GLUCOSE METABOLISM

What is Glucose Metabolism?

Glucose Metabolism is a Part of Carbohydrates Metabolism

- **Carbohydrate metabolism** includes the various biochemical processes responsible for the formation, breakdown and interconversion of carbohydrates in living organisms.
- The most important carbohydrate is glucose, a simple sugar (monosaccharide) that is found in foods and metabolized by nearly all known organisms.

“Glucose” is the Carbohydrate Currency of the Body

- Dietary Carbohydrates are Digested

in the

Gastrointestinal Tract

to

Simple Monosaccharide Abundantly Glucose

which are then all

Absorbed by the Intestinal Cells.

“Glucose” is the Carbohydrate Currency of the Body …..cont.

- **Monosaccharides** other than glucose after the absorption by the intestine they are converted to glucose in the liver.

GLUCOSE

↓ Absorption by Intestine

Carried by the Blood to Different body tissues

Function of Glucose

- **The Principal Biochemical Function of Glucose is to Provide Energy for Life Processes.**

- **Glucose Oxidation**

is the primary source of energy for the biosynthesis of

Adenosine Triphosphate (ATP).

Which is

The Universal Energy Source for Biological Reactions.

Routes of Glucose Metabolism Controlled by Insulin

❑ ***Here is a Very Simple Explanation of how we Convert Glucose into Energy.***

- In response to the rise in **blood-glucose levels** after a meal

↓

The beta cells of the islets of Langerhans of the **Pancreas** release

Insulin

A protein hormone which enhances glucose uptake by the different body cells.

Effect of Insulin on Glucose Uptake by Cells

- *The cells that need glucose have **specific insulin receptors*** on their surface so that insulin can bind to them, encouraging glucose entry and utilization in the cells.
- The glucose enters the cell by special protein molecules in the plasma membrane called **" glucose transporters "** (**facilitated transport**).

Effect of Insulin on Glucose Uptake by Cells …..cont.

- Glucose can not enter the cells of most body tissues in the absence of insulin.
- **The main target tissues of insulin are:**

1. Liver.

2. Muscles.

3. Adipose tissues.

Aerobic and Anaerobic Metabolism of Glucose

- **Once inside the cells, glucose is metabolized to produce energy. This may occur by either:**

1. **Aerobic Metabolism** that occurs in combination with oxygen. It takes place in the cytosol and mitochondria.
2. **Anaerobic Metabolism** which do not need oxygen. Takes place in the cytosol only.

- ***Red blood cells*** **do not have mitochondria, so they convert glucose into energy without the use of oxygen.**

- Both Aerobic and Anaerobic Metabolic Pathways of Glucose Starts with Glycolysis

- What is Glycolysis?

Both Aerobic and Anaerobic Metabolic Pathways of Glucose Starts with Glycolysis

❑ Glycolysis

is a metabolic process by which

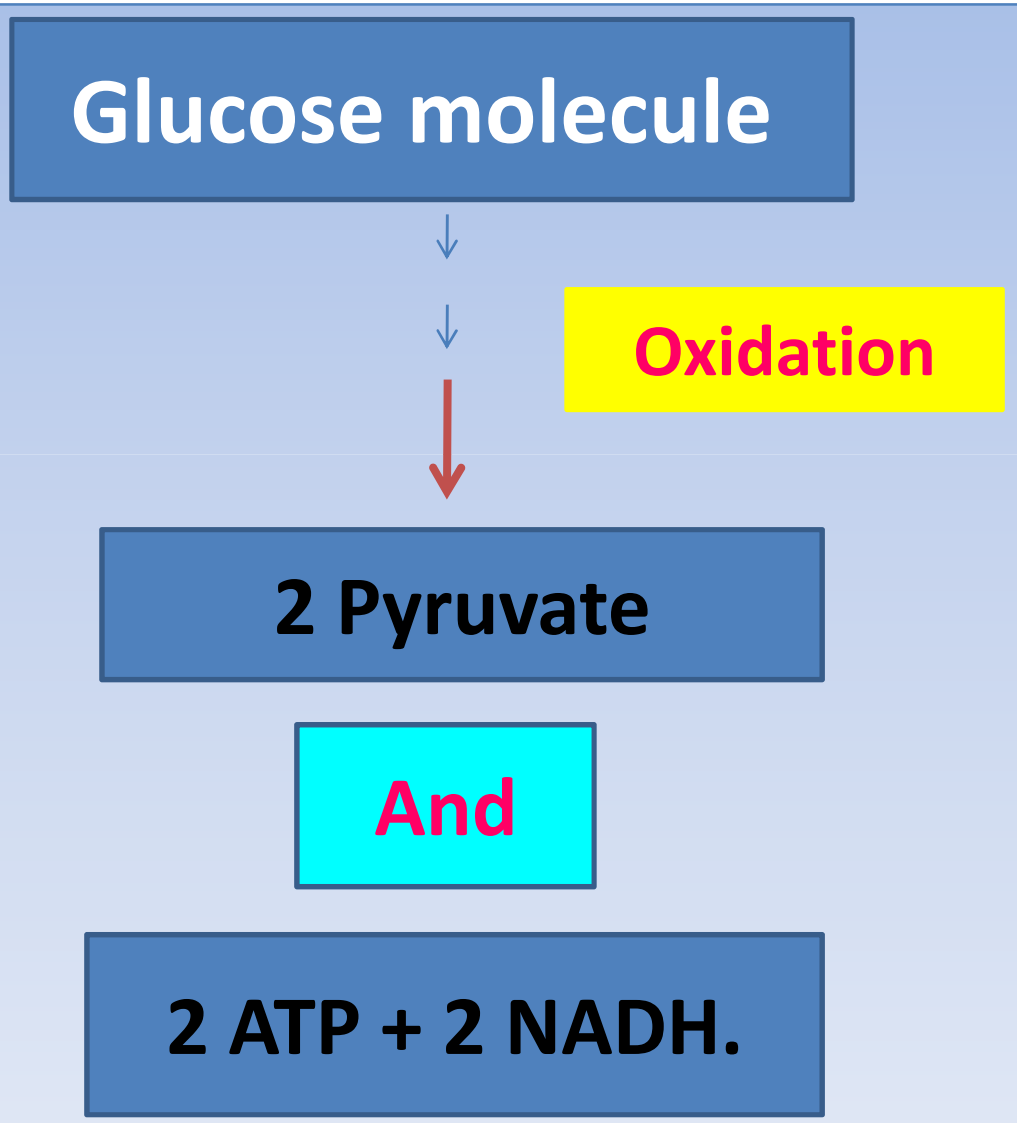
6-Carbon Glucose

molecule is oxidized to

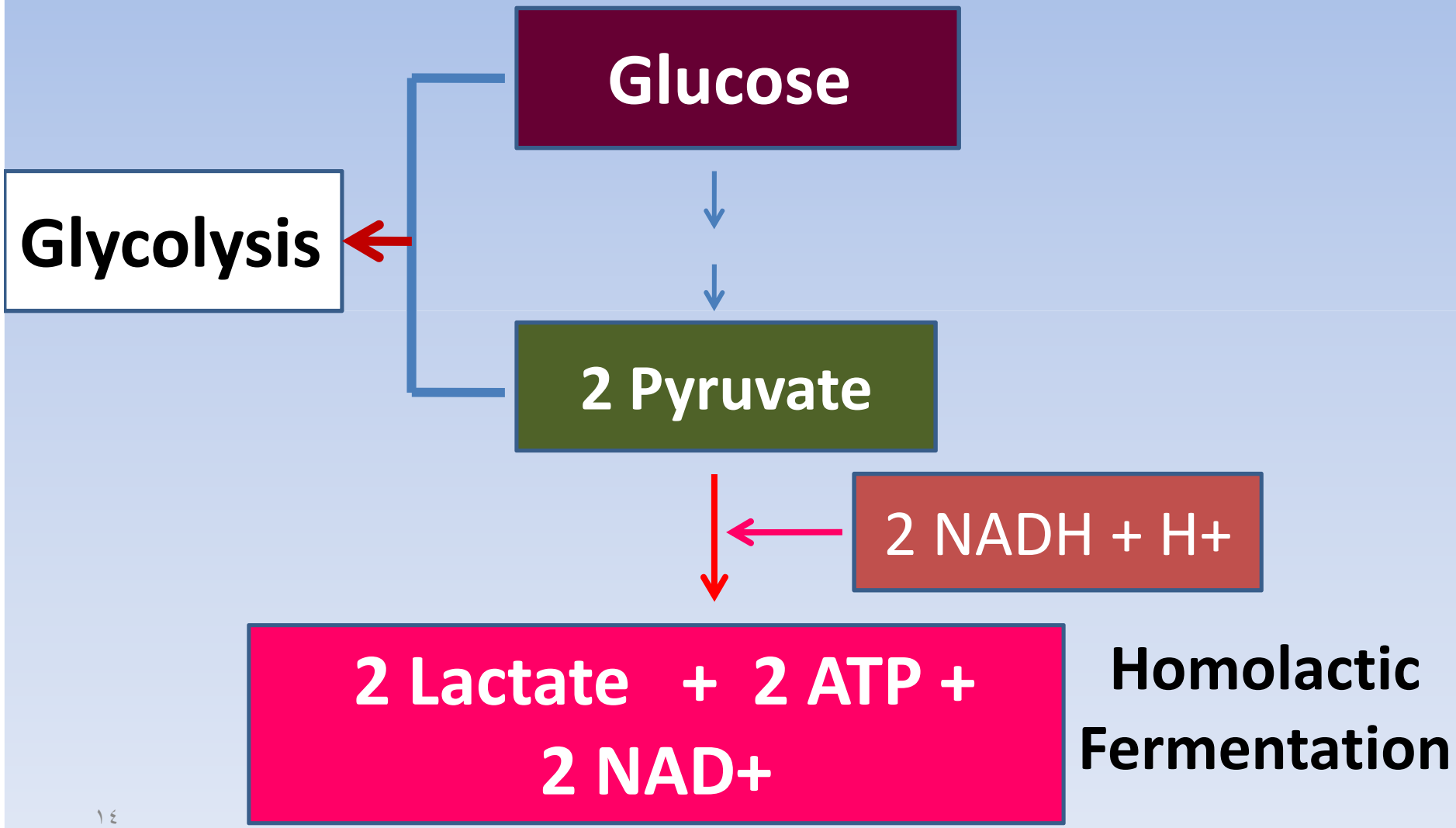
Two 3-carbon molecules of pyruvate.

- For every glucose converted to 2 pyruvate:
  2 net ATP and 2 net NADH are formed.

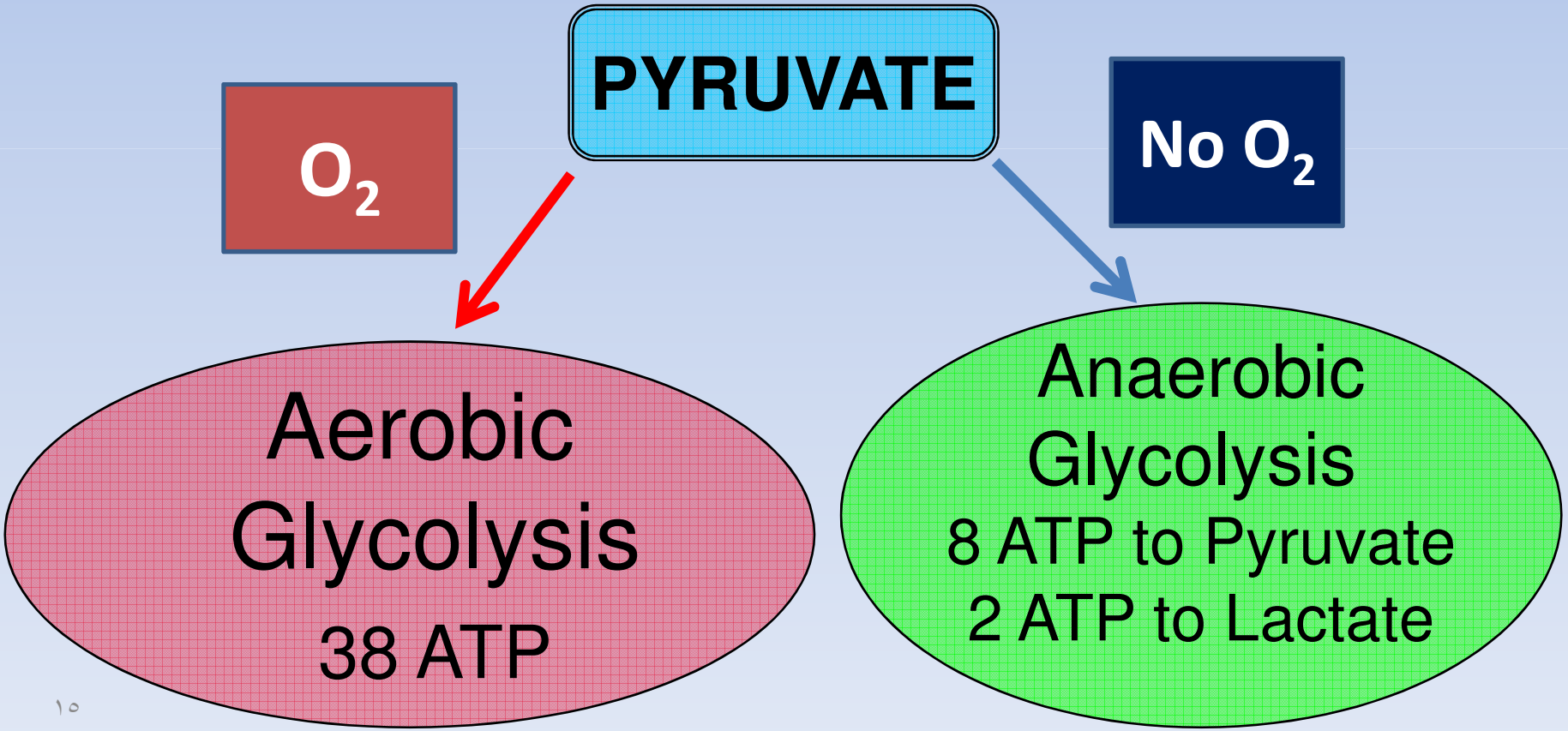
Glycolysis



Anaerobic Glycolytic Pathway



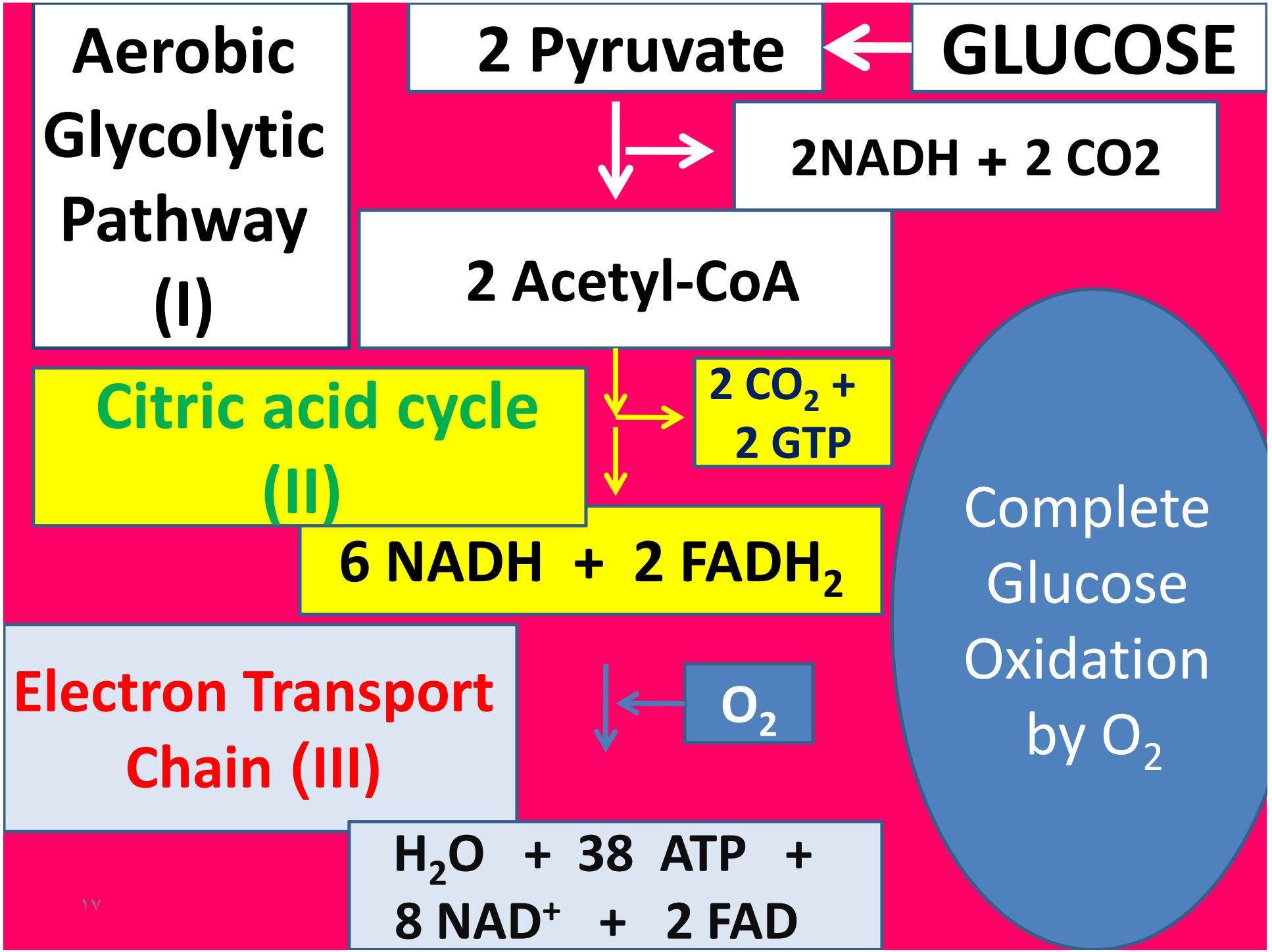
Both Aerobic and Anaerobic Metabolic Pathways of Glucose Starts with Glycolysis



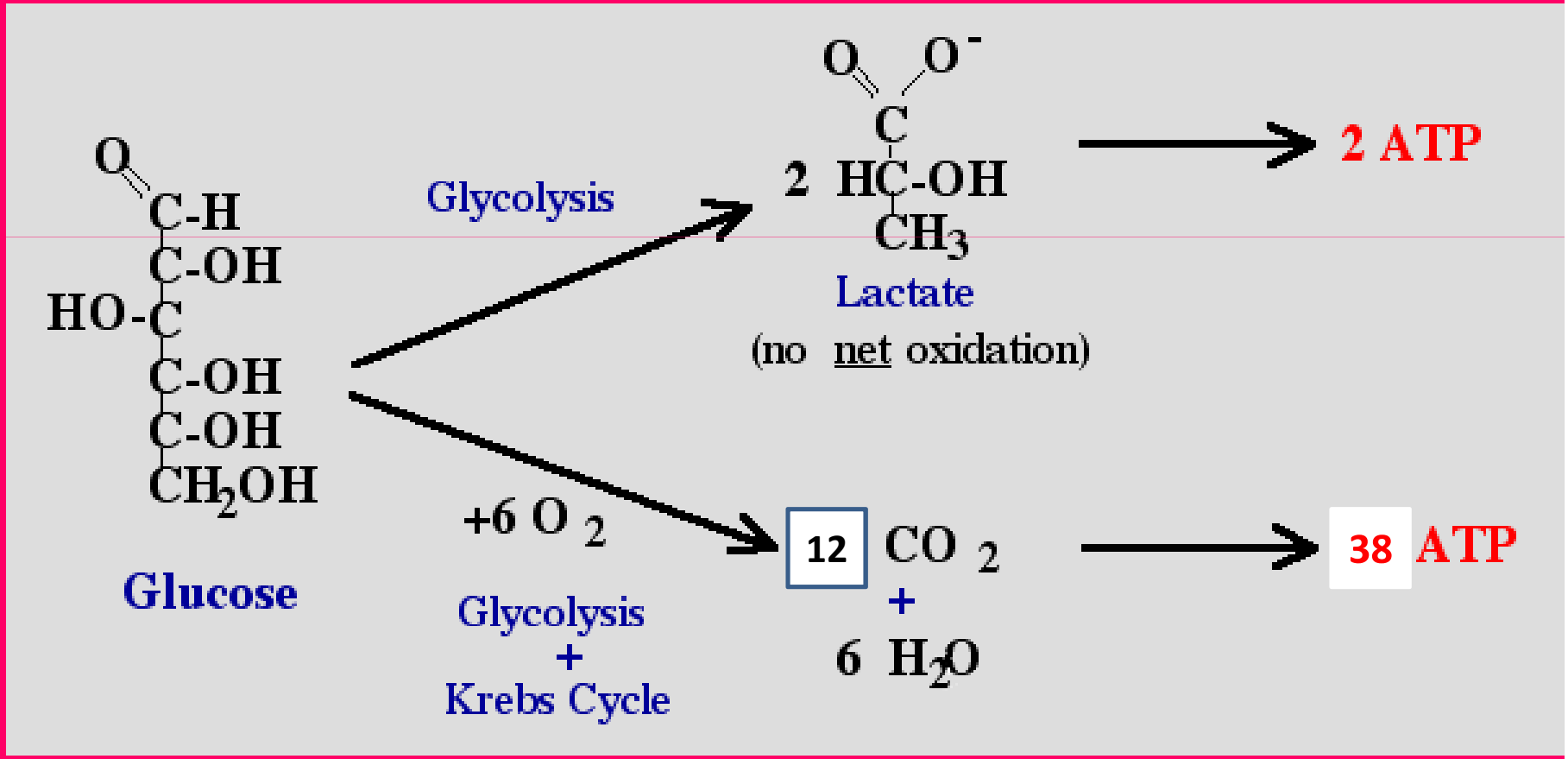
Aerobic Glycolytic Pathway

One molcule of Glucose gives 38 ATP

Glycolysis (Pyruvate Formation)	**2 ATP** **2 NADH (6 ATP)**
Acetyl- CoA Formation	**2 NADH (6 ATP)**
Krebs Cycle Citric Acid Cycle	**6 NADH (18 ATP)** **2 FADH2 (4ATP)** **2 GTP (2ATP)**


Aerobic Glycolytic Pathway (I)
2 Pyruvate
GLUCOSE
2NADH + 2 CO2
2 Acetyl-CoA
Citric acid cycle (II)
2 CO2 + 2 GTP
6 NADH + 2 FADH2
Electron Transport Chain (III)
O2
H2O + 38 ATP + 8 NAD+ + 2 FAD
Complete Glucose Oxidation by O2

الطاقة الإجمالية (ATP) الناتجة من الجلايكوليسز و دورة كريبس



Physiological Importance of Glucose

- Energy is required for the normal functioning of the organs in the body.
- ***Many tissues can use fat or protein instead of glucose as a source of energy but others such as the:***

Brain mainly uses glucose **And** ***Red blood cells can only use glucose***

As a source of energy

Physiological Importance of Glucose

❑ Glucose Metabolism

- Glucose is the Body's Fuel.

- Without glucose or without being able to convert it into energy rapidly and efficiently, we cannot survive in a good health. So it's very important that our

Glucose - Energy-Metabolism System

works efficiently.

What are the Hormones that their Effects Opposed Insulin Effects?

- ❑
- ❑The Effects of insulin are opposed by other hormones: *Glucagon*, Adrenaline Glucocorticoides and Growth hormone.

These hormones sometimes are called

Stress Hormones

Insulin and Glucagon Have Opposite Actions on Blood Glucose Level

- ***A Meal Rich in Carbohydrates:***

1- Induces insulin secretion.

2- Suppresses glucagon release.

Effects of Insulin on Body Metabolism

- **Insulin Correlates with the Fed State**

It Switches on

Pathways and Processes Involved in

The Cellular Uptake and Storage of Metabolic Fuels

and

switches off pathways involved in

Fuel Breakdown.

Effects of Insulin on Body Metabolism

- **In Normal Individuals**
- **Insulin acts as the body's only**

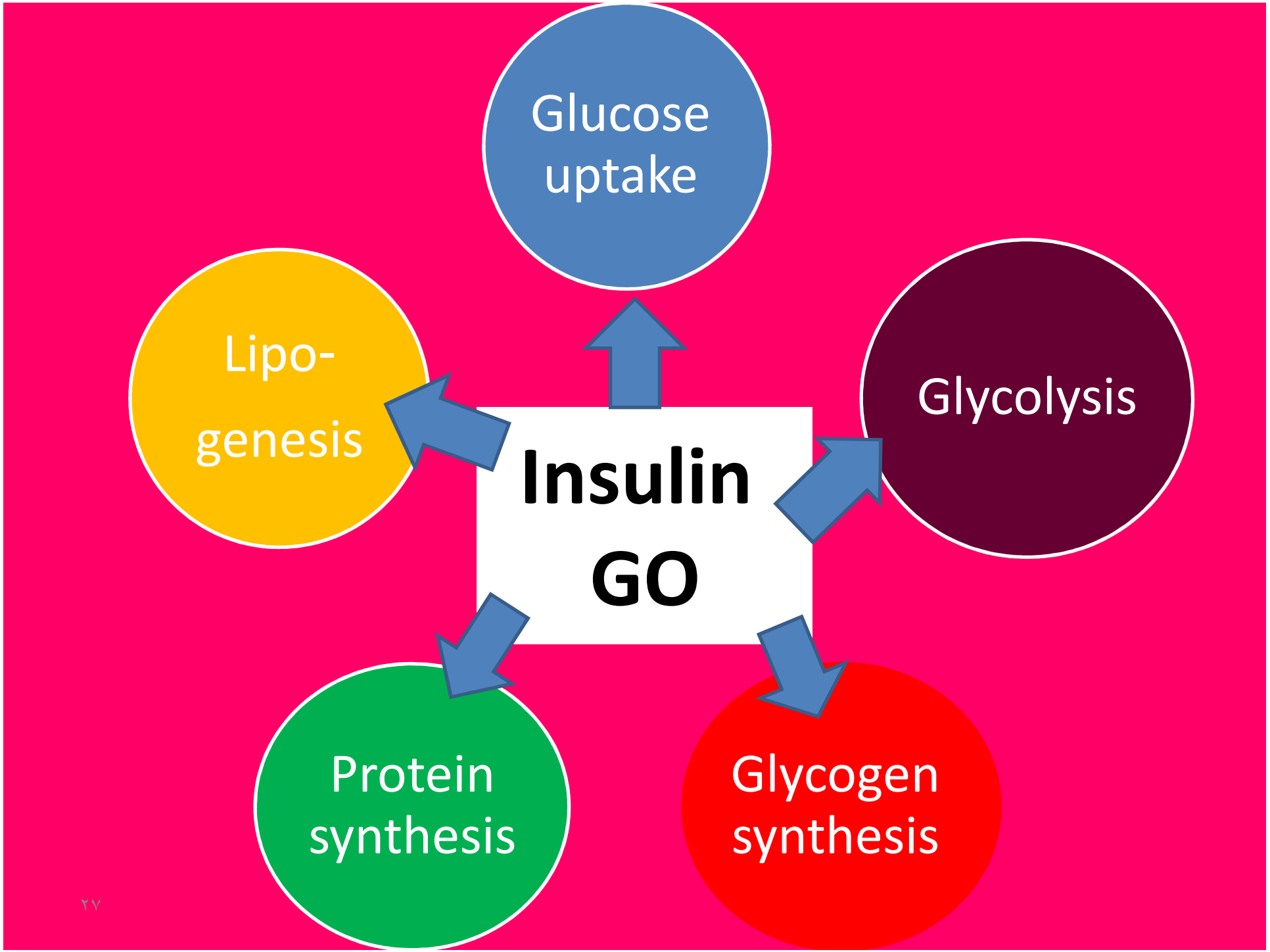
Hypoglycemic Agent

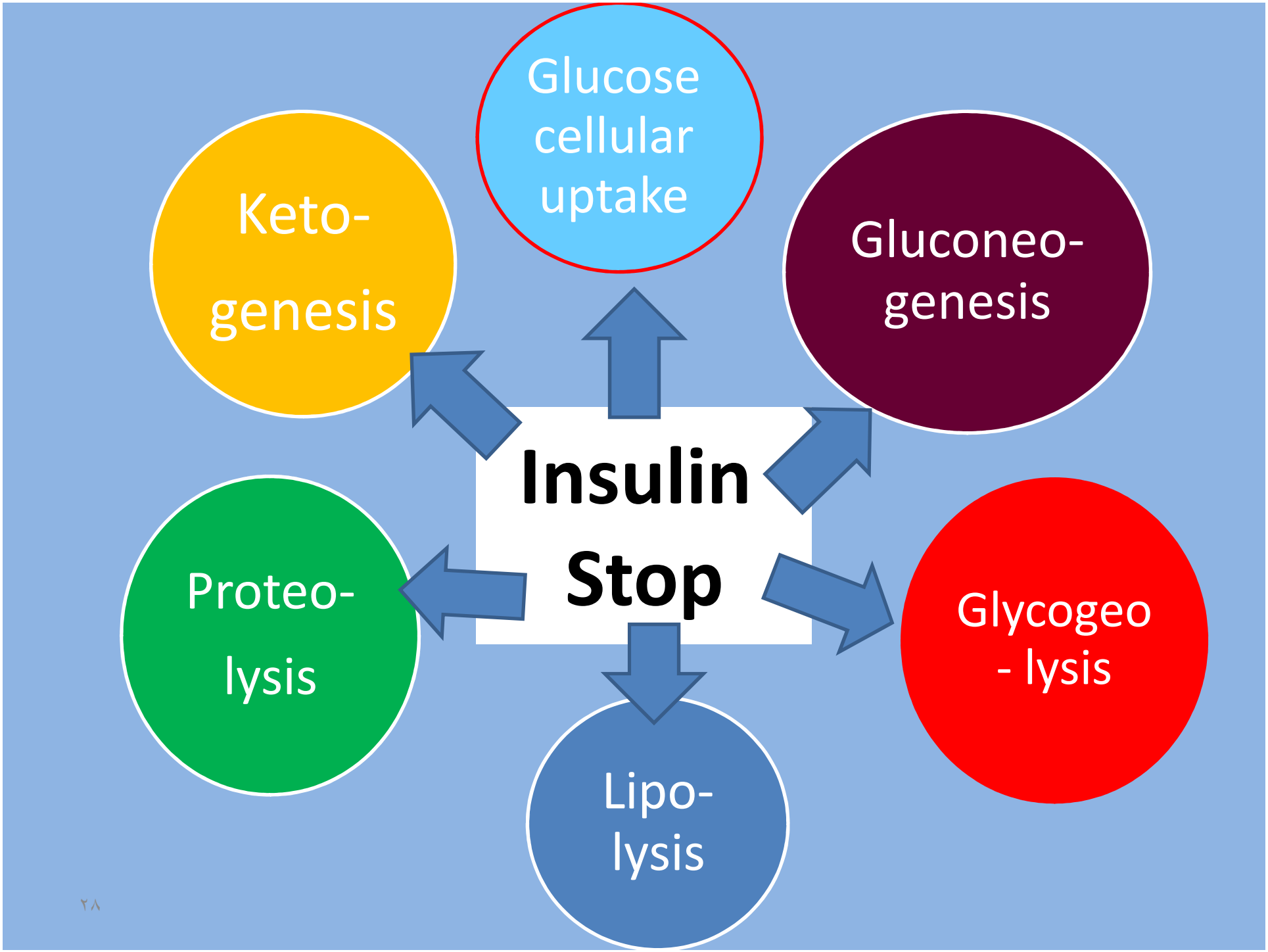
Insluin reduces blood glucose level.

The Metabolic Actions Of Insulin .....?

METABOLIC ACTIONS OF INSULIN

TISSUE			
	Liver	**Adipose**	**Muscle**
Inhibits :	**Glycogenolysis Gluconeogenesis ketogenesis**	lipolysis	-Protein breakdown -Amino acid release
Stimulates :	**- Glycogen and fatty acid synthesis**	Glycerol fatty acid synthesis	**- Glucose uptake and metabolism** -Amino acid uptake -Synthesis of protein **-Glycogenesis**


Glucose uptake
Lipo-genesis
Glycolysis
Insulin GO
Protein synthesis
Glycogen synthesis


Glucose cellular uptake
Keto-genesis
Gluconeo-genesis
Insulin Stop
Proteo-lysis
Glycogeo- lysis
Lipo-lysis

The Insulin-Opposite Effects of Glucagon on the Blood Level of Glucose

II . Function of Glucagon:

1- Stimulates Gluconeogenesis

2- Stimulates Glycogenolysis

- *Glucagon is a hyperglycemic agent*

  it increases blood glucose level .

- **After a Meal Rich in CHO, glucagon secretion is reduced.**

The Relationship Between Glucose Metabolism And Diabetes Mellitus is Very Important

Glucose Metabolism in Diabetes Mellitus

In Diabetic Patients

The hormonal regulation of blood glucose levels and metabolic processes are abnormal and results in the classic sign of **DIABETES MELLITUS:**

Elevated Blood Glucose Levels.

- The measuring of blood glucose levels is an important test in diabetes (and also other disorders).

Metabolic Processes of Glucose in Normal Individuals

Just Minutes After Ingestion of a Meal:

(1) Blood glucose levels increase, however by only 20% to 40% in nondiabetic individuals.

(2) Blood insulin levels **rapidly increase.** Most peripheral cells respond to the rise of blood glucose in the presence of insulin by rapidly increasing glucose transport into cells.

Metabolic Processes of Glucose in the Diabetics

***In the diabetic, both the production and* metabolism of glucose are increased.**

Thus, in the fasting state in diabetics, hepatic glucose release is greatly elevated, causing the diagnostic, fasting hyperglycemia of diabetics

Metabolic Processes of Glucose in the Diabetics

- The decreased control of glucose metabolism by insulin causes the diabetic to be in

Semistarvation State

with an increased dependence on triglycerides as a source of fuel and on protein as a source of glucose precursors.

Types of Diabetes Mellitus …..cont.

There are 2 Types of Diabetes Mellitus:

1- Type I Diabetes.

- It accounts for 5% to 10% of the diagnosed cases of diabetes.
- This type of diabetes is caused by insufficient insulin secretion (insulinopenia).
- Insulin injections are necessary to maintain normal glucose metabolism.
- Individuals with type I diabetes are especially prone to **ketoacidosis**. Ketoacidosis refers to excessive formation of ketone bodies and low blood pH (acidosis).

Types of Diabetes Mellitus

There are 2 Types of Diabetes Mellitus:

2- Type II Diabetes.

- The occurrence of type II diabetes has no correlation with blood insulin levels, however there is **insulin resistance.**
- **The type II individual is usually (i) not traeted with insulin injection, (ii) less prone to ketoacidosis, and (iii) is often in obese.**

Metabolic Processes of Glucose in the Diabetic ……cont.

After a meal, the inhibition of hepatic glucose output is

↓

Much smaller in the diabetic

There is diminished insulin output and/or insulin resistance in diabetics

↓

Abnormal and prolonged rise in blood glucose after a meal

Oral Glucose Tolerance Test

- **Oral Glucose tolerance test (OGTT)** is used
- **OGTT** is not always necessary to diagnose diabetes as most patients have both significantly high blood sugar and symptoms of diabetes and don't require further testing.

- **OGTT** used to diagnose prediabetes (patients at higher risk for developing DM in the future and currently have no symptoms of DM and their blood sugar is upper limit of normal).

Oral Glucose Tolerance Test

- **Oral Glucose tolerance test (OGTT)** is a laboratory method to check how the body breaks down (metabolizes) blood sugar.
- OGTT is used to diagnose prediabetes and diabetes.

Metabolic Processes of Glucose in the Diabetics

- **In summary**, the carbohydrate metabolism in a diabetic is strikingly similar to that of a nondiabetic in the fasting state.

  - In both cases metabolism of fatty acids has replaced the metabolism of glucose as the principal source of energy for the cell.

Diabetic Patients Suffer from Different Abnormalities

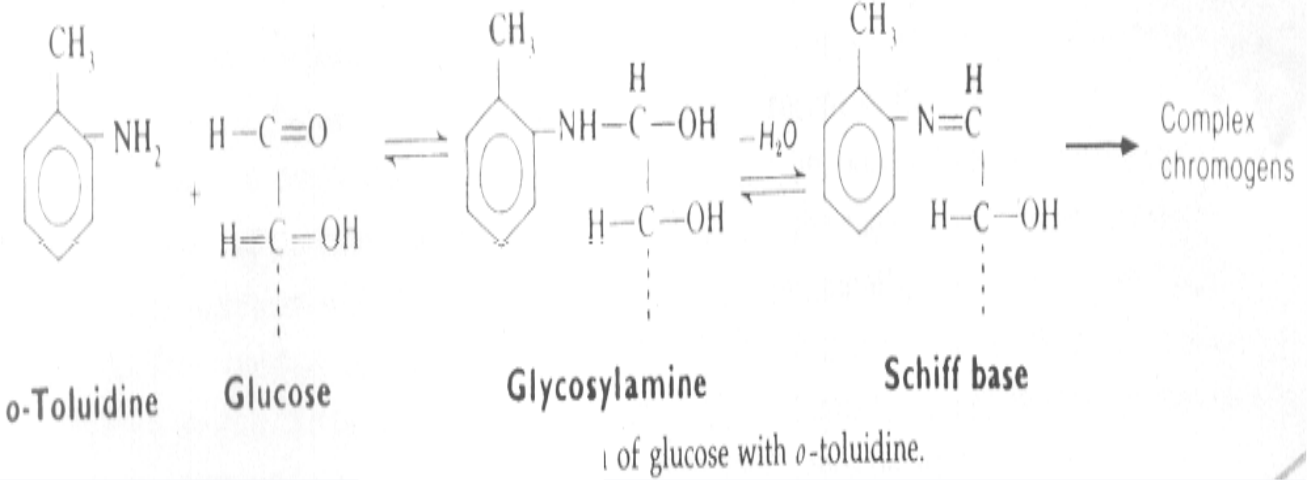
- **Late Complications of Diabetes Mellitus:**

1. Microangiopathy.
2. Retinopathy.
3. Nephropathy.
4. Neuropathy.
5. Macroangiopathy.

Principle of Method

- Various aromatic amines react with glucose in hot acetic acid solution to produce colored derivatives. Among those used is **o-toluidine**.
- The **o-toluidine** condenses initially with the aldehyde group of glucose to form an equilibrium mixture of a **glycosylamine** and the **corresponding Schiff base**, as illustrated Figure 1.

Figure 1



of glucose with *o*-toluidine.

Principle of Method

- Further rearrangements and reactions take place after the original condensation to produce a mixture of blue green chromogens with an absorption maximum at 625 nm.

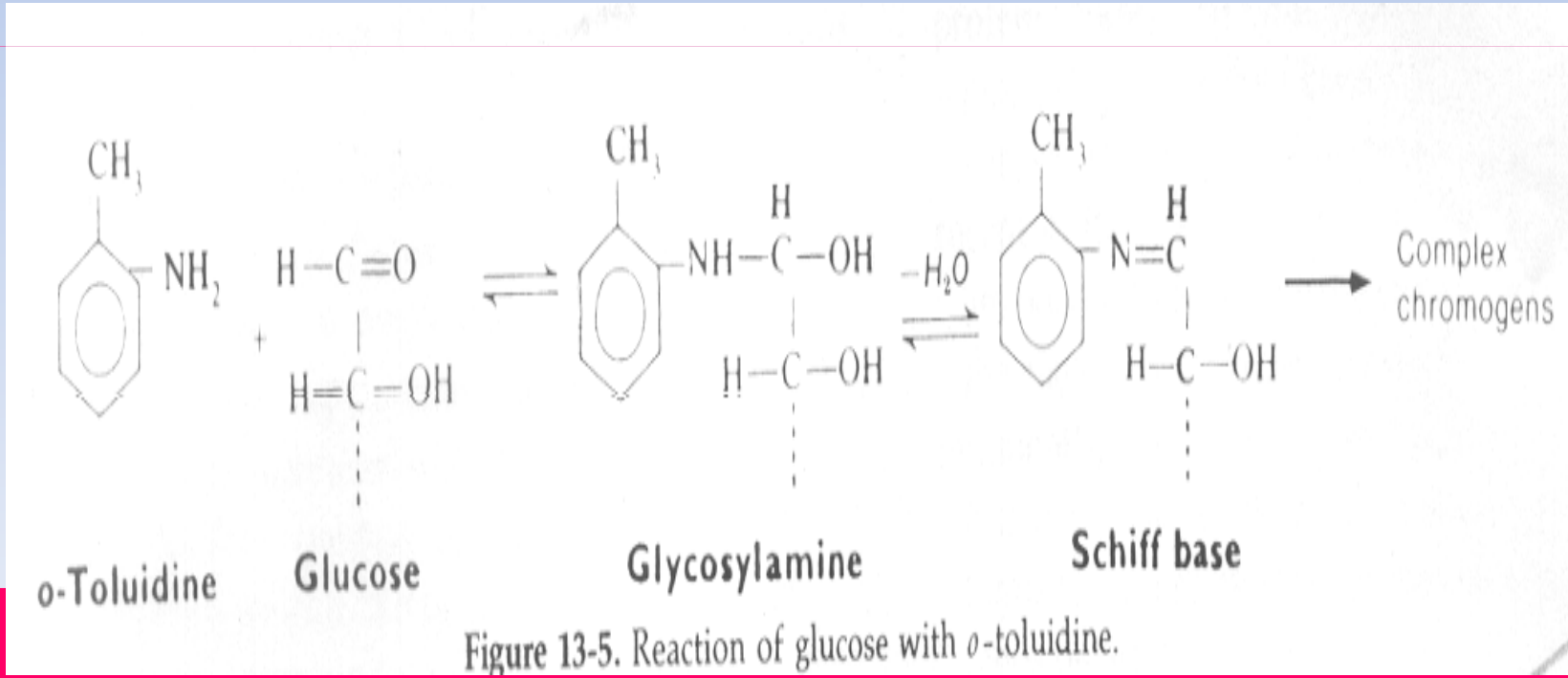


Figure 13-5. Reaction of glucose with *o*-toluidine.

Method

- **Routine laboratory methods:**

1- Fasting blood glucose: not more than 100mg/dl

2- **Glucose tolerance test** (GTT) : the test involves the administration of a standard oral glucose dose (1 g glucose/kg body weight) after an over night fast, blood is collected at frequent intervials (usually 0, 0.5, 1, and 2 hours) and analyzed for blood glucose concentration. The peak value should be less than 160 mg/dl and occurs between 15 – 30 minutes after glucose administration.

Materials

Reagents :

- O – toluidine
- Working standard (100 mg/dl)
- Blood samples
- Distilled water

Method

- Take 4 test tubes and label them T1 (test #2), T2(test #2), S (standard glucose), and B (blank), to each tube add 5 ml of)

  o – toluidine, then pipette:
- 0.1 ml of sample # 1 in T1
- 0.1 ml of sample # 2 in T2
- 0.1 ml of standard glucose in S
- 0.1 ml of water in B
- Shake the tubes very well and put them in a boiling water bath for 10 minutes, remove tubes, cool under tab water and read the absorbance of T1, T2 and S against the blank tube B at 625 nm, record your results.

Results

Calculation :

❖ **Blood glucose level in a test sample:**

- Absorbance of test X 100 (mg/dl) = -------- mg/dl

  Absorbance of std **(Concentration of Standard)**