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UNIT – II

DISORDERS OF CARBOHYDRATE METABOLISM

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Disorders Of Carbohydrate Metabolism:

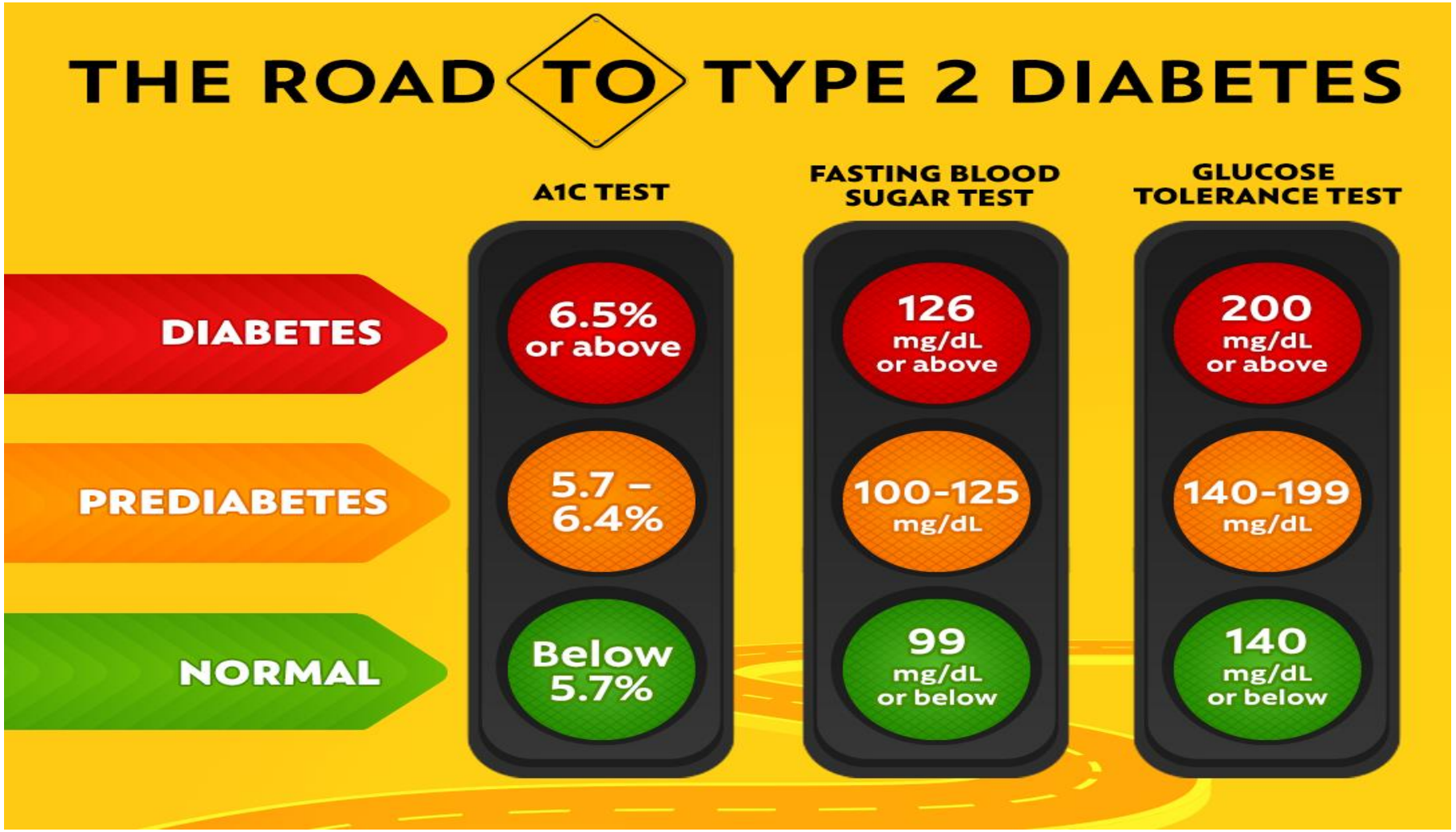
- ✓*Glucose level in normal blood*
- ✓*Renalthreshold level*
- ✓*Hyper & Hypoglycemia*
- ✓*Glycosuria*

Metabolic Disorder

- Metabolism is the process that body make energy from the food.
- Food is made up of proteins, carbohydrates, and fats.
- Chemicals in digestive system (**enzymes**) break the food into sugars and acids, that is used as energy.
- Whether the energy can be used or it can be stored in our tissues.
- Something went wrong in that process leads to metabolic disorder.

Glucose level in normal blood

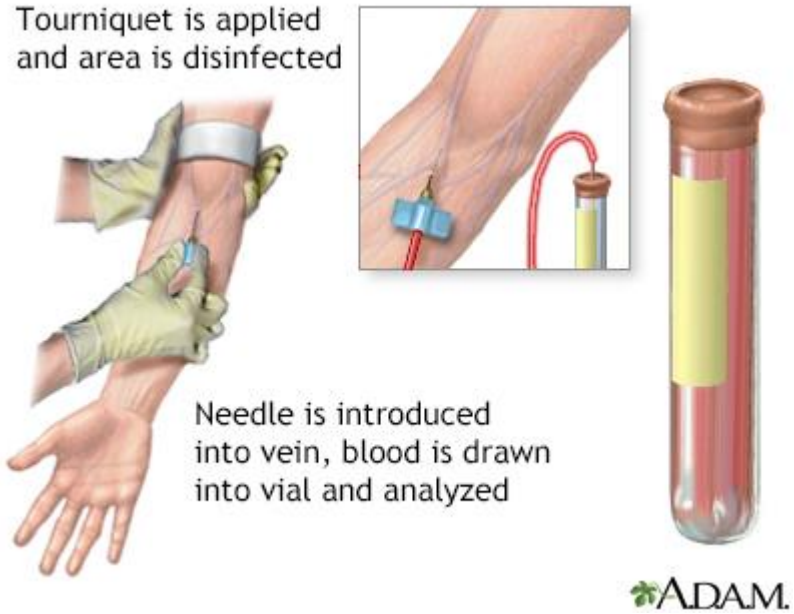
According to American Diabetes Association (ADA)



BLOOD SUGAR TEST

- A blood sugar test measures the amount of a sugar called glucose in a sample of your blood.
- Glucose is a major source of energy for most cells of the body, including brain cells. Glucose is a building block for carbohydrates. Carbohydrates are found in fruit, cereal, bread, pasta, and rice. Carbohydrates are quickly turned into glucose in your body. This can raise your blood glucose level.
- The hormone insulin made in the body helps control the blood glucose level.

COLLECTION METHOD



METHODS

- The test may be done in the following ways:
- After you have not eaten anything for at least 8 hours **(fasting)**
- At any time of the day **(random)**
- Two hours after you drink a certain amount of glucose **(2 hour post-prandial glucose test or oral glucose tolerance test)**

RESULTS

Normal Results

- In fasting blood glucose test, a level of 70 to 99 mg/dL (3.9 and 5.5 mmol/L) is considered normal.
- In random blood glucose test, a normal result depends on when you last ate. Most of the time, the blood glucose level will be 125 mg/dL (6.9 mmol/L) or lower.
- In post prandial after 2 hours of eating, a level is less than 140mg/dl is normal.

ABNORMAL RESULTS INDICATES

In fasting,

- A level of 100 to 125 mg/dL (5.6 to 6.9 mmol/L) means you have impaired fasting glucose, a type of prediabetes. This increases your risk of developing type 2 diabetes and you should consult with your provider.
- A level of 126 mg/dL (7 mmol/L) or higher usually means you have diabetes.

In random blood glucose test:

- A level of 200 mg/dL (11 mmol/L) or higher often means diabetes.
- After , a fasting blood glucose, A1C test, or glucose tolerance test, depending on random blood glucose test result.

HYPOGLYCEMIA

- Hypoglycemia is often defined by a plasma glucose concentration below 70 mg/dL; however, signs and symptoms may not occur until plasma glucose concentrations drop below 55 mg/dL.
- During fasting, glucose levels are maintained via gluconeogenesis and glycogenolysis in the liver.
- Hypoglycemia is most often seen in patients who have diabetes and are undergoing pharmacologic intervention. Among this group, patients with type 1 diabetes are 3 times as likely to experience hypoglycemia than patients with type 2 diabetes when receiving treatment.

Etiology

- In patients who do not have diabetes, hypoglycemia is uncommon. Still, when it occurs, there are a few major causes of hypoglycemia:
- pharmacologic, (medication like insulin)
- alcohol, (Alcohol inhibits gluconeogenesis)
- critical illness,(end-stage liver disease, sepsis, starvation, or renal failure,)
- counter-regulatory hormone(cortisol & epinephrine) deficiencies,(adrenal insufficiency)
- non-islet cell tumors(increased insulin-like growth factor 2 (IGF-2) secretion)

Symptoms

If blood sugar levels become too low, hypoglycemia signs and symptoms can include:

- Looking pale
- Shakiness
- Sweating
- Headache
- Hunger or nausea
- An irregular or fast heartbeat
- Fatigue
- Irritability or anxiety
- Difficulty concentrating
- Dizziness or lightheadedness
- Tingling or numbness of the lips, tongue or cheek

Causes

- Taking too much insulin
- The amount and timing of physical activity
- The amount and timing of physical activity

Prevention

- Monitor your blood sugar.
- Don't skip or delay meals or snacks

Symptoms

- Fast heartbeat
- Shaking
- Sweating
- Nervousness or anxiety
- Irritability or confusion
- Dizziness
- Hunger

Complication

Complications of untreated hypoglycemia can lead to

- Confusion, unusual behavior or both, such as the inability to complete routine tasks
- Loss of coordination
- Slurred speech
- Blurry vision or tunnel vision
- Nightmares, if asleep
- serious neurologic consequences, like
- seizures,
- brain damage, and
- even death.

Treatment / Management

- Hypoglycemia can be treated with intravenous (IV) dextrose followed by an infusion of glucose. For conscious patients able to take oral (PO) medications, readily absorbable carbohydrate sources (such as fruit juice)
- Glucagon can be given intramuscularly or intra nasal.

HYPERGLYCEMIA

- Hyperglycemia is blood glucose greater than 125 mg/dL while fasting and greater than 180 mg/dL 2 hours postprandial.
- A patient has impaired glucose tolerance, or pre-diabetes, with a fasting plasma glucose of 100 mg/dL to 125 mg/dL. A patient is termed diabetic with a fasting blood glucose of greater than 125 mg/dL.
- When hyperglycemia is left untreated, it can lead to many serious life-threatening complications.

CAUSES

The secondary causes of hyperglycemia include the following:

- Destruction of the pancreas from chronic pancreatitis(inflammation of pancreas), hemochromatosis(absorb too much iron), pancreatic cancer, and cystic fibrosis(production of faulty protein).
- Endocrine disorders that cause peripheral insulin resistance like Cushing syndrome(high level of cortisol hormone), acromegaly(high level of GH), and pheochromocytoma (tumor in adrenal gland).
- Use of medications like glucocorticoids, phenytoin, and estrogens.
- Gestational diabetes is known to occur in 4% of all pregnancies and is primarily due to decreased insulin sensitivity
- Total parental nutrition and dextrose infusion

Prevention

- Both type 1 and type 2 diabetes can manage hyperglycemia by eating healthy, being active, and managing stress.
- Oral medications and eventually insulin to help them manage hyperglycemia.
- Diet plan
- Excersice
- Taking your insulin (or glucose-lowering medication) as prescribed
- Avoiding consuming too many calories (i.e., through sugary beverages)
- Controlling stress
- Staying active

PATHOPHYSIOLOGY

- Hyperglycemia in a patient with type 1 diabetes is a result of genetic, environmental, and immunologic factors. These lead to the destruction of pancreatic beta cells and insulin deficiency.
- In a patient with type 2 diabetes, insulin resistance and abnormal insulin secretion lead to hyperglycemia.

SYMPTOMS

Symptoms of hyperglycemia

- increased thirst and a dry mouth.
- needing to pee frequently.
- tiredness.
- blurred vision.
- Unintentional weight loss.
- Recurrent infections, such as thrush, bladder infections (cystitis) and skin infections.

COMPLICATIONS

Complications of untreated or uncontrolled hyperglycemia over a prolonged period of time include:

Microvascular Complications

- Retinopathy
- Nephropathy
- Neuropathy

Macrovascular Complications

- Coronary artery disease
- Cerebrovascular disease
- Peripheral vascular disease

Prevention

- Both type 1 and type 2 diabetes can manage hyperglycemia by eating healthy, being active, and managing stress.
- Oral medications and eventually insulin to help them manage hyperglycemia.
- Diet plan
- Excersice
- Taking your insulin (or glucose-lowering medication) as prescribed
- Avoiding consuming too many calories (i.e., through sugary beverages)
- Controlling stress
- Staying active

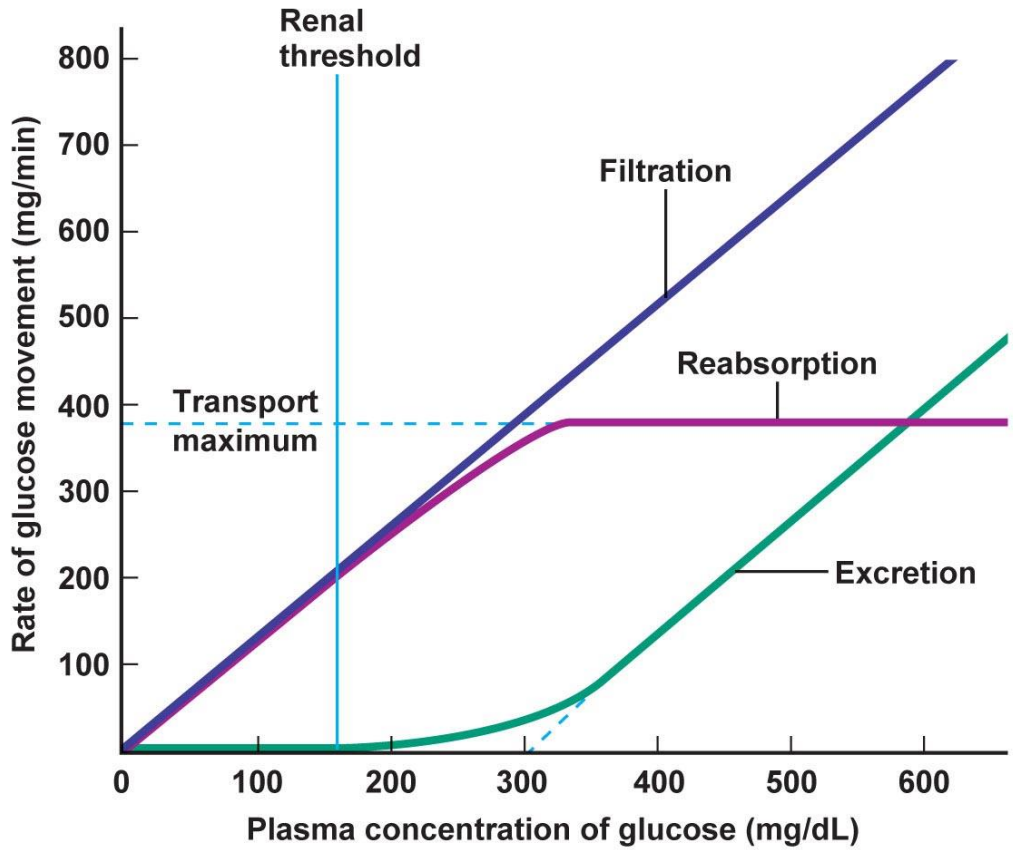
TREATMENT

Treatment goals are to reduce the following complications associated with hyperglycemia:

- Kidney and eye disease by regulation of blood pressure and lowering hyperglycemia
- Ischemic heart disease, stroke, and peripheral vascular disease by control of hypertension, hyperlipidemia, and cessation of smoking
- Reduce the risk of metabolic syndrome and stroke by control of body weight and control of hyperglycemia

RENAL THRESHOLD

- *Glucosuria*, glucose in the urine, results from the glomerular filtration of more glucose than the renal tubule can absorb.
- It occurs in all normal individuals in amounts up to 25 mg/dl. Abnormally increased glucosuria [more than 25 mg/dl in random fresh urine], results from either an elevated plasma glucose, an impaired renal glucose absorptive capacity, or both.
- The plasma glucose concentration above which significant glucosuria occurs is called the *renal threshold* for glucose.
- Its value is variable, and deviations occur both above and below the commonly accepted "normal" threshold of 180 mg/dl. In diabetic patients, the value is reported to vary from 54 to 300 mg/dl



TOPIC:GLYCOSURIA QUALITATIVE TESTS FOR SUGARS IN URINE INTRAVENOUS AND OTHER TYPE OF GLUCOSE TOLERANCE TESTS FRUCTOSE LEVEL IN BLOOD,PENTOSURIA GALACTOSEMIA


Glycosuria
CHAHAT MIDDHA
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INTRODUCTION

- Normally, the urine contains about 0.05gm% of sugar. Such a small quantity cannot be detected by benedicts test, but under certain circumstances, a considerable amount of sugar may be excreted in the urine.
- Excretion of detectable amount of sugar in the urine is called glycosuria.
- Glycosuria results from the rise of blood glucose above its renal threshold.

CLASSIFICATION

- Glycosuria may be due to various reasons on the basis of which is classified into following groups:

1. Alimentary glycosuria
2. Renal glycosuria
3. Diabetic glycosuria

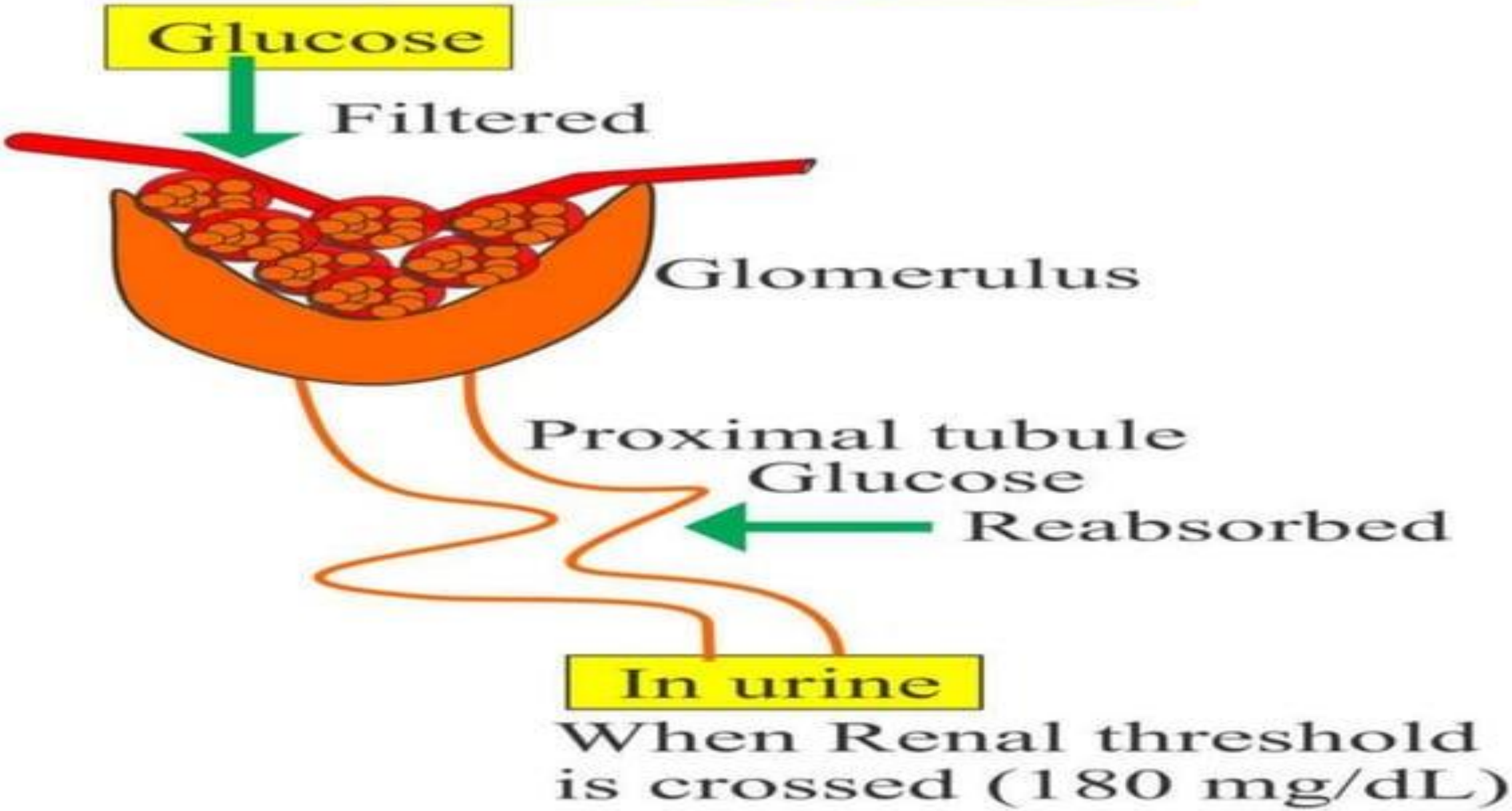
ALIMENTARY GLYCOSURIA

- The blood sugar level of some individuals after meal rises rapidly above the normal renal threshold and results in glycosuria and know as alimentary glycosuria.
- This is due to an increased rate of absorption of glucose from the intestine.
- High blood glucose level returns to normal at 2 hours after a meal. This type of glycosuria is benign (harmless).

RENAL GLYCOSURIA

- This is observed due to impairment tubular reabsorption of glucose and have lowered renal threshold for glucose.
- In such cases, blood glucose level is below.
- 80mg% i.e. Below normal renal threshold for glucose, but glucose appears in the urine due to lowered renal threshold.
- Renal glycosuria is benign condition, unrelated to diabetes and it may occur temporarily in pregnancy without symptoms of diabetes.

Renal Glycosuria



DIABETIC GLYCOSURIA

- Diabetic glycosuria is a pathological condition and is due to deficiency or lack of insulin which causes diabetes mellitus.
- Although the renal threshold id normal, as blood glucose level exceeds the renal threshold, the excess glucose passes into urine to produce glycosuria.

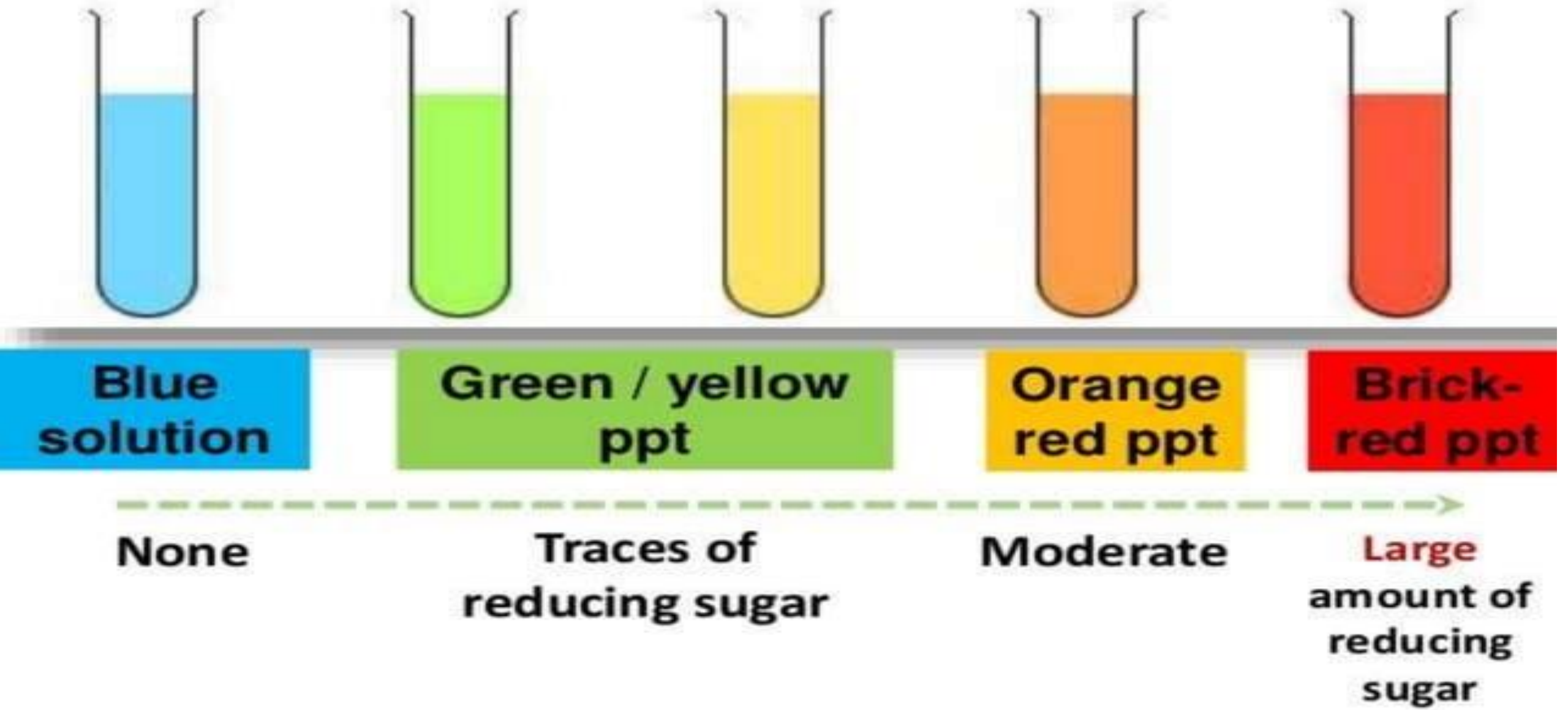
Benedict Test

For Urine

PROCEDURE

- Take 5 ml of Benedict's reagent.
- Add 8 drops of urine sample.
- Boil for 2 minutes or keep it in water bath for 5 minutes.
- A light green, yellow and brick red color is produced depending on the concentration of urinary glucose.

Benedict's Test :
can be used to find out the amount of reducing sugar



GLUCOSE TOLERANCE TEST

Introduction

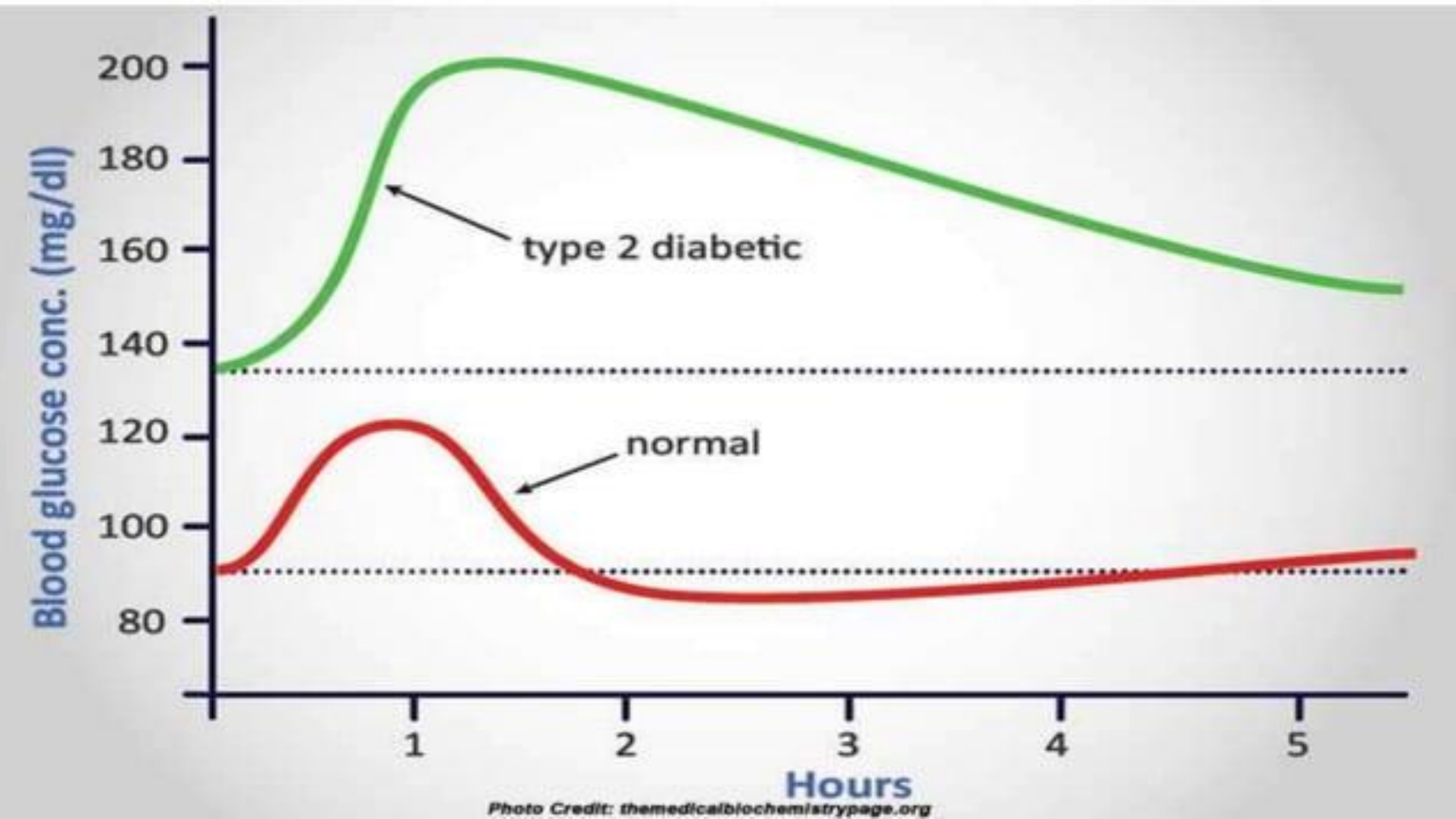
- OGTT measures the body's ability to use glucose, that is the body's main source of energy.
- An OGTT can be used to **diagnose prediabetes and diabetes**.
- Used to test for **diabetes, insulin resistance, impaired beta cell function,** and sometimes **reactive hypoglycemia and acromegaly**, or rarer disorders of carbohydrate metabolism.
- An OGTT is most commonly done to **check for diabetes that occurs with pregnancy (gestational diabetes).**
- Many variations of the GTT have been devised over the years for various purposes, with **different standard doses of glucose**, **different routes of administration**, **different intervals and durations of sampling**, and **various substances measured**

High glucose levels may be caused by

- Diabetes.
- Gestational diabetes.
- Hyperthyroidism.
- Some medicines, such as corticosteroids, niacin, phenytoin (Dilantin), some diuretics, and some medicines used to treat high blood pressure, HIV, or AIDS.
- Large amounts of the hormone cortisol in the blood (Cushing's syndrome).
- Inherited diseases, such as hemochromatosis.

Low glucose levels may be caused by

- Certain medicines, such as medicines used to treat diabetes, someblood pressure medicines (such as propranolol), and some medicines for depression (such as isocarboxazid).
- Decreased production of the hormones cortisol and aldosterone (Addison's disease).
- Problems with the thyroid gland or an underactive pituitary gland.
- A tumor or other problems of the pancreas.
- Liver disease.


Blood glucose conc. (mg/dl)
200
180
160
140
120
100
80
type 2 diabetic
normal
1
2
3
4
5
Hours
Photo Credit: themedicalbiochemistrypage.org

Insulin tolerance test

- An insulin tolerance test (ITT) is a medical diagnostic procedure during which insulin is injected into a patient's vein, after which blood glucose is measured at regular intervals.
- This procedure is performed **to assess pituitary function, adrenal function, and sometimes for other purposes**.
- An ITT is usually ordered and interpreted by endocrinologists.
- Insulin injections are intended to **induce extreme hypoglycemia below 2.2 mmol/l (40 mg/dl).**
- In response, **ACTH and GH are released** as a part of the stress mechanism.
- **ACTH elevation causes the adrenal cortex to release cortisol**. Normally, **both cortisol and GH serve as counterregulatory hormones, opposing the action of insulin, i.e. acting against the hypoglycemia**.

GALACTOSEMIA

Introduction

- Galactosemia is a rare, hereditary disorder of carbohydrate metabolism that affects the body's ability to convert galactose (a sugar contained in milk, including human mother's milk) to glucose (a different type of sugar).
- The disorder is caused by a deficiency of an enzyme galactose-1-phosphate uridylyl transferase (GALT) which is vital to this process.
- Early diagnosis and treatment with a lactose-restricted (dairy-free) diet is absolutely essential to avoid profound intellectual disability, liver failure and death in the newborn period.

Synonyms and Subdivisions

- **Synonyms of Galactosemia**
- Galactose-1-phosphate uridylyl transferase deficiency
- Transferase deficiency galactosemia
- GALT deficiency

- **Subdivisions of Galactosemia**
- Classic galactosemia
- Clinical variant galactosemia
- Biochemical variant galactosemia (Duarte variant galactosemia)

LAB DIAGNOSIS OF EARLY AND LATENT DIABETES MELLITUS-DIABETIC COMA, SECONDARY DEGENERATIVE CHANGES ASSOCIATED WITH DIABETES MELLITUS, GLYCOGEN STORAGE DISORDERS

Diabetes Mellitus

Definition:

- ✓ Diabetes is a complex multigenic syndrome primarily due to beta-cell dysfunction associated with defects in the synthesis, secretion and action of insulin
- ✓ Metabolic disorder characterized by hyperglycaemia (↑*in blood glucose)*

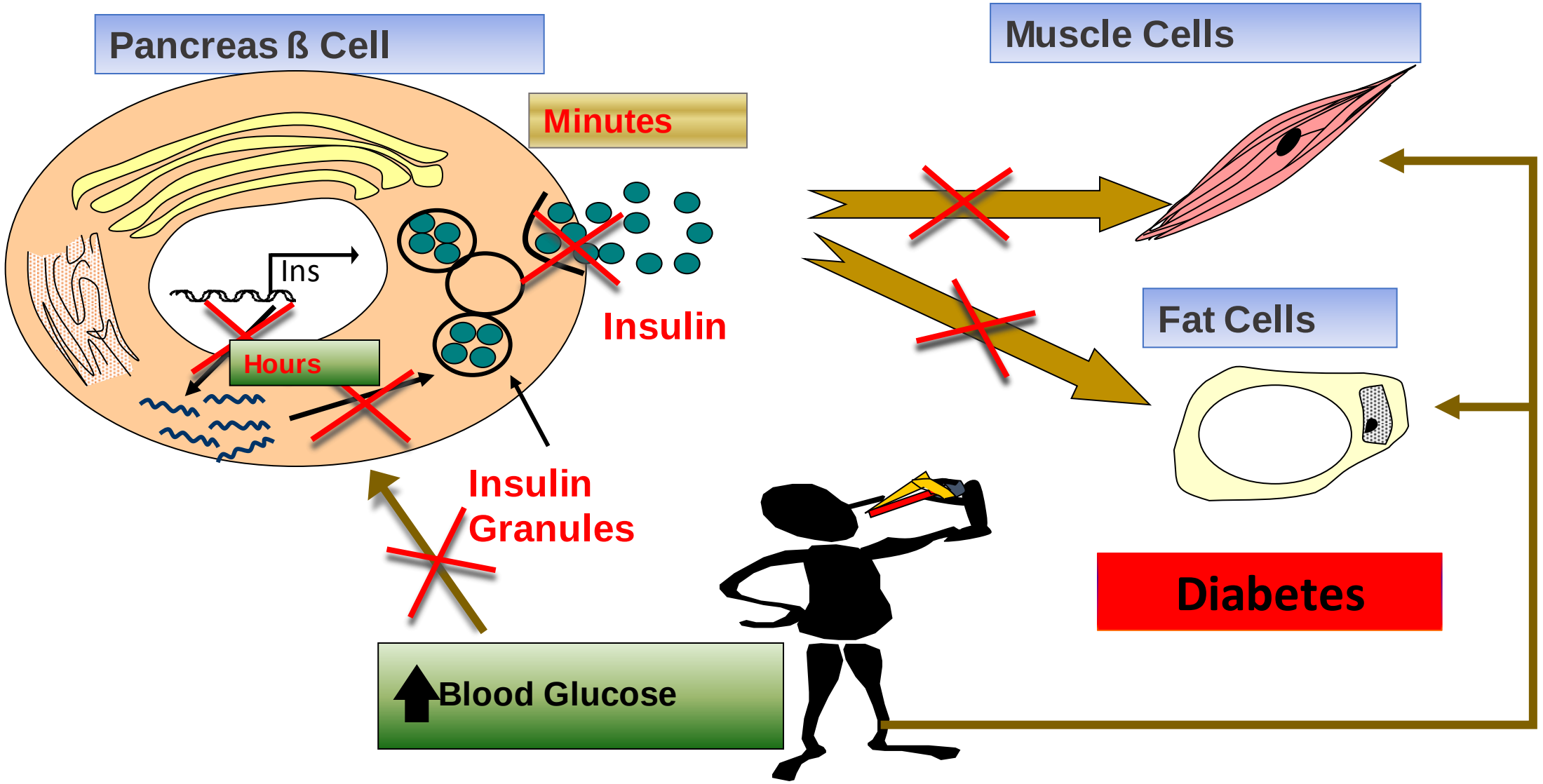
Diabetes = "siphon" or "running through"

(Large urine volume)

Mellitus = "sweet"

(Glucose in urine)

Maintaining Glucose Homeostasis:



Types of Diabetes

1. Type 1 Diabetes

- Insulin-dependent diabetes mellitus (IDDM)
- Juvenile-onset diabetes
- pancreas unable to produce enough insulin.

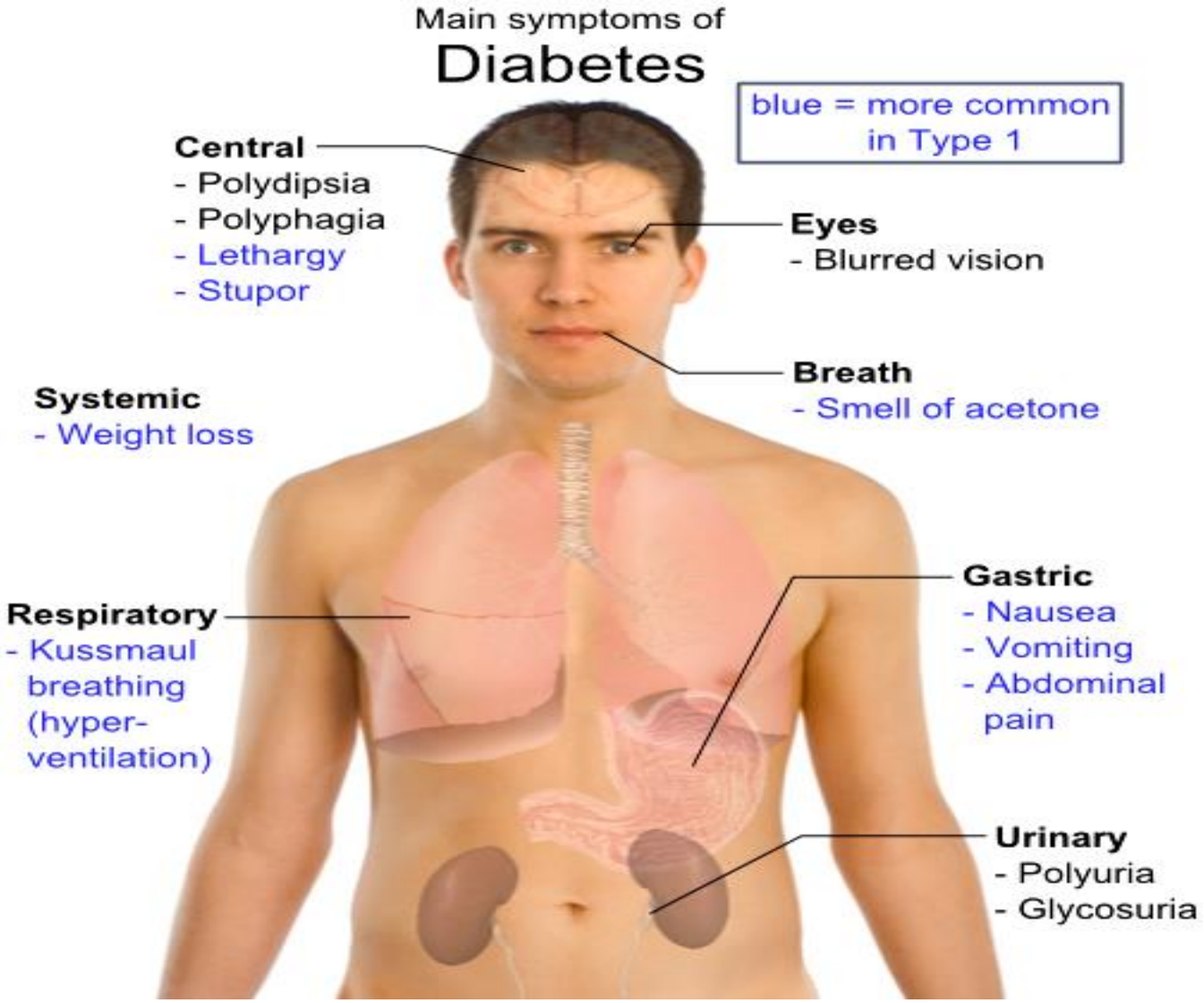
2. Type 2 Diabetes

- Non-insulin-dependent diabetes mellitus (NIDDM)
- Adult-onset diabetes
- pancreas produces insulin but cell receptors become insulin resistant.

3. Gestational diabetes

- diabetes develops during pregnancy and mostly disappear after delivery.
- It may precede development of type 2 DM.

Signs and Symptoms



Risk factors

- **Family history of diabetes**
- **Obesity**
- **Older than 30 years of age**
- **Lack of physical activity**
- **Sedentarism (person with little or no physical activity)**
- **Stress**
- **Poor diet**
- **Excessive weight**
- **Consumption of alcohol and drugs**
- **Smoking**

Complications of Diabetes

1. Acute complications:

- Glucosuria : glucose appears in urine
- Polyuria : frequent urination
- Polydipsia : excessive thirst
- Polyphagia : excessive food intake
- Ketoacidosis : The condition develops when the body can't produce enough insulin.

2.Chronic complications:

- Neuropathy:

  -loss of sensation due to damage of nerve fibres

  (e.g. heat, cold, pain)

- Cardiovascular disease:

  -atherosclerosis, myocardial infarction

- Retinopathy:

  -damage of retina

- Cataract:

  -damage of lens

- Nephropathy:

  -severe kidney, proteinuria

Diagnosis

The most common diagnostic tests include the

- Fasting Plasma Glucose Test
- Random Plasma Glucose Test
- Glycosylated Hemoglobin
- Glycosylated Albumin
- Oral Glucose Tolerance Test.

Tests should be repeated every 3 years, or more often for individuals with a family history of diabetes, certain ethnic groups, history of gestational diabetes, low HDL cholesterol, high levels of triglycerides, high blood pressure, or pre-diabetes

Treatment of Diabetes

Type 1 Diabetes

- Insulin therapy
- Pancreatic islet transplantation

Type 2 Diabetes

- Exercise, diet & weight loss
- Oral glucose lowering drugs

Blood Sugar Management

Maintaining blood glucose levels through proper dietary changes, exercise and/or medication and insulin therapy is essential for effective diabetes control.

Diabetes and Diet

Type 2 DM can usually be controlled with diet and exercise, in addition to monitoring any other body system condition that may exist.

Diabetes and Exercise

- Exercise reduces stress, enhances your mood, improves body image, and promotes a sense of well-being.
- Diabetics can benefit from participating in at least 30 to 60 minutes of physical activity on most days of the week.
- Always consult your health care practitioner before starting a new exercise or fitness routine to determine which activities are safe and compatible with your individual health profile.

To Remember

- Type 2 Diabetes is mainly a disease of “lifestyle.”
- You can prevent many of the complications of diabetes through diet, exercise and stress reduction.

Early Diabetes mellitus:

- Early diabetes refers to the initial phase where blood glucose levels are starting to become abnormal but are not yet high enough to be classified as diabetes.
- This stage may include conditions like impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).

Characteristics

- Blood glucose levels are higher than normal but not in the diabetic range.
- Individuals might begin to show some symptoms of diabetes, like mild fatigue or increased thirst, but these symptoms are often subtle or absent.
- There is usually insulin resistance, where the body's cells do not respond effectively to insulin.

Latent diabetes mellitus:

- Latent diabetes, often referred to as pre-diabetes, is a stage where blood glucose levels are elevated above normal but still below the threshold for a diabetes diagnosis.
- It indicates a high risk of developing type 2 diabetes in the future.

Characteristics:

- Blood glucose levels are consistently higher than normal, especially after eating, but they have not yet crossed the diagnostic threshold for diabetes.
- Individuals with latent diabetes are often asymptomatic.
- There is a significant risk of progression to type 2 diabetes within a few years if no intervention is made.

1. **Fasting Plasma Glucose (FPG) Test:**

- Blood is drawn after an overnight fast (at least 8 hours).
- **Normal Range**: < 100 mg/dL (5.6 mmol/L).
- **Prediabetes**: 100–125 mg/dL (5.6–6.9 mmol/L).
- **Diabetes**: ≥ 126 mg/dL (7.0 mmol/L) on two separate occasions.

2. **Oral Glucose Tolerance Test (OGTT):**

- After fasting, the patient consumes a glucose solution (usually 75 g of glucose). Blood glucose levels are then measured at intervals, typically at 2 hours.
- **Normal Range**: < 140 mg/dL (7.8 mmol/L) after 2 hours
- .**Prediabetes**: 140–199 mg/dL (7.8–11.0 mmol/L) after 2 hours.
- **Diabetes**: ≥ 200 mg/dL (11.1 mmol/L) after 2 hours.

3. **Glycated Hemoglobin (HbA1c) Test:**

- Measures the percentage of glucose attached to hemoglobin in the blood over the past 2–3 months.
- **Normal Range**: < 5.7%
- .**Prediabetes**: 5.7%–6.4%.
- **Diabetes**: ≥ 6.5%.

Diabetic Coma

- diabetes-related coma is a life-threatening complication that can result from very high blood sugar (hyperglycemia) or very low blood sugar (hypoglycemia).
- A coma is a prolonged, deep state of unconsciousness.
- People in comas are unresponsive but still alive.
- **Impaired Glucose Tolerance (IGT)** and **Impaired Fasting Glucose (IFG)** are considered early or latent stages of diabetes.
- They can be detected through FPG, OGTT, or HbA1c tests.

- Three diabetes complications can lead to a coma, including:
- Hyperosmolar hyperglycemic state (HHS).
- Diabetes-related ketoacidosis (DKA).
- Severe low blood sugar (hypoglycemia).

Hyperosmolar hyperglycemic state

- Hyperosmolar hyperglycemic state (HHS) is a life-threatening complication of diabetes — mainly Type 2 diabetes. HHS happens when your blood glucose (sugar) levels are too high for a long period, leading to severe dehydration and confusion. Blood sugar levels are usually over 600 milligrams per deciliter (mg/dL).
- If you don’t get treatment for HHS in time, it can lead to a coma.

Diabetes-related ketoacidosis (DKA)

- Diabetes-related ketoacidosis (DKA) is a life-threatening complication that mainly affects people with diagnosed or undiagnosed Type 1 diabetes. But it sometimes affects people with Type 2 diabetes as well.
- DKA happens when your body doesn't have enough insulin (natural or synthetic). Your body needs insulin to make glucose in your blood enter your cells, where it's used as fuel for energy. If there's no insulin or not enough insulin, your body starts breaking down body fat for energy instead. As your body breaks down fat, it releases ketones into your bloodstream.

- For a person with diabetes, a high amount of ketones causes their blood to become acidic. If you don’t get treatment for DKA in time, it can lead to a coma.
- Someone who has DKA usually has blood sugar levels above 250 mg/dL. But the main causes of DKA are a lack of insulin and ketones, not just high blood sugar. People with diabetes can have blood sugar over 250 mg/dL and not have DKA.

Severe hypoglycemia

- Severe hypoglycemia happens when your blood sugar is below 40 mg/dL. This is life-threatening.
- Glucose is the main source of energy for your body and brain. When your blood glucose is low, your body can't function properly. If your blood sugar drops really low (like below 40 mg/dL), you likely won't be able to function because of the physical and mental changes that occur. Prolonged severe hypoglycemia that's not treated in time can lead to a coma.
- Most cases of severe hypoglycemia affect people with diabetes who take insulin or certain oral diabetes medications, like sulfonylureas.

Symptoms and Causes

- The three main symptoms of a coma include:
- **Unconsciousness**: This is like a very deep sleep, and it’s impossible to wake you up.
- **Lack of eye response**: This means your eyes stay closed, and someone holding your eye open doesn’t cause you to react. Your eyes might have some reflex responses, such as reacting to light.
- **Lack of motor (movement) response**: This means you don’t consciously move. You may still have some reflex responses

- Severe symptoms of DKA that could happen before a diabetes-related coma include:
- Nausea and vomiting.
- Abdominal pain.
- Rapid, deep breathing at a consistent pace (Kussmaul breathing).
- Fruity-smelling breath.
- Feeling very tired or weak.
- Feeling disoriented or confused.
- Decreased alertness.

- Symptoms of HHS that could happen before a diabetes-related coma include:
- Mental changes, such as confusion, delirium or hallucinations.
- Loss of consciousness.
- Dry mouth and extreme thirst (polydipsia).
- Frequent urination.
- Blurred vision or vision loss.
- Weakness or paralysis that may be worse on one side of your body.

- Symptoms of severe low blood sugar that could happen before a diabetes-related coma include:
- Blurred or double vision.
- Slurred speech.
- Clumsiness or difficulty with coordination.
- Being disoriented.
- Seizures.

I. Immediate: Diabetic ketoacidosis and coma is one of the most important and dreaded complication specially in Type-I.

II. Late complications: Other complications are late to appear and are due to changes in blood vessels.

These are two types:

- Involvement of large vessels
- Involvement of small vessels.

(a) Large vessels involvement: Atherosclerosis and its effects:

Involvement of coronary vessels can produce myocardial infarction.

Involvement of cerebral vessels can produce “stroke”.

(b) Small vessels changes involve:

Thickening of basement membrane

Microvascular changes

1. **Diabetic retinopathy (70%):** Tiny haemorrhages, punctate or flame-shaped, exudates. Haemorrhage in vitreous humour can cause sudden blindness.
2. **Diabetic cataract:** Is due to:

- Non-enzymatic glycosylation of lens protein, α-crystallin;
- Osmotic damage to lens protein due to accumulation of sorbitol

3. **Diabetic nephropathy (50% cases):** Characterised by (a) Proteinuria, (b) Hypertension and (c) Oedema. The triad is called as Kimmelsteil-Wilson syndrome. Microscopic lesions are called as ‘Kimmelsteil-Wilson lesions/disease’.

   Lesions are often present when syndrome is not developed. Sometimes kidney lesions may be shown as:

- Papillary necrosis: A dangerous complication.
- Pyelonephritis: When secondary infections occur

4. **Peripheral neuritis (neuropathy):** Manifestated by loss of sensation and tingling. Biochemically probably the cause is myoinositol deficiency. Sometimes there may be associated myopathies, weakness of muscles.
5. **Diabetic gangrene:** Cause is due to diminished blood supply due to atherosclerotic changes in blood vessels. Also associated tissue hypoxia due to formation of HbA1C (glycosylated Hb), less oxygen carrying capacity.

6. **Skin lesions**: Prone to infections: boils/ulcers and carbuncles. There may be necrosis of skin, Necrobiosis diabeticorum.

• May be punctate depigmented atrophy

• Wound healing is delayed.

7. **Pulmonary tuberculosis**: Susceptible to pulmonary tuberculosis

Table 21.1 Glycogen-storage diseases

Type	Defective enzyme	Organ affected	Glycogen in the affected organ	Clinical features
I Von Gierke	Glucose 6-phosphatase or transport system	Liver and kidney	Increased amount; normal structure.	Massive enlargement of the liver. Failure to thrive. Severe hypoglycemia, ketosis, hyperuricemia, hyperlipemia.
II Pompe	α-1,4-Glucosidase (lysosomal)	All organs	Massive increase in amount; normal structure.	Cardiorespiratory failure causes death, usually before age 2.
III Cori	Amylo-1,6-glucosidase (debranching enzyme)	Muscle and liver	Increased amount; short outer branches.	Like type I, but milder course.
IV Andersen	Branching enzyme (α-1,4 $\longrightarrow$ α-1,6)	Liver and spleen	Normal amount; very long outer branches.	Progressive cirrhosis of the liver. Liver failure causes death, usually before age 2.
V McArdle	Phosphorylase	Muscle	Moderately increased amount; normal structure.	Limited ability to perform strenuous exercise because of painful muscle cramps. Otherwise patient is normal and well developed.
VI Hers	Phosphorylase	Liver	Increased amount.	Like type I, but milder course.
VII	Phosphofructokinase	Muscle	Increased amount; normal structure.	Like type V.
VIII	Phosphorylase kinase	Liver	Increased amount; normal structure.	Mild liver enlargement. Mild hypoglycemia.

Note: Types I through VII are inherited as autosomal recessives. Type VIII is sex linked.

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THANK YOU