Glucose metabolism and diabetes mellitus

Dr Zainab Sattar Ali

Al muthanna University

Pharmacy college

* Glucose is the common carbohydrate currency of the body. the different metabolic processes that affect the blood glucose concentration.
* This level is, as always, the result of a balance between input and output, synthesis and catabolism.

Insulin

Insulin is the principal hormone affecting blood glucose levels, its actions is an important on diabetes mellitus. Insulin is a small protein synthesized in the beta cells of the islets of Langerhans of the pancreas.

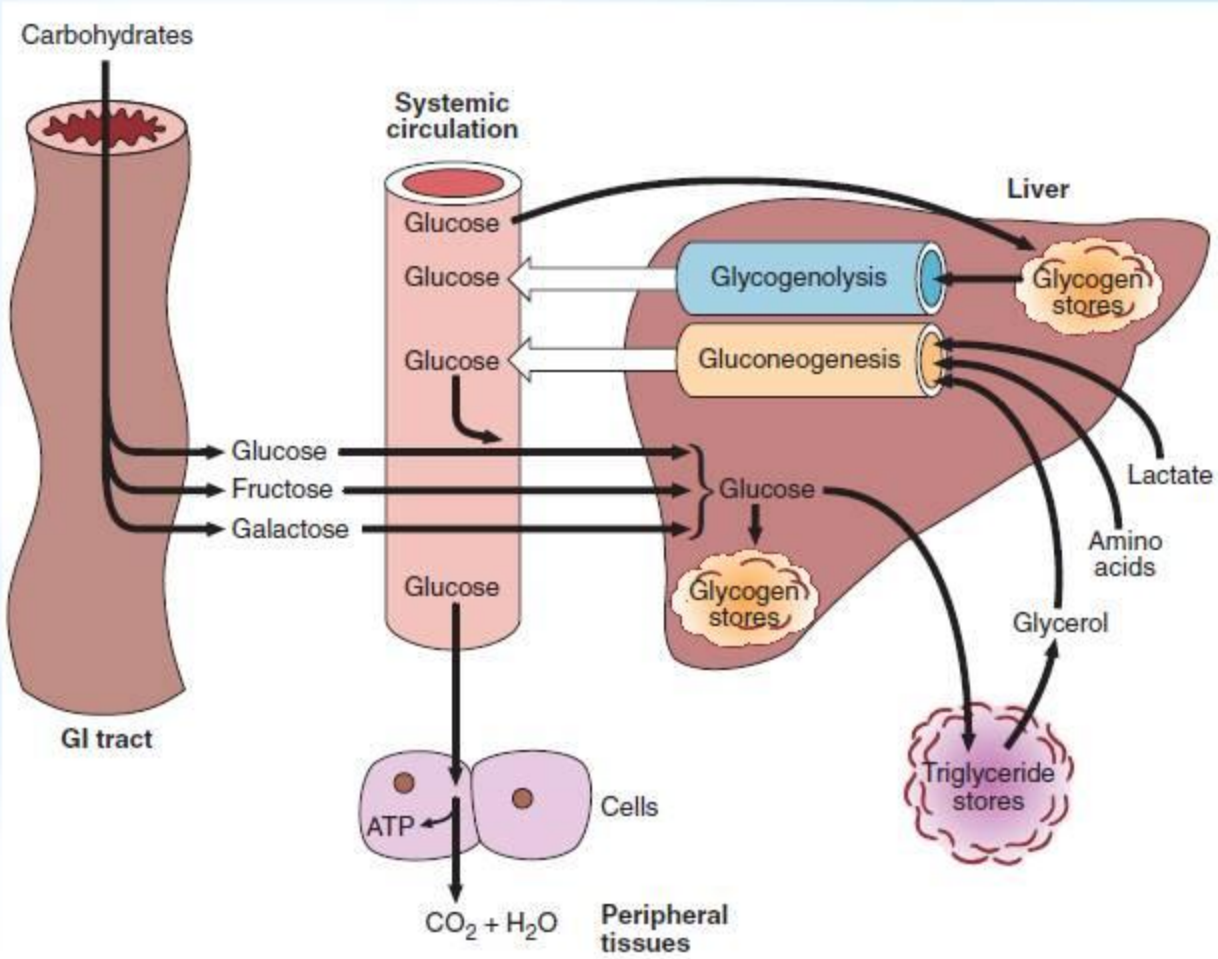
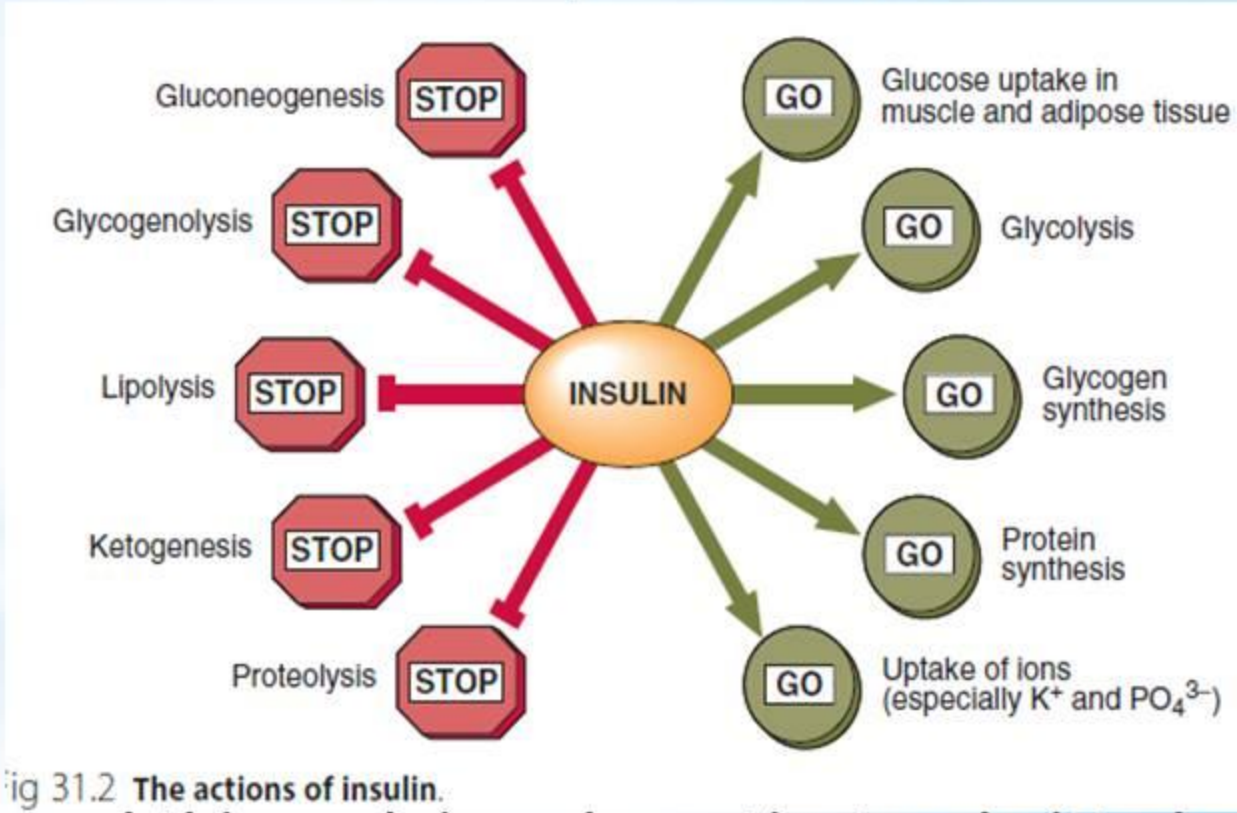


Fig 31.1 **Glucose homeostasis.**

It acts through membrane receptors and its main target tissues are liver, muscle and adipose tissue. Insulin signals 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. It should be noted that glucose cannot enter the cells of most body tissues in the absence of insulin.

*The effects of insulin Are opposed by other hormones, e.g. glucagon, adrenaline, glucocorticoids and growth hormone. These are sometimes called stress hormones, and this explains why patients admitted acutely to hospital often have raised blood glucose.



ig 31.2 **The actions of insulin.**

Diabetes mellitus

Diabetes mellitus is the commonest endocrine disorder . It may be defined as a syndrome characterized by hyperglycaemia due to an insulin resistance and an absolute or relative lack of insulin. Primary diabetes mellitus is generally sub classified into Type 1 or Type 2. diabetes mellitus are shown in Secondary diabetes mellitus may result from pancreatic disease, endocrine disease such as Cushing's syndrome,
drug therapy, and, rarely, insulin receptor abnormalities.

Type 1 diabetes mellitus

Type 1 diabetes accounts for approximately 15% of all diabetic patients. It can occur at any age but is most common in the young, with a peak incidence between 9 and 14 years of age. The absolute lack of insulin is a consequence of the autoimmune destruction of insulin producing beta cells. There may be an environmental precipitating factor such as a viral infection. The presence of islet cell antibodies in serum predicts future development of diabetes.

Type 2 diabetes mellitus

Type 2 diabetes accounts for approximately 85% of all diabetic patients and can occur at any age. It is most common between 40 and 80 years but is now being reported in adolescent and even paediatric populations. In this condition there is resistance of peripheral tissues to the actions of insulin, so that the insulin level may be normal or even high. Obesity is the most commonly associated clinical feature.

Late complications of diabetes mellitus

- Microangiopathy is characterized by abnormalities in the walls of small blood vessels(thickening of the basement membrane).
- Retinopathy may lead to blindness because of vitreous haemorrhage from proliferating retinal vessels, and maculopathy or oedema affecting the macula
- Nephropathy leads in the early stage increased GFR, increased glomerular size and microalbuminuria and ultimately to renal failure.
- Neuropathy may become evident as diarrhoea, postural

foot ulcers due to microangiopathy of nerve blood vessels and abnormal glucose metabolism in nerve cells.

■ Macroangiopathy (or accelerated atherosclerosis) leads to premature coronary heart disease. the dyslipidaemia seen in these patients (increased triglycerides, decreased HDL-cholesterol, and a shift towards smaller, denser LDL) is considered highly atherogenic.

Table 31.1 **Type 1 versus Type 2 diabetes mellitus**

Main features	Type 1	Type 2
Epidemiology		
Frequency in northern Europe	0.02–0.4%	1–3%
Predominance	N. European Caucasians	Worldwide Lowest in rural areas of developing countries
Clinical characteristics		
Age	<30 years	>40 years
Weight	Low/normal	Increased
Onset	Rapid	Slow
Ketosis	Common	Under stress
Endogenous insulin	Low/absent	Present but insufficient
HLA associations	Yes	No
Islet cell antibodies	Yes	No
Pathophysiology		
Aetiology	Autoimmune destruction of pancreatic islet cells	Impaired insulin secretion and insulin resistance
Genetic associations	Polygenic	Strong
Environmental factors	Viruses and toxins implicated	Obesity, physical inactivity

Diagnosis of diabetes mellitus

1. Fasting blood glucose

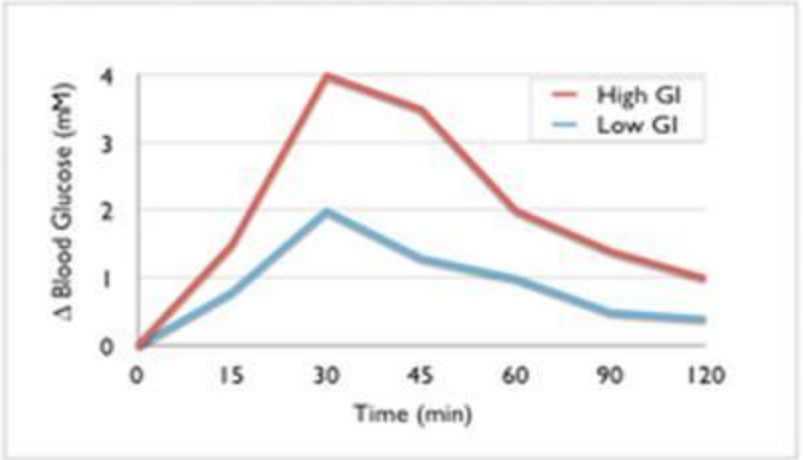
fasting blood glucose concentration of ≥7.0 mmol/L(126 mg/dl) is regarded as diagnostic of diabetes, whether or not hyperglycaemic symptoms are present. The patient should be fasted overnight (at least 10 hours). If the result falls between 6.0 and 6.9 mmol/L, the patient is said to have 'impaired fasting glycaemia'

2- A postprandial glucose test is a blood Glucose test that determines the amount of a glucose in the blood after a meal.

measures blood glucose exactly 2 hours after eating a meal, timed From the start of the meal. By this point blood sugar has usually gone back down in healthy people, but it may still be elevated in people with

Postprandial glucose test

Medical diagnostics



Changes in blood glucose over time following a high and low glycemic index (GI) carbohydrate.

Purpose determines the amount of a type of sugar after a meal

3- The oral glucose tolerance test(OGTT): This was often done where diagnostic confusion still existed despite repeat glucose measurement. glucose tolerance test (OGTT), a standard dose of glucose is ingested by mouth and blood levels are checked two hours later.

Preparation

The patient is instructed not to restrict carbohydrate intake in the days or weeks before the test. The test should not be done during an illness, as results may not reflect the patient's glucose metabolism when healthy. A full adult dose(75 g) should not be given to a person weighing less than 42.6 kg , or the excessive glucose may produce a false positive result. Usually the OGTT is performed in the morning as glucose tolerance can exhibit a diurnal rhythm with a significant decrease in the afternoon. The patient is instructed to fast (water is allowed)

for 8–12 hours prior to the tests. Medication such as large doses of salicylates, diuretics, anticonvulsants, and oral contraceptives affect the glucose tolerance test.

Procedure

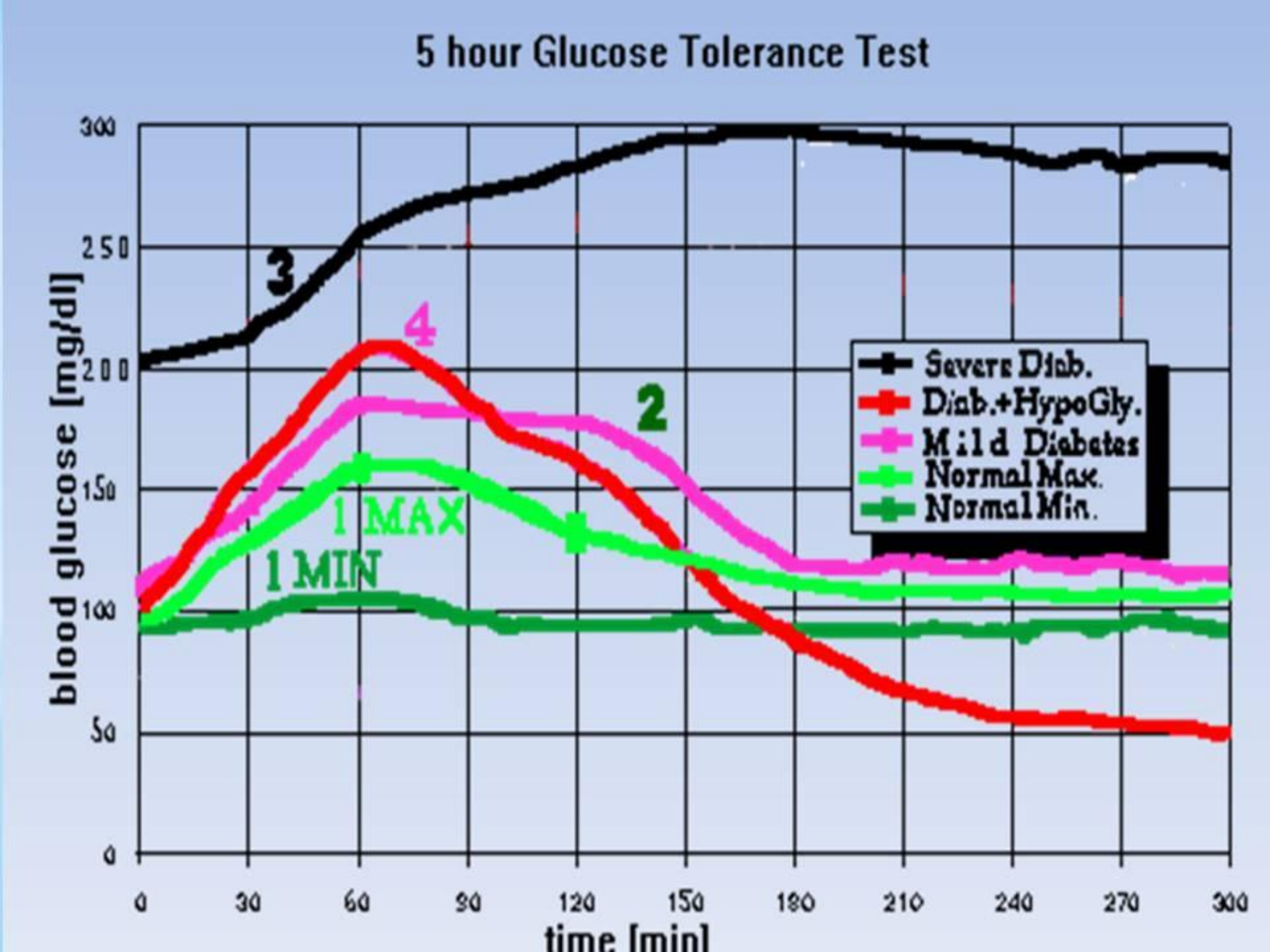
A zero time (baseline) blood sample is drawn.

The patient is then given a measured dose (below) of glucose solution to drink within a 5-minute time frame. Blood is drawn at intervals for measurement of glucose (blood sugar), and sometimes insulin levels. the most important sample is the 2

Table 32.1 **Criteria for the diagnosis of diabetes mellitus**

Fasting blood glucose		
Non-diabetic	**Impaired fasting glycaemia**	**Diabetes**
<6.0	6.0–6.9	≥7.0
Oral glucose tolerance test		
	Fasting	**2-hour**
Impaired glucose tolerance	<7.0	7.8–11.0
Diabetes	≥7.0	≥11.1

All figures refer to glucose concentrations (mmol/L) in venous plasma.


5 hour Glucose Tolerance Test
blood glucose [mg/dl]
time [min]
300
250
200
150
100
50
0
0
30
60
90
120
150
180
210
240
270
300
3
4
2
1 MAX
1 MIN
Severe Diab.
Diab.+HypoGly.
Mild Diabetes
Normal Max.
Normal Min.

4. Measurement of glycosylated –Hb (HbA1C)

- Glycosylated Hb (HbA1c) results from non enzymatic binding of glucose with Hemoglobin .The process is irreversible and continues during the half life of RBCs.
- Normal subjects and controlled cases of DM have 4-8% glycosylated –Hb .
- The increase in the percent of HbA1c is related to the blood glucose level.
- The test is used for follow up of diabetic patients.
- Not affected by fasting or feeding or any factor that affect blood glucose immediately so it gives an idea about the glycemic control of the patient throughout the life span of RBCs (120 days).Also it gives an idea about the efficiency of the drugs used in treatment and adjustment of proper dose.