Glucose Metabolism & Diabetes

Glucose metabolism:

- Glucose is simple sugar or monosaccharide derived from breakdown of dietary carbohydrates and the one that can be easily absorbed
- Non-glucose monosaccharaides including galactose and fructose are converted to glucose by the liver.
- Glucose is the primary source of energy for most body cells; the blood glucose level at any given time is under the control of a number of hormones.
- Insulin a hormone secreted by pancreas, after a meal the hormone responds to high glucose levels, promoting glucose entry into cells depending on the cells need.
- Glucose may undergo anaerobic or aerobic metabolism to yield energy as adenosine triphosphate (ATP).
- Alternatively glucose may be converted to and stored as glycogen (Glycogenesis).
- Most body cells have limited glycogen stores but the liver and skeletal muscles store larger amounts of glycogen.
- Glucose may also be converted under the action of the insulin to protein and fat (Lipogenesis) with the latter stored in adipose tissue.

Important Terms:

Glycolysis: is the metabolism of glucose to obtain energy in the form of ATP and pyruvate

Glycogenesis: is the conversion of glucose into glycogen which is then to be stored in the liver and muscle tissues

Glycogenolysis: is the breakdown and conversion of glycogen into glucose which is then utilized by cells as a source of energy

Gluconeogenesis: is the synthesis of glucose molecules from sources other than carbohydrates like proteins, amino acids and lipids.

The Function of Pancreas:

1. Exocrine function:

   Secretion of digestive enzymes including α-amylase, lipase and protease; which are responsible for the breakdown of carbohydrates (starch and glycogen), lipids and proteins respectively.

2. Endocrine function:
   - Insulin: secreted by the β-cells of islets of Langerhans, which causes the utilization of glucose by body tissues as source of energy and storage
   - Glucagon: secreted by α-cells of islets of Langerhans, which causes the elevation of blood glucose level by releasing it from the storages
   - Somatostatin: secreted by delta cells of the pancreas, this hormone inhibits the secretion of insulin and glucagon. It is also a growth hormone – inhibiting hormone and also has an inhibitory effects on parietal cells of the stomach

Metabolic Effects of Insulin and Glucagon:

Organ	Effect of Insulin	Effect of Glucagon
Whole body	Glycolysis	Inhibit glycolysis
Liver	Promote glucose storage as glycogen (glycogenesis), increase level of triglyceride and VLDL formation	Promote glycogen breakdown and formation of glucose (glycogenolysis) and gluconeogenesis
Muscles	Promote protein synthesis, increase glycogen synthesis and storage (glycogenesis)	Promote protein and amino acid breakdown and formation of glucose as well as glycogenolysis
Adipose tissue	Promote TG and fatty acids storage (lipogenesis)	Stimulate fatty acids breakdown (lipolysis) and formation of keto acids

- Many diseases alter normal glucose metabolism, the most frequent cause of an increase in blood glucose or hyperglycemia is diabetes.
- Hypoglycemia defined as a blood glucose level less than 50mg/dl; and may have severe consequences; one cause of hypoglycemia in-diabetic patients is an excessive dose of insulin.
- The body secrets a number of hormones that increase blood glucose levels but only insulin lowers the blood sugar.

Diabetes Mellitus:

Is defined as an elevated blood glucose associated with absent or inadequate pancreatic insulin secretion, with or without impaired insulin action.

Tests used in the diagnosis of diabetes:

Type of test	Normal Range
Fasting glucose	90 – 110mg/dl
2hr post prandial	<140mg/dl
Oral glucose tolerance	<140mg/dl
Glycated hemoglobin Hb A1c	4-6%

Criteria for testing Diabetes in Adult Individuals:

There are some risk factors contributing in the development of diabetes in the adults, these are:

- Individuals aging 45 and older and specially with body mass index (BMI greater than 25 kg/m^2)
- Family history of diabetes in a first degree relative
- History of gestational diabetes or having a baby heavier than 9 pounds (about 4kg or greater)
- Hypertension (>140/90 mm Hg)
- Low concentration of high density lipoprotein (HDL) (<35 mg/dl) cholesterol and/or elevated triglyceride concentrations (>250 mg/dl)
- History of impaired fasting glucose or impaired glucose tolerance
- Diagnosis of other clinical conditions associated with insulin resistance
- History of vascular disease

Other causes of Hyperglycemia or DM:

In some cases high blood glucose values are caused by conditions other than diabetes. Hyperglycemia can be secondary to traumatic brain injury, febrile disease, and certain liver diseases and over activity of adrenal, pituitary or thyroid Gland and certain drugs like doxazocin (anti-hypertensive).

Symptoms of diabetes:

The primary symptoms of diabetes are:

- excessive urination (polyuria)
- abnormally high blood glucose (hyperglycemia)
- abnormally high urine glucose (glycosuria)
- excessive thirst (polydipsia)
- constant hunger (polyphagia)
- sudden weight loss during acute episodes of disease
- excessive blood ketones (ketonemia)
- excessive urinary ketones (ketonuria) may be detected

These symptoms are all caused by the body's inability to metabolize glucose levels; glycosuria is a consequence of hyperglycemia when the blood glucose exceeds l60 -170mg/dl (the renal threshold for glucose), so glucose appears in the urine.

Hypoglycemia:

Hypoglycemia is a blood glucose concentration below the fasting value with a transient decline in blood sugar 2 hours after a meal. It could be caused by one of the followings:

- Glycogen storage disease associated with impaired breakdown of stored glycogen in the liver causing hypoglycemia
- islet cell hyperplasia and insulinoma

A decrease in blood glucose is life threatening because the brain and cardiac cells depend on glucose in the blood and interstitial fluids.

Long Term Complications of Diabetes Mellitus:

- Cardiovascular Disturbance
- Diabetic macro-angiopathy: like myocardial infarction, stroke, and peripheral vascular disease
- Diabetic micro-angiopathy: like peripheral vascular disease (Diabetic foot), diabetic retinopathy, diabetic nephropathy and peripheral neuropathy
- Infection
- Renal failure
- Blindness

Oral Glucose Tolerance Test (OGTT)

Background:

In a healthy individual the insulin response to a large oral glucose dose is almost immediate. It peaks in 30 to 60 minutes and returns to normal levels within 3 hours when sufficient insulin is present to metabolize the glucose ingested at the beginning of the test.

Indications for OGTT:

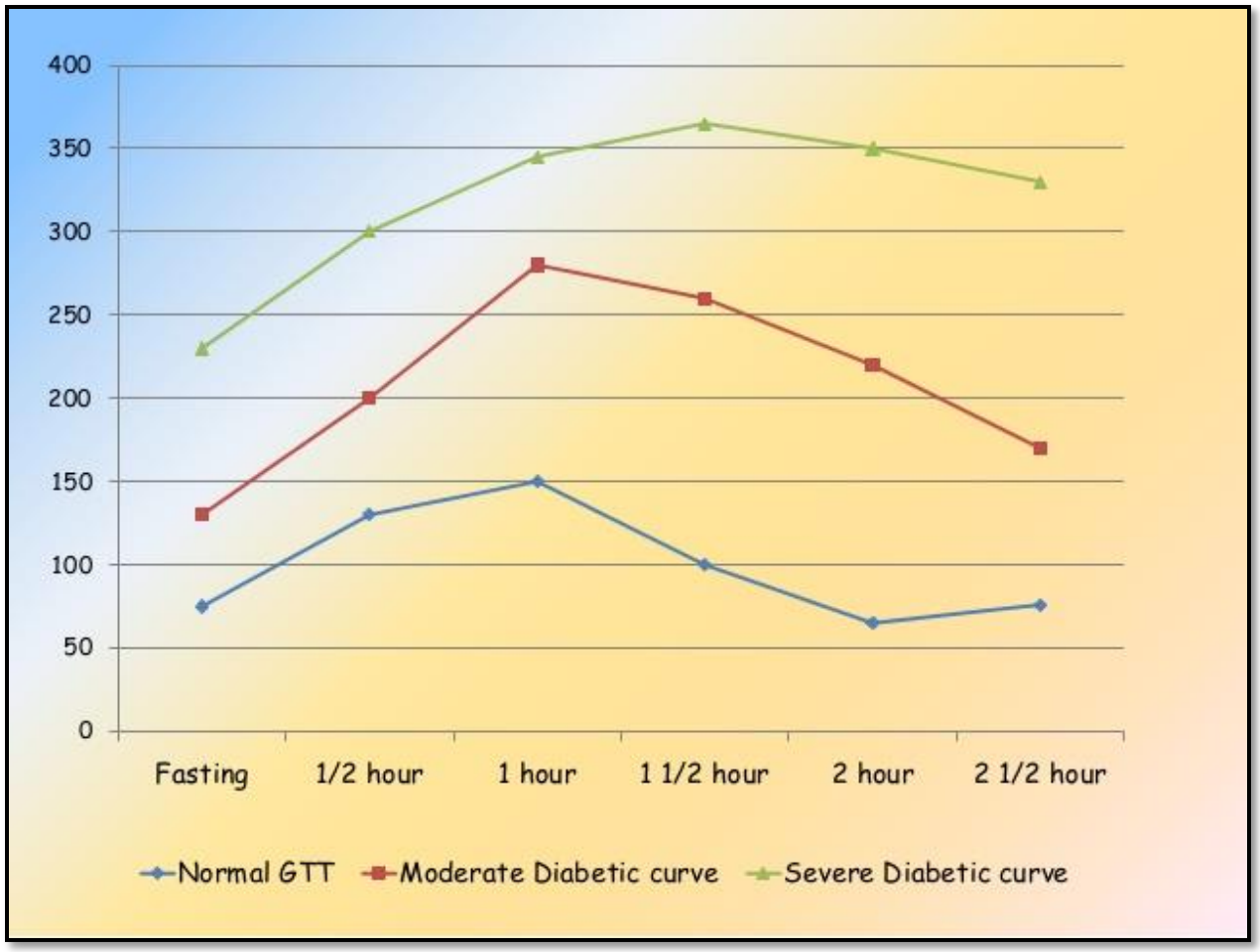
1. Patient has symptoms suggestive of diabetes mellitus
2. Fasting blood sugar value is inconclusive (between 110 – 126mg/dl)
3. During pregnancy, excessive weight gaining is noticed with a past history of big baby (more than 4 kg) or past history of miscarriage
4. To rule out benign renal glycosuria
5. Patients with neuropathies, retinopathies, nephropathies and hypertriglyceridemia of unknown origin

Procedure:

1. Before executing the test, the individual should be fasting for not more than 10 hours
2. Take a blood sample and measure the serum glucose, this reading is considered at zero time (either venous blood or capillary blood)
3. Dissolve about 75gm of glucose in a full glass of water (about 250ml of water) and administer it to the patient (taking in consideration that the whole glass of glucose in water should be drunk)
4. After 30 min take another sample of blood and measure the serum glucose (there should be a sharp increase in blood glucose)
5. Repeat the measurement of blood glucose every 30 min till you complete a full 2 hours and record the results

Normal Values of Glucose in OGTT:

- Fasting value: 90 – 110 mg/dl
- 30 min later: 110 – 170 mg/dl
- 60 min later: 120 – 170 mg/dl
- 2 hours later: 90 – 120 mg/dl
- 3 hours later: 90 – 120 mg/dl



Oral Glucose Tolerance Test Curve of Normal and Diabetic Patients