Urinary glucose

Glycosuria : concentration of urinary glucose detectable using relatively insensitive but specific screening test , this occurs only when glomerular reabsorptive capacity exceeded and this occurs because :-

1-plasma and glomerular filtrate glucose concentration more than 180 mg /dl (10 mmol/ L.

2-The glomerular reabsorptive capacity is reduced as in pregnancy (renal glycosuria)

Glycosuria should be sought in a urine specimen produced by the kidneys , collected about an hour after a meal (peak plasma concentration) by double void technique ,i.e. : the patient should empty the bladder and discard the specimen , then a further specimen passed after 10-15 minutes is collected and tested . Reducing substances in urine can be detected by using copper containing reagent (clinitest tablets) , in neonatal period we use this test rather than one specific test for glucose to detect inborn error metabolism such as Galactosemia .

Hyperglycemia and diabetes mellitus

Hyperglycemia may be due to :-

1- Diabetes mellitus .

2- Intravenous infusion of glucose-containing fluids .

3- Sever stress (temporary effect) such as cerebrovascular accident.

Diabetes mellitus

Diabetes mellitus is caused by absolute or relative deficiency of insulin . It is defined by WHO as:-

- a fasting plasma glucose concentration grater than 126 mg/dl or

- grater than 200mg/dl 2 hours after carbohydrate meal or 2 hours after oral ingestion of 75 g of glucose .

It is classified into the following categories :-

1-Insulin dependent diabetes mellitus (Type 1), insulin therapy is essential otherwise the patient prone to develop ketoacidosis .It is usually present during childhood so it may called juvenile diabetes . deficiency of insulin is due to b-cells destruction by autoimmunity or viral disease or unknown cause .

2- Non insulin dependent diabetes mellitus (Type 2) patient is less likely develop ketoacidosis , although insulin may some times needed but it is not essential for life .onset usually during adult life and there is a familial tendency .Some inherited disorders may cause it they are :- reducing insulin secretion , resistance to insulin action and post receptor defects despite high insulin concentration. Risk factors are obesity ,sustained stress and sedentary life style .

3-Diabetes mellites associated with other conditions includes :-

- Absolute insulin deficiency secondary to pancreatic disease i.e. :chronic pancreatitis .
- Relative insulin deficiency due to excessive growth hormone (acromegaly) or corticoid (Cushing's syndrome).
- Drugs such as steroids and thiazide .

Impaired glucose tolerance

It is a finding of a fasting venous plasma glucose concentration between 100 and 125 mg/dl and/or plasma glucose concentration of between 126 and 200 mg/dl 2 hours after taking a standard glucose load .

secondary causes should be sought and dietary advice given if necessary .

Clinical and metabolic features of insulin dependent diabetes mellitus

Hyperglycemia is an invariable finding . If plasma glucose concentration exceed about 10 mmol/L and renal function is normal there will be glycosuria , polyuria ,polydipsia , these classical symptoms of diabetes mellitus are only present in advanced cases

Abnormalities in lipid metabolism may be secondary to insulin deficiency . lipolysis is enhanced and plasma free fatty acids increase which is converted to acetyl co A and Ketones .or re-esterified to form endogenous triglycerides and incorporated into VLDL, This will accumulate because insulin is needed for activity of lipoprotein lipase for catabolism of VLDL ,chylomicronemia may occurs and cholesterol synthesis also increase with increase in in LDL , muscle westing due to protein breakdown

Long term effects

- Macrovascular disease .
- Microvascular disease , affect retina (diabetic retinopathy) and kidney .
- Kidney disease , including proteinuria and progressive renal failure , nephrotic syndrome . the presence of small amount of albumin in the urine (microalbuminuria) is associated with increased risk of developing progressive renal disease .
- Glycation of hemoglobin and plasma protein may also occur , and may assayed to assess , retrospectively , long term diabetic control .
- Infections and may aggravated the condition .
- Infants born to women with poorly controlled diabetes tend to be large at birth and to have an increased risks of fetal abnormalities .

Management of diabetes mellitus

Blood glucose concentration may be measured by the patients themselves using glucose oxidase strips read visually or by using portable reflectance meter which should be checked regularly by laboratory staff .

*Glycated hemoglobin(Hb A1c) expressed as a percentage of total hemoglobin concentration gives a retrospective assessment of the mean plasma glucose concentration during the last 6 to 8 weeks , the higher the percentage the poorer the diabetic control .

In type1 diabetes , insulin requirements vary in patients for example the dose may need to increase during illness or during pregnancy . type 2 diabetes may be controlled by diet , weight reduction or treated by sulphonylurea drugs(tolbutamide or glibenclamide) . biguanides (metformin or phenformin) may be given but they have risk of Lactic acidosis .

Ketosis

Adipose tissue cells in conjunction with liver convert excess glucose to triglycerides and store it in adipose tissue as a source of energy.

In the liver triglycerides are formed from : First -Glycerol 3 phosphate (from triose phosphate)

Second - Fatty acids (from acetyl co A)

The triglycerides are transported to adipose tissue cells incorporated in VLDL and stored in adipose tissue as a source of energy.

During fasting when exogenous glucose is unavailable , plasma insulin concentration will become low so endogenous triglycerides converted to free fatty acids and glycerol by lipolysis. Glycerol enters the hepatic gluconeogenesis pathway to give glucose thus minimizing the fall in glucose concentration

Most tissues other than the brain can oxidize fatty acids to acetyl co A which can be used in tricarboxylic acid cycle (TCA) as an energy source , when the rate of production exceeds the hepatic cells use, condensation of acetyl co A will give Acetoacetic acid which is converted to Acetone. these Ketones can be used as an energy source by brain and other tissues when glucose in short supply .

Therefor Ketosis occurs when fat stores used as the main source of energy as in fasting ,Vomiting ,Starvation (Ketotic hypoglycemia) , and in diabetic ketoacidosis which associated with hyperglycemia, diabetic hyperglycemia is due to low insulin activity.

Ketosis always reflects excessive use of fat as an energy source due to : -

1-intracellular glucose deficiency .

2- low insulin activity .

Lactic acidosis

Glucose which entered to muscle is stored as glycogen which can not be reconverted to glucose because of the absence of G 6 phosphatase in the muscle , and it can supply local needs only . during muscular activity glycogenolysis is stimulated by Adrenalin (Epinephrine) , the resultant G 6 P is metabolized by glycolysis and in

T C A cycle to supply energy .

The rate of glycolysis may exceed the availability of Oxygen needed in T C A cycle and glycolytic products may then accumulate , so in an aerobic glycolysis :-

Glucose ----------→ 2 Lactate + 2 H .

Under normal conditions this lactate go to the liver and converted to glucose (cori cycle) .Under aerobic conditions liver consumes much more lactate than it produced .