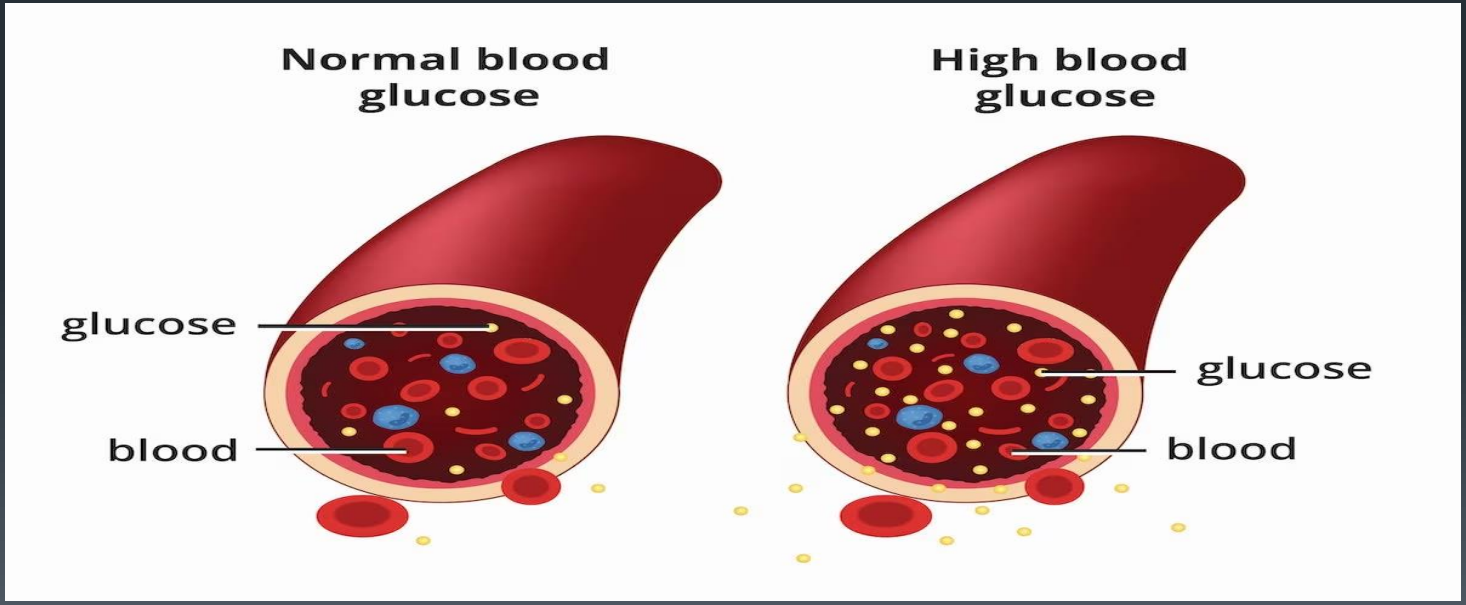
DIABETES MELLITUS

- As per the WHO, diabetes mellitus (DM) is defined as a metabolic diseases characterized by high levels of glucose in the blood (hyperglycemia) resulting from defects in insulin secretion, insulin action, or both.



Condition	Fasting blood sugar test	Glucose tolerance test	A1C test
Diabetes	126 mg/dl or above	200 mg/dl or above	6.5% or above
Prediabetes	100-125 mg/dl	140-199 mg/dl	5.7 – 6%
Normal	99 mg/dl or below	140 mg/dl or below	Below 5-7%

TYPE 1 DM

- Your body doesn’t make insulin.
- It constitutes about 10% cases of T1DM.
- Children and young adults are more likely to be diagnosed with T1DM.

- Subtype 1A (immune-mediated) DM characterized by autoimmune destruction of β-cells which usually leads to insulin deficiency.

- Subtype 1B (idiopathic) DM characterized by insulin deficiency with tendency to develop ketosis but these patients are negative for autoimmune markers.

TYPES

1. TYPE 1 DIABETES MELLITUS (10%) • (earlier called Insulin-dependent, or juvenile-onset diabetes).

- Type IA DM: Immune-mediated
- Type IB DM: Idiopathic

2. TYPE 2 DIABETES MELLITUS (90%) • (earlier called non-insulin-dependent, or maturity-onset diabetes

3. GESTATIONAL DIABETES MELLITUS (4%)

TYPE 1 DM

- Your body doesn’t make insulin.
- It constitutes about 10% cases of T1DM.
- Children and young adults are more likely to be diagnosed with T1DM.

- Subtype 1A (immune-mediated) DM characterized by autoimmune destruction of β-cells which usually leads to insulin deficiency.

- Subtype 1B (idiopathic) DM characterized by insulin deficiency with tendency to develop ketosis but these patients are negative for autoimmune markers.

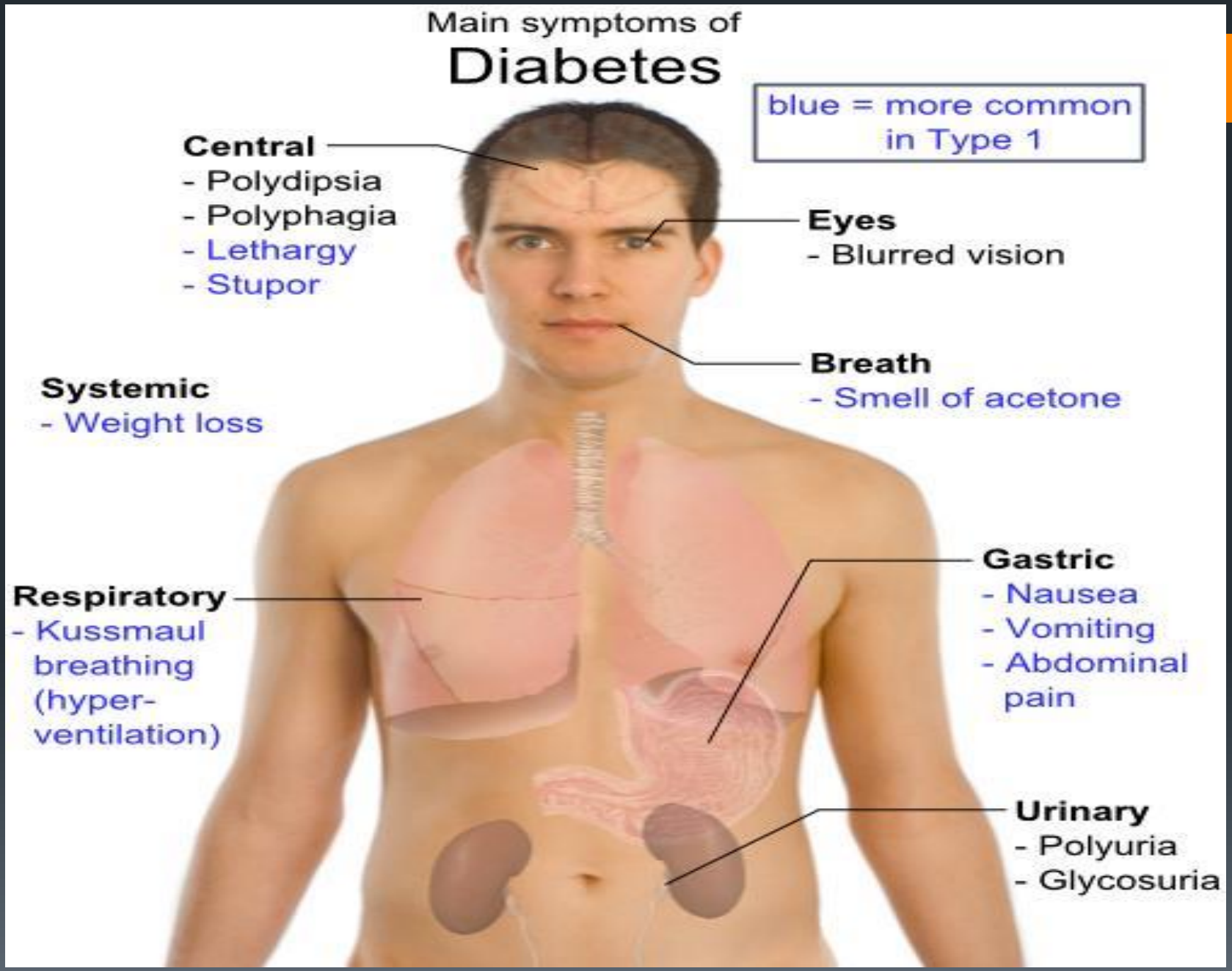
TYPE 2 DM

- Your body cell can’t use the insulin it makes(insulin resistant) or doesn’t make enough insulin.
- This type comprises about 90% cases of DM.
- It often occurs later in a client’s life due to obesity, inactivity, and hereditary.

GESTATIONAL DM

- About 4% pregnant women develop DM due to metabolic changes during pregnancy.
- Although they revert back to normal glycaemia after delivery.

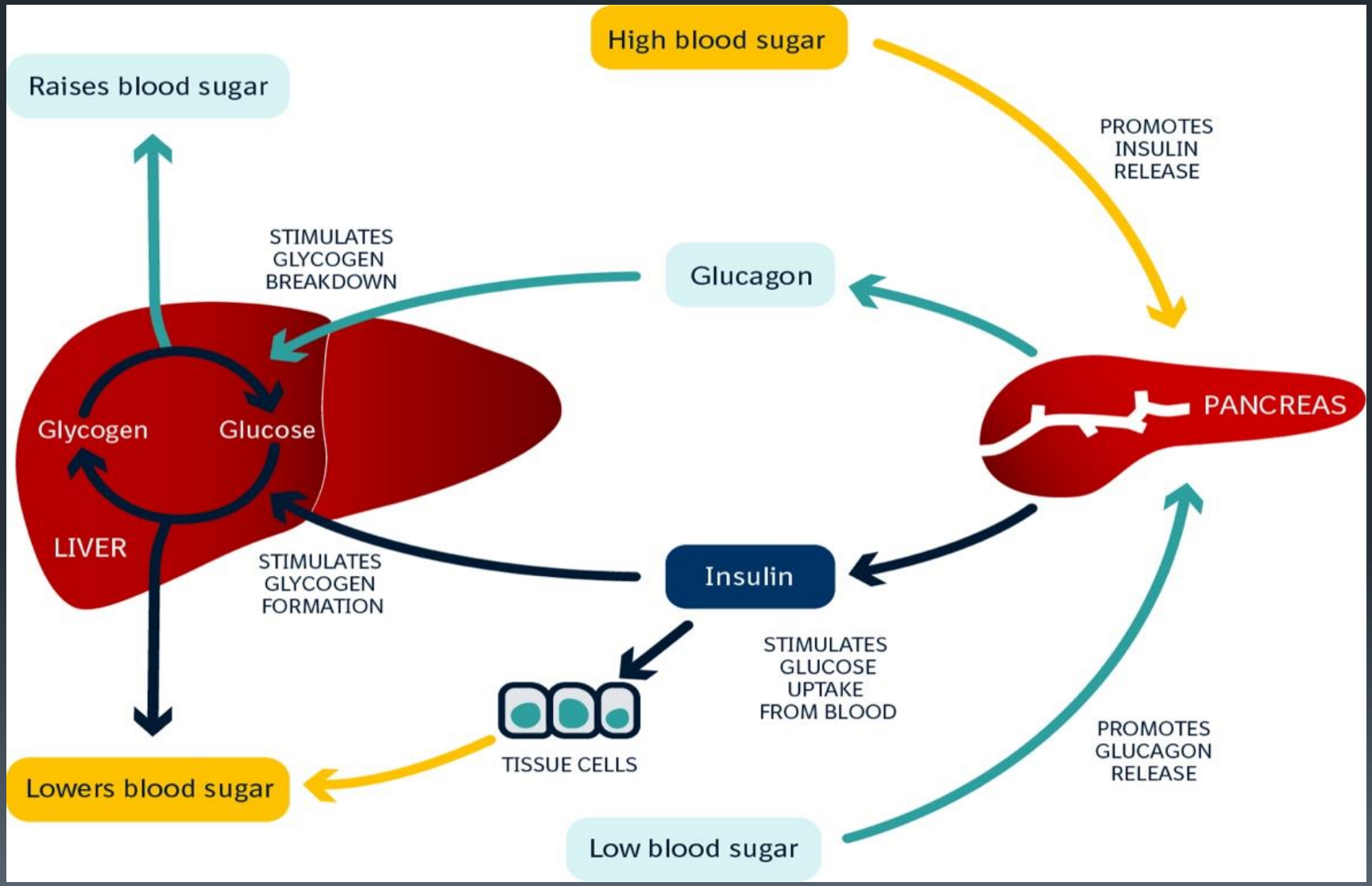
Comparison of type 1 and 2 diabetes		
Feature	**Type 1 diabetes**	**Type 2 diabetes**
Onset	Sudden	Gradual
Age at onset	Any age (mostly young)	Mostly in adults
Body habitus	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, decreased or increased
Concordance in identical twins	50%	90%
Prevalence	Less prevalent	More prevalent - 90 to 95% of U.S. diabetics


Main symptoms of
Diabetes
blue = more common in Type 1
Central
- Polydipsia
- Polyphagia
- Lethargy
- Stupor
Eyes
- Blurred vision
Breath
- Smell of acetone
Systemic
- Weight loss
Respiratory
- Kussmaul breathing (hyper-ventilation)
Gastric
- Nausea
- Vomiting
- Abdominal pain
Urinary
- Polyuria
- Glycosuria

COMPLICATIONS

- All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20)
- The major long-term complications relate to damage to blood vessels.
- Diabetes doubles the risk of cardiovascular disease
- About 75% of deaths in diabetics are due to coronary artery disease.
- Other "macrovascular" diseases (stroke - change in how blood flows through the brain).
- The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves.

PATHOPHYSIOLOGY



PATHOPHYSIOLOGY

- General Insulin is the principal hormone that regulates the uptake of glucose from the blood into cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the IGF-1 (Insulin-like growth factor – 1).

- Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all forms of diabetes mellitus.

- The body obtains glucose from three main places:
- The intestinal absorption of food
- The breakdown of glycogen, the storage form of glucose found in the liver
- Gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body.

- Insulin plays a critical role in balancing glucose levels in the body:
- It can inhibit the breakdown of glycogen or the process of gluconeogenesis.
- It can stimulate the transport of glucose into fat and muscle cells.
- It can stimulate the storage of glucose in the form of glycogen.

- Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating.

- Lower glucose levels result in decreased insulin release from the beta cells and results in the breakdown of glycogen to glucose.

- This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin.

- If the amount of insulin available is insufficient If cells respond poorly to the effects of insulin If the insulin itself is defective.
- Then glucose will not be absorbed properly by the body cells.
- The net effect is persistently high levels of blood glucose, poor protein synthesis, and break down of fat storage
- Acidosis.

- When the glucose concentration in the blood remains high over time, the kidneys will reach a threshold of reabsorption

↓

Glycosuria.

↓

- This increases the osmotic pressure of the urine ⟶polyuria increased fluid loss

↓

- Lost blood volume will be replaced osmotically from water held in body cells and other body compartments

↓

- dehydration

↓

- polydipsia

MANAGEMENT OR TREATMENT

- Good nutrition
- Regular exercise
- Diet control to maintain blood pressure.
- Medications
- Surgery
- Pancreas transplant
- kidney transplantation
- Weight loss surgery

UNIT – III
PEPTIC ULCER

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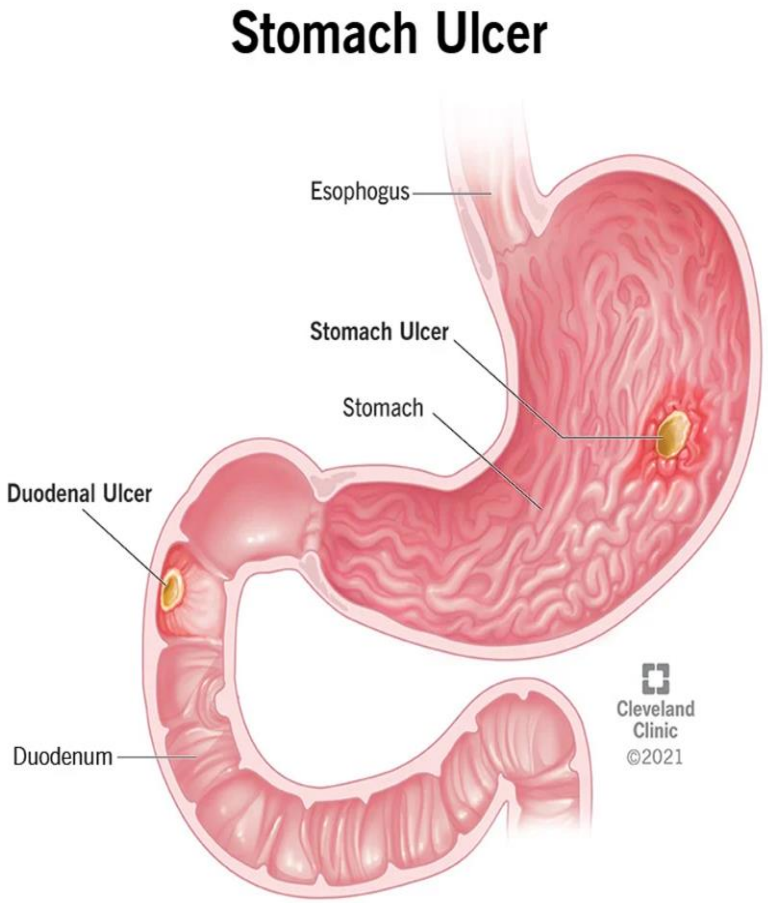
Introduction

Peptic ulcer disease is a condition in which painful sores or ulcers develop in the lining of the stomach or the first part of the small intestine (the duodenum)



Types of peptic ulcer

i. Esophageal ulcer

ii. Duodenal ulcer

iii. Gastric ulcer

Symptoms

- ✓ Symptoms of peptic ulcer very with location of the ulcer and the patient age.
- Abdominal discomfort/pain
- Nausea (feeling of vomit)
- Water brash (when an excessive(large) amount of saliva and mixes with stomach acids)
- Loss of appetite and weight loss
- Hematemesis (vomiting of blood) Rarely(small amount)

Complications of peptic ulcer

* Gastrointestinal bleeding (Sudden large bleeding can be life threatening)
* Cancer (Helicobacter pylori as the etiological factor making it 3-6 times likely to develop stomach cancer)
* Perforation (hole in the wall)

PATHOPHYSIOLOGY OF PEPTIC ULCER

H. pylori INDUCED ULCER (Helicobacter pylori bacteria)

* Gram negative bacteria produced heat shock proteins

↓

* Cytokines, histamine, lipopolysaccharides

↓

* 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

STEROIDS INDUCED ULCER

* Steroids (corticosteroids) acts on cell membrane (phospholipid)

↓

* Inhibit phospholipase

↓

* Inhibits arachidonic acid no prostaglandins and damaging of mucosal lining

Diagnosis of peptic ulcer

- **Radiological Diagnosis:**
  - Barium x-ray or upper GI series is a widely used for diagnosis.

- **Laboratory test:**
  - Serologic test for detecting H. pylori
  - Stool antigen test for non-invasive detecting the presence of H. pylori

- **Endoscopic diagnosis**

Treatment

* Proton pump inhibitors (PPI): These drugs reduce acid, which allows the ulcer to heal.(omeprazole and esomeprazole)
* Histamine receptor blockers (H2 blockers): These drugs also reduce acid production (cimetidine and famotidine)
* Antibiotics: These medications kill bacteria. (amoxicillin and ciprofloxacin)


THANK
YOU!