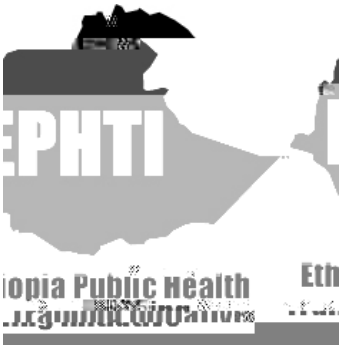
MODULE

# Diabetes Mellitus

For the Ethiopian Health Center Team

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**Important Guidelines for Printing and Photocopying**

# ACKNOWLEDGMENTS

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# UNIT ONE

# INTRODUCTION

## 1.1 Purposes and Use of the Module

This module is intended to serve as a general learning material for diabetes mellitus by the health center team.

This module can also be used by other categories of health professionals. It should be

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**2.1.2.2 Bsc Nurses**

Answer the following questions on the separate sheet

1. Which of the following is the best time for short acting insulin administration?
    A. Morning before meal
    B. Morning after meal
    C. At any time through a day
    D. Evening only
2. Which action would be **inappropriate** to include in diabetic teaching plan?
    A. Changing position hourly to increase circulation
    B. Inspect legs and feet's daily for any change
    C. Keep legs elevated on two pillows
    D. Keep insulin not in use in the refrigerator
3. Which statement is **true** regarding diabetes?
    A. Diabetes is an acute disorder that responds only to insulin treatment
    B. Diabetes is chronic disorder that responds only to insulin treatment
    C. Diabetes is an abnormality of carbohydrate, fat, protein metabolism
    D. All of the above
4. One of the following is **not** the site for subcutaneous injection during management of diabetes mellitus.
    A. Outer aspects of the upper arms
    B. Anterior thigh
    C. Abdomen
    D. All
    E. None
5. A boy age 7 recently was diagnosed with type 1 diabetes mellitus .He takes NPH and regular insulin. His mother asks the nurse if he can go on an after noon foot ball playing during an upcoming weekend. Which response by the Nurse would be the best?
    A. He should have a snack, such as cheese, sandwich and a glass of milk, an hour before the play and should carry a fast acting source of glucose

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## Part II True / False questions

a. There is no cure for Diabetes T/F
b. Glucose is mainly made in the kidney T/F
c. 'A' cells in the Islets of Langerhans produce insulin T/F
d. Many complications of Diabetes are avoidable T/F
e. Diabetes is more common in obese people T/F
f. Glucagon is used to treat hyperglycemia T/F
g. In infections the blood sugar level goes down T/F
h. Raised blood pressure should always be treated in the
i. Diabetic patient T/F
j. Diabetics should routinely test their urine for ketones T/F
k. Ketoacidosis and vomiting in a diabetic is a life-threatening
l. situation T/F
m. Short-acting insulin acts for about 1 hour T/F
n. The main problem to address in diabetes is the normalization
o. of blood sugar levels T/F
p. Blisters on a diabetic foot are often painless T/F
q. All available insulin's contain 100U per ml T/F
r. Refined carbohydrates are unrestricted in a diabetic diet T/F
s. Fiber is unrestricted in a diabetic patient T/F
t. Hypertension is only important when proteinuria is present T/F
u. The ischaemic foot is characterized by absent pulses T/F
v. Diabetic Autonomic Neuropathy can cause impotence T/F
w. The feet should be checked at every follow up visit T/F
x. Infection can cause loss of glycaemic control T/F

**Part II Case study**

10. Ato Kebede, a newly diagnosed type1 patient is admitted to the medical ward. You further assessed him and found that patient has polyphagia polydypsia and weight loss. The physician ordered lente insulin for him.

A. You planned to teach Ato kebede about self-injection of insulin. What are the important points that should be included in your teaching plan?
B. One of the acute complications of diabetic mellitus is hypoglycemia. What are the causes of hypoglycemia in a diabetic patient like Ato Kebede?
C. How do you explain the signs of hypoglycemia for Ato Kebede?
D. How do you prevent the complication of hypoglycemia?
E. It is known that majority of lower extremity amputation are performed in a diabetic patient like Ato kebede. What are the diabetic complications contributing to foot infections?
F. Mention at least 6-foot care instruction to be given for Ato Kebede.

### 2.1.2.3 Medical laboratory technologists

**Instructions:** choose the appropriate answer from the alternatives given for each question and write the answers on a separate sheet of paper.

1. Why is there a discrepancy between the whole blood glucose concentration and the plasma glucose concentration?
    A. Because there is a different distribution of Glucose in whole blood and plasma
    B. Because there is a high amount of water in plasma
    C. Because the cellular component in whole blood use glucose frequently
    D. None

2. One of the following methods of Glucose determination does use enzymatic reaction
    A. Folin- MU copper Reduction method
    B. Alkaline ferric cyanide method
    C. Hexokinase n.v. method
    D. Somogyi-Nelson method

3. Which of the following method is highly specific for glucose determination
    A. Alkaline ferric cyanide method
    B. Copper Reduction method
    C. Glucose oxidase method
    D. O-Toluidine method
4. When does glucose appear in the wine
    A. When the urine glucose level higher than blood glucose level
    B. When blood glucose level is between 60-11omg/de
    C. When the blood glucose level is greater than 180-200 mg/dl
    D. When a person is started
5. One of the following methods for urinary glucose determination is highly specific
    A. Copper reduction method
    B. O-Toluidine method
    C. Reagent strip Tests
    D. A and B
6. Sodium fluoride additive used in a specimen collected for Glucose
    A. Inhibits glycol tic enzymes from destroying the glucose
    B. Precipitates the protein present
    C. Prevents non glucose reducing substances from interfering with the testing
    D. None of the above
7. In a person with normal glucose metabolism, the blood glucose level usually increases rapidly after carbohydrates are ingested, but returns to a normal level after
    A. 30 minute
    B. 60 minute
    C. 90 minute
    D. 15 minute
8. Which of the following organs uses glucose from digested carbohydrates and stores it as glycogen for later use as a source of immediate energy by the muscles?

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abdominal pain, easy fatigability and blurred vision of one-week duration. His condition slowly deteriorated in the period of time that he has been ill and he was drowsy.

The health officer on duty examined him and the findings were an acutely sick looking

**DEFINITION**

Diabetes Mellitus is a clinical syndrome comprising a heterogeneous group of metabolic diseases that are characterized by chronic hyperglycemia and disturbances in carbohydrate, fat and protein metabolism secondary to defects in insulin secretion, insulin action or both.

**CLASSIFICATION OF DIABETES MELLITUS**

Based on the pathologic process considered to be responsible for hyperglycemia, diabetes mellitus can be classified into

- **Type 1 Diabetes Mellitus**
  - Autoimmune destruction of the pancreatic islet β-cells with absolute loss of insulin secretion
  - In few patients the pathogenesis remains idiopathic

- **Type 2 Diabetes Mellitus**

  - is a heterogeneous group of disorders usually characterized by variable degrees of insulin resistance, impaired insulin secretion, β-cell dysfunction and dysregulated hepatic glucose production

- **Other specific subtypes of Diabetes Mellitus**

  Genetic defects of β-cell function
  Genetic defects of insulin action
  Diseases of the exocrine pancreas
  - when the majority of pancreatic is

only 0.5%. 86% of the study subjects were under 20 years of age, however, and the figure for those above 40 was found to be 2.4%.

**CLINICAL FEATURES**

Classical symptoms

- Thirst
- Polyuria
- Nocturia
- Rapid weight loss
- Increased susceptibility to infection in patients with uncontrolled diabetes
- Chronic fatigue and malaise

Signs

-

**DIAGNOSIS**

Criteria for the Diagnosis of Diabetes Mellitus

Symptoms of diabetes plus random blood glucose concentration ≥200 mg/dL

Or

Fasting plasma glucose≥ 126 mg/dL

Or

Two-hour plasma glucose≥ 200 mg/dL during an oral glucose tolerance test

In the absence of unequivocal hyperglycemia and acute metabolic decompensation, these criteria should be confirmed by repeat testing on a different day.

**COMPLICATIONS OF DIABETES MELLITUS**

- May be classified into acute and chronic complications
- Acute complications are
  - Á Diabetic ketoacidois
  - Á Nonketotic hyperosmolar state
  - Á Hypoglycemia
- Chronic complications
  - Á Affect many organ systems
  - Á Are responsible for the majority of morbidity and mortality associated with the disease
  - Á Can be subdivided into vascular and non-vascular complications
  - Á This division is rather arbitrary since it is likely that multiple pathogenic processes are involved in all forms of complications.
  - Á The vascular complications are further subdivided into

Á Microvascular complications that includes

- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy

Á Macrovascular complications

- Coronary artery disease

## MANAGEMENT

## OVERALL PRINCIPLES

The goals of therapy for patients with type 1 or type 2 diabetes mellitus are to:

- eliminate symptoms related to hyperglycemia,
- reduce or eliminate the long-term microvascular and macrovascular complications of diabetes mellitus and
- allow the patient to achieve as normal a life-style as possible

The care of an individual with either type 1 or type 2 diabetes mellitus requires a multidisciplinary team.

Patient education, dietary management and exercise play a central role in managing diabetic patients in addition to pharmacologic therapy.

### Patient Education

- It should be viewed as a continuing process with regular visits for reinforcement and not just a one-time affair.
- Involves education of the patient and family members about a number of issues important for optimal diabetes care, including
    - self-monitoring of blood glucose
    - urine ketone monitoring ( for those with type 1 diabetes mellitus)
    - insulin administration, if necessary
    - guidelines for diabetes management during illnesses
    - management of hypoglycemia
    - foot and skin care
    - diabetes management before, during, and after exercise
    -

**Dietary Management**

This involves optimal coordination of caloric intake with other aspects of diabetes therapy like insulin, exercise and weight loss

**Aims of Dietary Management**

- Abolish symptoms of hyperglycemia
- Avoid hypoglycemia associated with therapeutic agents (insulin, oral glucose lowering agents)
- Reduce overall blood glucose and minimize fluctuations
- Avoid atherogenic diets or those which may aggravate diabetic complications (e.g. high protein intake in nephropathy)
- For a patient with type 1 diabetes mellitus the aim of dietary management is to coordinate and match the caloric intake, both temporally and quantitatively, with the appropriate amount of insulin.
- In type 2 patients, it should address the greatly increased prevalence of cardiovascular risk factors (hypertension, dyslipidemia, obesity) and disease in this population. The majority of these individuals are obese, and weight loss is strongly encouraged and should remain an important goal
- Food intake must be spread evenly throughout the waking hours and taken at regular times in relation to the insulin dose.
- Patients should be advised to spread whatever food is available through the day and the reasons explained.
- The diet should be balanced in relation to its composition of fats

**General Dietary Instructions**

Food items the diabetic should avoid (rapidly absorbed carbohydrates)

Sugar, honey, jams, candy, marmalade

Cakes, Sweet Biscuits

Soft drinks (Coca Cola, Mirinda etc )

Alcohols

Foods which the diabetic can take with restrictions

Food items from grains: enjera, bread, kinche, kita, atmit

Foods items prepared from peas, beans, lentils, chick peas

Potato, sweet potato, kocho, bulla

Food items the diabetic can take fr

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Insulin antibodies

Local allergy

Lipodystrophy at insulin injection sites

Insulin Preparations

Main types of therapeutic insulin

| | |
|---|---|
| Species | Bovine |
| | Porcine |
| | Human |
| Purity | Conventional |
| | Single peak |
| | Highly purified |
| Duration of action | Short |
| | Intermediate |
| | Long |

**MANAGEMENT OF THE TYPE 2 DIABETIC PATIENT**

**Goals of Therapy**

- Improved glycemic control
- Treatment of conditions associated with type 2 diabetes mellitus
    - Obesity
    - hypertension
    - Dyslipidemia
    - Cardiovascular disease
- Detection and management of diabetes mellitus related complications

In a newly diagnosed type 2 diabetic, one should resort first to dietary management and exercise before embarking on pharmacologic measures.

Glycemic control is reassessed and if response is not achieved, pharmacologic agents may be tried.

Oral glucose lowering agents are preferred as the initial choices to lower serum glucose levels.

As type 2 diabetes is a progressive illness, monotherapy is seldom successful in the long term.

Therapy is initiated with one class of agent, depending on patient characteristics and a second agent is added if adequate glycemic contro6gen42y5Tchieved.

**Groups of Oral Antidiabetic Agents with Examples**

Sulphonylureas

Glibenclamide

Biguanides

Metformin

Alpha-glucosidase inhibitors

Acarbose

Thiazolidinediones

Troglitazone

**PREVENTION AND CONTROL**

**Screening**

Many patients with diabetes mellitus are unaware that they have diabetes mellitus and type 2 diabetes mellitus may be present for up to a decade before diagnosis.

Many patients with type 2 diabetes mellitus have one or more of diabetes mellitus related complications at diagnosis.

For the above reasons, it is recommended to screen those at risk of developing diabetes mellitus using fasting blood glucose.

This includes

- Those above 45 years of age every three years
- Those with family history of diabetes mellitus (parent or sibling with type 2 diabetes mellitus)
- Obesity as evidenced by BMI$\geq$ 27Kg/$m^2$

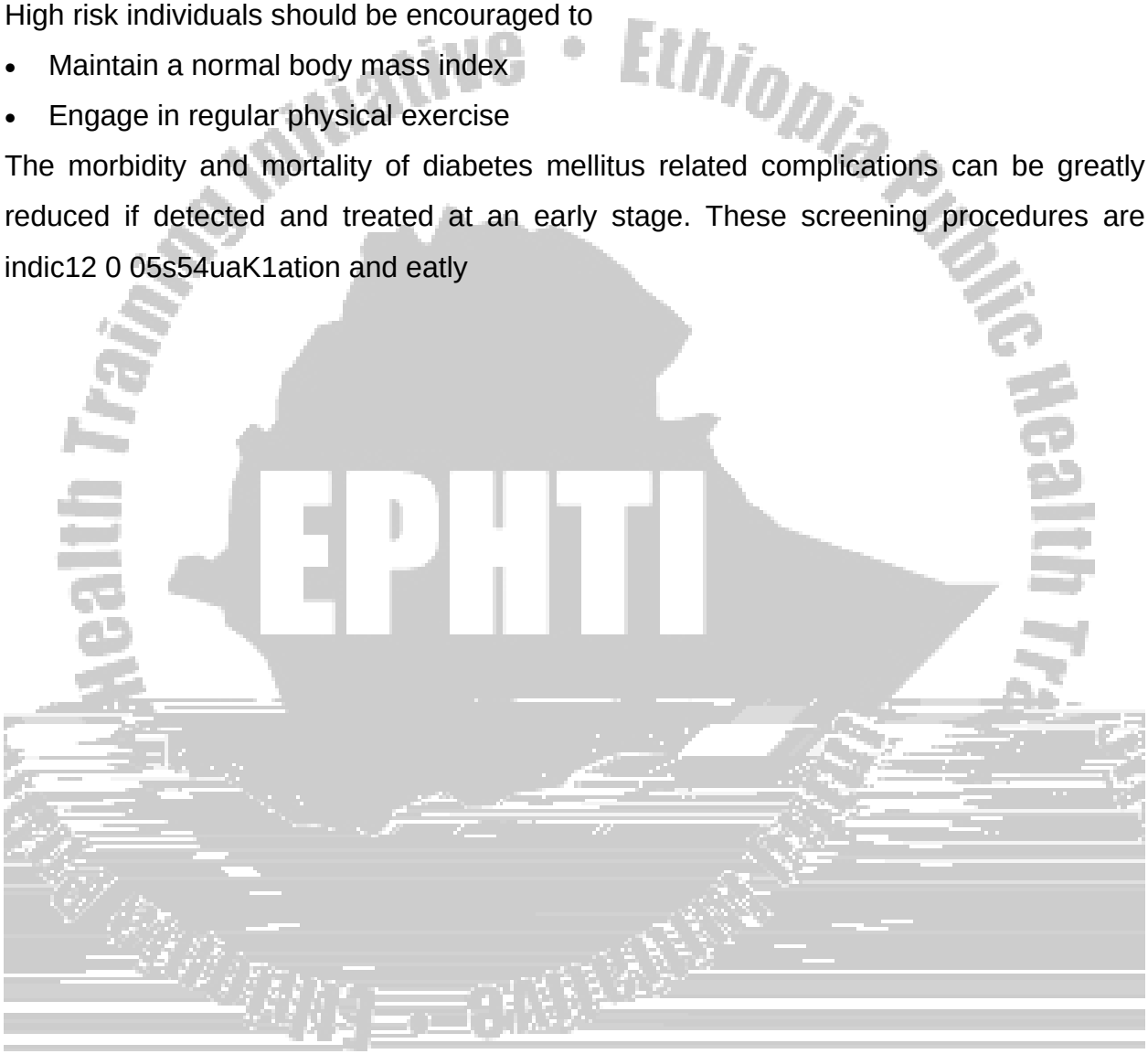
- History of delivering a baby weighing above 4Kg or previous episode of gestational diabetes mellitus
- Hypertension

A number of lifestyle modification and pharmacologic agents are suggested to prevent or delay its onset.

High risk individuals should be encouraged to

- Maintain a normal body mass index
- Engage in regular physical exercise

The morbidity and mortality of diabetes mellitus related complications can be greatly reduced if detected and treated at an early stage. These screening procedures are indic12 0 05s54uaK1ation and eatly



- Abdominal pain
- Shortness of breath
- Blurred vision
- Weight loss
- Altered mental state

**Physical findings**

- Tachycardia
- Hypotension
- Tachypnea/respiratory distress

- Impaired peripheral glucose utilization

Ketosis results from a marked increase in free fatty acid release from adipocytes, with a resulting shift toward ketone body synthesis in the liver. Reduced insulin levels, in combination with elevations in catecholamines and growth hormone, lead to an increase in lipolysis and release of free fatty acids. Normally, these free fatty acids are converted to triglycerides or very low density lipoproteins (VLDL) in the liver, but in DKA, hyperglucagonemia alters hepatic metabolism to favor ketone body formation.

Average losses of Fluid and Electrolyte in DKA of moderate severity

- Water: 6 Liters
- Sodium: 500 mmol
- Chloride: 400 mmol
- Potassium:350 mmol

**Precipitating Events**

- Inadequate insulin administration
- Infection (pneumonia, UTI, gastroenteritis, sepsis)
- Infarction (cerebral, coronary, mesenteric, peripheral)
- New onset diabetes
- Drugs

**Laboratory Abnormalities and Diagnosis**

DKA is characterized by

- Hyperglycemia RBS>250mg/dL,
- Ketosis
    - Ketone bodies positive at serum dilution of $\geq$1:2
    - Ketonuria of 2+ or above
- Metabolic acidosis (increased anion gap)
    - $P^H$ of 7.3 or lower and a bicarbonate level of $\leq$15 mEq/L

Despite a total-body potassium deficit, the serum potassium at presentation is typically at the high end of the normal range or mildly elevated secondary to the acidosis.

**TREATMENT**

- Rehydration
- Insulin
- Treatment of the precipitating cause when applicable
- Management of acid base disturbance
- Management of electrolyte imbalance
- Supportive care
- Resumption of subcutaneous insulin therapy once patient is out of the state of DKA
- Patient education

With appropriate therapy, the mortality of DKA is low (<5%).

Mortality is related more to the underlying or precipitating event, such as infection or myocardial infarction.

**Complications of DKA**

- The major non-metabolic complication of DKA therapy is cerebral edema, which most often develops in children as DKA is resolving.
    - Over replacement of free water should be avoided.
- Venous thrombosis and adult respiratory distress syndrome occasionally complicate DKA.
- Disseminated intravascular coagulation (rare)
- Acute circulatory failure

**NON-KETOTIC HYPEROSMOLAR COMA**

It is the second major clinical presentation of uncontrolled diabetes mellitus.

It is almost exclusively seen in patients older than 60.

Precipitating factors include

Drugs like beta-blockers

Parenteral and enteral feeding

Excessive intravenous glucose administration

As with DKA, osmotic diuresis is central to the pathogenesis but this develops more slowly.

Dehydration is made worse by limited access to water and by the reduced perception of thirst in the elderly.

Non-ketotic heperosmolar coma is characterized by marked hyperglycemia and loss of water up to 25% of body weight in severe cases.

**Differences between DKA and Non-Ketotic Hyperosmolar Coma (HONK)**

| | DKA | HONK |
|---|---|---|
| Age | Any age | >60 |
| Presentation | Hours to days | Days or weeks |
| Mortality | 5%overall | 50% |
| Serum glucose | High | Very high |
| Serum osmolality | High | Very high |
| Serum sodium | Normal or low | Normal or high |
| Bicarbonate | Low | Normal or slightly low |
| Ketonuria | Present | Absent |

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**CAUSES**

Most commonly occurs as a side effect of the treatment of diabetes mellitus. Incidence increases with attempts to achieve euglyemia with tight control of glucose concentrations

Other causes in patients with diabetes include

- Overdose of insulin or oral agents
- ill timed administration of insulin or oral agents
- administration of the wrong type of insulin
- Missed or delayed meals or snacks
- Uncompensated exercise
- Alcohol consumption
- Concomitant chronic renal failure
    - insulin clearance is reduced in patients with chronic renal failure

Hypoglycemia can cause significant morbidity and can be lethal, if severe or prolonged. It should be considered in any patient who presents with confusion, altered level of consciousness, or seizures.

The central nervous system can not synthesize glucose or store enough glycogen for more than a few minutes' glucose supply.

The brain cannot use free fatty acids as an energy source, and ketone bodies, which are generated late, are not useful in acute hypoglycemia. Significant hypoglycemia, therefore, can cause both acute and chronic brain dysfunction.

**Morbidity related to severe hypoglycemia in diabetic patients**

CNS

- Coma
- Convulsions
- Brain damage
- Impaired cognitive function, Intellectual decline
- Vascular events: TIA, stroke

Adrenergic symptoms are mediated by norepinephrine released from sympathetic postganglionic neurons and the release of epinephrine from the adrenal medullae. Increased sweating is mediated by cholinergic sympathetic nerve fibers.

**Neuroglycopenic signs and symptoms**

Neuroglycopenic symptoms are the direct result of central nervous system neuronal glucose deprivation.

Signs and symptoms include

- Confusion
- Odd behavior
- Inability to concentrate
- Drowsiness
- Visual disturbance
- Tingling around the mouth
- Convulsions
- Focal neurologic deficits e.g. hemiplegia
- Coma

**TREATMENT**

Urgent treatment is necessary in patients with suspected hypoglycemia.

Blood should be drawn, whenever possible, before the administration of glucose to allow documentation of the plasma glucose level.

Oral treatment with glucose tablets or glucose-containing fluids, candy, or food is appropriate if the patient is able and willing to take these. A reasonable initial dose is 20 g of glucose. If neuroglycopenia precludes oral feedings, parenteral therapy is necessary. Intravenous glucose (25 g) should be given using a 50% solution followed by a constant infusion of 5 or 10% dextrose. If intravenous therapy is not practical, subcutaneous or intramuscular glucagon can be used, particularly in people with type 1 diabetes mellitus. Because it acts primarily by stimulating glycogenolysis, glucagon is ineffective in glycogen-depleted individuals (e.g., those with alcohol-induced hypoglycemia). These treatments raise plasma glucose concentrations only transiently,

and patients should be encouraged to eat as soon as they are alert in order to prevent a recurrence.

## CHRONIC COMPLICATIONS OF DIABETES MELLITUS

The microvascular complications of both type 1 and type 2 DM result from chronic hyperglycemia. It is also suspected that a genetic susceptibility for developing particular complications exists.

Evidence implicating a causative role for chronic hyperglycemia in the development of macrovascular complications is less conclusive.

Dyslipidemia and hypertension also play important roles in macrovascular complications.

Three major theories have been proposed to explain how hyperglycemia might lead to the chronic complications of diabetes mellitus. These are

- formation of advanced glycosylation end products (AGEs) via the nonenzymatic glycosylaton of cellular protein
- increased glucose metabolism via the sorbitol pathway
- increased formation of diacylglycerol leading to activation of certain isoforms of protein kinase C (PKC), which, in turn, affect a variety of cellular events that lead to diabetes mellitus-related complications

Studies have provided definitive proof that reduction in chronic hyperglycemia can prevent many of the early complications of type 1 DM.

The development of chronic complications correlates with the duration of diabetes and glycemic control

### Ophthalmologic Complications of Diabetes Mellitus

Diabetes mellitus is a leading cause of blindness in the working population in the developed world

Blindness is primarily the result of progressive diabetic retinopathy and clinically significant macular edema.

Diabetic retinopathy is classified into two stages. These are non-proliferative and proliferative retinopathy.

- Microalbuminuria
    - defined as excretion in a 24-h period of 30 to 300 mg/d of albumin (incipient nephropathy)
- Established nephropathy
    - Á Overt proteinuria (Urinary protein >300 mg/d)
- Á Dipstick positive
- End stage renal disease
    - Á Renal failure that requires dialysis or transplantation

The optimal therapy for diabetic nephropathy is prevention.

Interventions effective in slowing progression from microalbuminuria to overt nephropathy include near normalization of glycemia, strict blood pressure control and administration of ACE inhibitors.

**Diabetic Neuropathy**

Manifests as polyneuropathy, mononeuropathy, and/or autonomic neuropathy. The most common form of diabetic neuropathy is distal symmetric polyneuropathy often described as having a glove and stocking distribution.

tachycardia and orthostatic hypotension. Gastroparesis and bladder-emptying abnormalities are also likely related to the autonomic neuropathy seen in DM (discussed below). Hyperhidrosis of the upper extremities and anhidrosis of the lower extremities result from sympathetic nervous system dysfunction. Anhidrosis of the feet can promote dry skin with cracking, which increases t

Preventive management is as important as correct treatment of established lesions. The main aim is to prevent excessive pressure on particular areas of skin.

A greater proportion of cardiac infarcts seem painless in patients with diabetes than in non-diabetics.

Heart disease is the major cause of deat

3. In the hypothetical case already mentioned the health officer requested the following laboratory investigations with the results shown below.

RBS = 450mg/dL

U/A - glucose = 4+

- ketones =4+
- Albumin =negative

3.1. Do the findings on laboratory investigation support (refute) your clinical suspicion?

3.2. What additional investigation would you request if resources permit?

**III. Diagnosis**

1. Clinical features

The presentation of patients depends on the type of diabetes and the stage of pathologic process.

1.1. Type 1 DM

Patients with type 1 DM commonly present with the classic acute symptoms of hyperglycemia: excessive thirst (polydipsia), polyuria, polyphagia and weight loss. Twenty five percent of type 1 diabetics present for the first time with diabetic ketoacidosis (DKA) characterized by hyperglycemia, ketosis and acidosis.

1.2. Type 2 DM

The presentation of type 2 diabetes is less acute than type 1 with “poly” symptoms and

2.2. Type 2 DM

Provided pharmacologic therapy is not required immediately all patients should be given at least a one month trial of diet, exercise and weight management. If this regimen does not lead to adequate blood glucose control, oral antihyperglycemic agents with or without insulin are indicated. Insulin may be needed in symptomatic patients who have type 2 DM with FBG values greater than 250 mg/dl. The common antihyperglycemic agents in use are discussed below.

**a. Glibenclamide**

Dosage

- 2.5– 20mg daily or in two divided doses

Side effect

- hypoglycemia.

Contraindications

- hepatic and renal impairment.

Drug interactions

- alcohol – flushing

Dosage form

- tablets of 5mg

**b. Metformin**

Dosage

- 500 – 2000 mg PO daily in divided doses

Side effects

- anorexia, nausea, vomiting, abdominal discomfort and diarrhea

Contraindications

- renal disease, hepatic disease, alcoholism

Dosage forms

- tablets of 500mg.

## V. Complications

The complications of DM can be divided into acute and chronic complications

1. Acute complications

1.1 Diabetic ketoacidosis (DKA)

It is a clinical condition that may be defined as a triad of

- Hyperglycemia
- Ketosis
- Acidosis

It usually occurs in the setting of type 1 DM and is primarily caused by relative or absolute insulin deficiency.

Common precipitating factors are infection and omission of insulin dose. Patients may also come with DKA on initial presentation.

Symptoms include nausea, vomiting, polydipsia, polyuria, abdominal pain and weakness. On examination, signs include tachycardia, orthostatic hypotension, poor skin turgor, warm or dry skin and mucous membranes, deep and fast breathing

urinary ketones) regular insulin is given 6 hours subcutaneously according to random blood sugar (RBS) level as follows:

RBS> 250mg/dl- 12u

RBS: 180-250mg/dl-8u

RBS – 120-180mg/dl –4u

RBS < 120 but >70 mg/dl-70mg/dL-no insulin

RBS<70mg/dL- Hold insulin and give juice or meal and recheck blood glucose in one hour.

**Fluid Replacement**

Normal saline IV should be given rapidly as soon as the patient arrives.

Total fluid given may be as high as 10 litres depending on the patient's response & urine output.

Fluid replacement may proceed in the following manner.

2-3L of 0.9% saline over first 1-3 hour (5-10mL/Kg per hour); subsequently, 0.45% saline at 150-300mL/hr; change to 5% glucose and 0.45% saline at 100-200mL/hr when plasma glucose reaches 250mg/dL.

**Electrolyte Replacement**

Potassium replacement should be according to serum potassium values. Potassium, 20 meg 1h is generally safe if renal function is normal

SE. renal failure

Dosage forms, injection 20 meg /10 ml ampoule of kc/

# 3.2 SATELLITE MODULE FOR BSC NURSES

## Directions for using the module

Before starting to read this module, please follow the directions given below

- ü Go through all the contents of the Core Module by starting with the pre test
- ü Use a separate sheet of paper to write your answers and label it as pre-test answers

## Learning objectives

On completion of this module, the learner will able to

1. Differentiate between type 1 and type 2 diabetes
2. Describe etiologic factors associated with diabetics
3. Understand the function of glucose and insulin
4. Relate the clinical manifestation of diabetic mellitus to the associated pathophysiologic alteration
5. Recognize the seriousness of DM with reference to morbidity and mortality
6. Identify the diagnostic and clinical significance of blood glucose tests
7. Describe the various type of insulin
8. Explain the dietary modification used for management of person with diabetes
9. Describe the relationship between diet, exercises and modification for persons with diabetes
10. Develop a plan for teaching insulin self administration
11. Learn on the pharmacological calculation of insulin to reach on accurate dose (units to milliliter from a vial containing 40,80 or100 units)
12. Differentiate between hypoglycemia and Diabetic ketoacidocis and HHNS
13. Describe the major macrovascular, micr

## Diabetes Mellitus

Definition: - is a chronic multifactorial, systemic metabolic disorder characterized by hyperglycemia and abnormal insulin production and /or action.

Insulin is a hormone produced by the pancreas. it controls the level of glucose in the blood by regulating the production and storage of glucose.

-Beta cells are responsible for production and secreting insulin and glucagons.

-It is anabolic or storage hormone

- When a meal is eaten, insulin secretion increases and moves glucose from the blood into the muscle, liver, and fat cell.

  In those cells insulin has the following effect.

  - Stimulate storage of glucose in the liver and muscle
  - Enhance storage of dietary fat in the adipose tissue
  - Accelerate transport of amino acid in to the cells

Also inhibit the break down of stored glucose, protein and fat

**Glucagon-**a relative or absolute excesses of glucagons are an essential factor in the development of DM. It increases blood glucose concentrations

**Classification of diabetes**

Type 1-IDDM

Type 2-NIDDM

Other specific subtype- like malnutrition related Diabetic Mellitus (MRDM), gestational DM

**Characteristics of type 1 & type 2 DM (compare& contrast)**

- But it is thought that a combination of
  - × Genetic susceptibility
  - × Environmental factors that contribute to beta cell destruction and
  - × Genes regulating immune response are involved

**Type 2 DM**

- Is related to insulin resistance (a decreased sensitivity to insulin) and impaired insulin secretion
- But the exact mechanism is unknown
- Risk factors include:

→ Age (insulin resistance tends to increase with age over 65)

→ Obesity

→ Family history is strongly associated or environmental factors, e.g. Viruses

## Diagnostic Criteria for Diabetic Mellitus

Fasting plasma glucose (FPG) >126mg/dl

Random blood glucose (RBS) >200mg/dl with symptoms

2hr post load glucose >200mg/dl

See the Core Module for the details

## Management

**Goal:** - to try to normalize insulin activity & blood glucose levels in an attempt to reduce the development of the vascular & Neuropathic complications.

There are five components of management for diabetes: -

- Diet
- Exercise
- Monitoring blood glucose
- Medication (as needed)
- Education

**I. Dietary Management**

Goal: - provision of all the essential food co

*__Foods which diabetic should take with restriction (cereals or starch 50 - 60 %)__

a. Foods from grain e.g. injera, bread, kinche, dabo kolo, kita ,atemit
b. Foods prepared from peas, beans, lentils
c. Potato, sweat potato, kocho, bulla
d. All fruits except lemons and grape fruit
e. Macaroni, pasta, rice

**Foods, which diabetics can take freely or with minimal restriction (protein 10-20%)**

A) Lean meat and fish (with minimal restriction)
B) Eggs and milk (with minimal restriction)
C) Green leafy vegetables (kale, salad, cabbage
D) Lemon, grape fruit
E) Tea, coffee, lemon juice without sugar, ambo water, other mineral water and clear soup
F) Spices pepper, berbere
G) Tomato, pumpkin, carrot, Onion, chili pepper

**II. Exercise**

- Is extremely important in the management of diabetes because of its effect on lowering blood glucose and reducing cardiovascular risk factors
- Lowers blood glucose level by increasing the uptake of glucose by body muscles and by improving insulin utilization
- Pre or post exercise snack may be required to prevent hypoglycemia after exercise
- Patients should be taught to do regular, moderate exercise at the same time and in the same amount for at least 30 minutes each day. Exercise recommendations must be altered as necessary for patients with diabetic complications
- Blood glucose level should be measured before any exercise activity is initiated.

- Exercise should not be initiated with fasting plasma glucose>250mg/dl or<100mg/dl (because it may precipitate diabetic ketoacidosis and hypoglycemia respectively)

-Patient is advised to:

- Use proper footwear and if appropriate other Protective equipment
- Avoid exercise in extreme heat or cold
- Inspect feet daily after exercise
- Avoid exercising during periods of poor metabolic control.

**III. Monitoring of Glucose and Ketones**

- Blood glucose level should be assessed frequently by the patient or by having follow up in the health unit
- Urine and ketone checks are appropriate if blood glucose is greater or equal to 250 mg/dl

**IV. Medications**

**Insulin therapy**

- In type 1 diabetes, the body loses the ability to produce insulin, thus, exogenous insulin must be administered indefinitely. A standard insulin treatment consists of one or two injection/day, using intermediate or long acting insulin with or with out regular insulin.
- In type 2 diabetes, insulin may be necessary on a long term basis to control glucose levels if diet and oral agents have failed. In addition, some patients whose type 2 diabetes is usually controlled by diet alone or diet and an oral agent may require insulin temporarily during illness, infection, pregnancy, surgery or some other stressful events.

*Insulin preparation*

A number of insulin preparation are available. They vary according to four main characteristics, that is

1) Concentration –U-40
-U-80
-U-100
-U-500

2) Species (source)- Human source
-Animal source (beef/pork)

3) Manufacturer –Lilly
-Novo nordisk companies

4) Time course of action –Rapid acting(regular)
-Intermediate acting (NPH and lente)
-Long acting(ultra lente)
-Mixed (e.g 70%NPH/30%Reg)

| **Time course** | **Agent** | **Onset** | **Peak** | **Duration** | **Indications** |
|---|---|---|---|---|---|
| Short acting | Regular (R) | ½ -1 hr | 2-3hr | 4-6hr | Usually administered 20-30 minutes before meal |
| Intermediate acting | NPH (Neutal protamine Hagedorn)Lente(L) | 3-4hr | 4-12hr | 16-20 hr | Usually taken after food |
| Long acting | Ultralente (“UL”) | 6-8 hr | 12-16 hr | 20-30hr | Used primarily to control fasting glucose level |

Patient education -about Insulin Injection

- Insulin injections are administered into the **subcutaneous** tissue
- Equipment: - Insulin
  - Short acting insulin is clear in appearance and long acting insulin are cloudy and white
- The long acting must be mixed (gently inverted or rolled in the hands) before use
- Before injection it should have room temperature, which may require rolling it in the hands or removing it from a refrigerator for a time before the injection. Actually there is no significant difference in the biologic activity between insulin put in the refrigerator and in the temperature (25-34oc). It would seem safe to conclude that unless insulin in Africa is stored for a long period at very high temperature, there is no potential problem (5).
- If a frosted, adherent coating is present, some of the insulin is bound and should not be used

**Syringes**

- Should be matched with the insulin concentration
- 1 ml syringes – hold 100 units
- ½ ml syringes – hold 50 units
- 3/10 ml syringes – hold 30 units

**Preparing the injection**

Mixing insulin: - when short and long acting

- Arms (posterior surface)
- Thighs (anterior surface)
- Hips

Absorption is greatest in abdomen and decreases progressively in the arm, thigh, and hips.

**Rotation**

- Rotation of injection site is required to prevent lipodystrophy, localized changes in fatty tissue,

The patient is instructed as:

1. Do not use a site > once every 4 to 6 weeks
2. Sites should be 1 to 1 ½ inches apart

Treatment involves: - desensitization, gradually increasing the amount of insulin under cautious observation.

3. Insulin lipodystrophy

- Refers to a localized disturbance of fat metabolism in the form of lipoatrophy (loss of subcutaneous fat and appears as slight dimpling or more serious pitting of subcutaneous fat) or lipohyperthrophy (is the development of fibro fatty masses at the injection site and is caused by the repeated use of injection site)
- If insulin is injected in to scarred areas the absorption may be delayed

Treatment: Patient should avoid injection on the areas and prevent by rotating injection sites

3. Insulin Resistance

- Insulin requirements up to 1u/kg can be seen with obesity, stress, aging
- Modest insulin resistance-2-3u/kg wt-can be seen frequently with type 2
- Extreme insulin resistance (>3u/kg)-is rare and may be caused by a variety of autoimmune and genetic disorder

**Oral Anti diabetic agents**

Effective for type 2 DM patients who do not respond to diet and exercise alone and who are able to produce some insulin

**A. Glibenclamide**

Dosage: 2.5 – 20mg daily or in two divided doses

Side effect: hypoglycemia.

Contraindications: hepatic and renal impairment.

Drug interactions occur with alcohol leading to flushing

Dosage form: tablet 5mg

**B. Metformin**

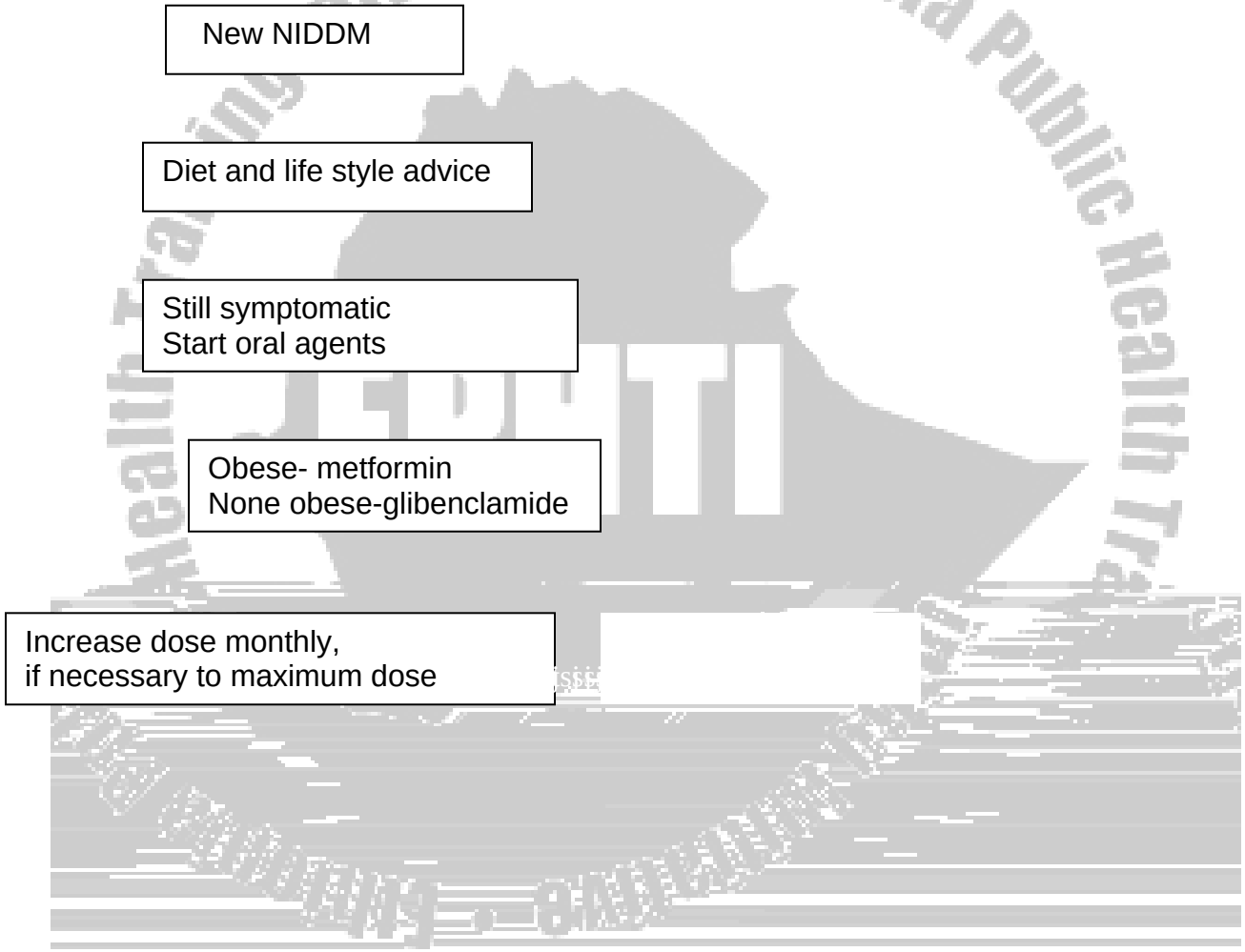
Dosage, 500 – 2000 mg Po daily in divided doses

Side effects: anorexia, nausea, vomiting, abdominal discomfort and diarrhea.

Contra-indication: renal disease, hepatic disease alcoholism

Dosage form: tablet, 500mg and 850mg

**Fig1: Algorithm for the control of type 2(NIDDM)**



### A. Acute complications of diabetes

1. Hypoglycemia (Insulin Reactions)

- Occurs when blood glucose level falls below 50 to 60 mg /dl (2.7 to 3.3 mmol/L )

**Caused by**: Too much insulin or hypoglycemic agents

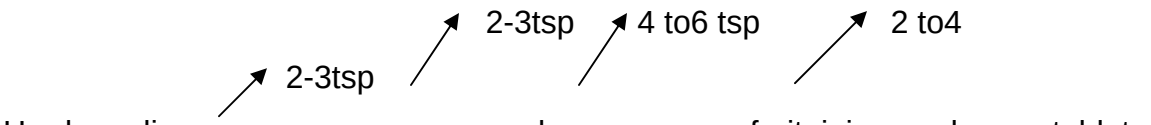
-Too little food or

-Excessive physical exercise or excessive alcohol

-Occurs also if meals are delayed or snacks are omitted 002 Tw02 Tw6-uirbe

**Treatment for Mild and moderate hypoglycemia**

10 to 15 mg of a fast acting sugar orally




**Treatment for Severe hypoglycemia**

The initial treatment of a confused, comatose patient is to infuse a bolus of 50 ml of 50% glucose; preferably after a blood sample for lab analysis has been obtained. This bolus is followed by the continuous infusion of 5 to 10 % of glucose at a rate sufficient to keep the plasma glucose level> 100mg/dl

Patient education: - prevented by following a regular pattern for eating, administering insulin, and exercising

- Because unexpected hypoglycemia may occur all patients treated with insulin should wear an identification **bracelet or tag** indicating that they have diabetes and should keep sugar or candy in their pocket
- Patient and family members should be aware of signs of hypoglycemia

**2. Diabetic Ketoacidosis (DKA)**

DKA is caused by an absence or markedly inadequate amount of insulin. Patients with sever DKA can become severely dehydrated with the loss of electrolyte. Volume loss is highly variable as is $Na^+$ and $K^+$ decreasing. Paradoxically potassium appear elevated as a response to acidosis, though this is a temporary shift of potassium from intra to extra cellular space

Sign and symptoms: - anorexia, nausea, and vomiting & abdominal pain

- Acetone breathe
- Kussmaul respiration (very deep& and fast respiration)
- Lab.value : Blood glucose level 300 to 800 mg /dL

Causes: - A reduced or missed dose of insulin, an illness or infection

Treatment of DKA includes

- Fluid replacement if kidney functions is normal and there is no concern for heart disease

-

times more likely to experience kidney failure) and blood supply to peripheral nerves (Neuropathy).

**Foot and leg problems**

-50-70% of lower extremity amputations are performed on people with diabetes. 50% of which are preventable, provided patients are taught preventive foot care on daily basis

-Diabetic complications contributing to foot infections are: Neuropathy, peripheral vascular disease and immunocompromised.

- **Neuropathy**

A group of disease that affect all types of nerves including peripheral, autonomic and spinal nerves

- Leading to loss of pain and pressure sensation and autonomic neuropathy

9. Measures that increase circulation to the lower extremities should be instituted, including
    - Avoid smoking
    - Avoid crossing legs when sitting
    - Protect extremities when exposed to cold
    - Avoid immersing feet in cold water
    - Use socks or stockings that do not apply pressure to the legs at specific sites or constrict.
    - Apply pressure to the legs at specific sites
    - Institute an exercise regimen
10. Use a light when walking at night
11. Do not place feet near sources of heat
    e.g fireplace, heater , hot water bottle, etc.
12. Wear shoes when outdoors that protects toes and soles of feet from cuts and bruises.
13. Referral to a specialist when necessary.

**Nursing Process**

The Patient with Newly Diagnosed Diabetic Mellitus

**Assessment**

- The history and physical assessment focus on
    - sign and symptom of prolonged hyperglycemia and
    - physical, social and emotional factors that may affect the patient ability to learn and perform diabetes self care activities
- The patient is interviewed and asked for a description of

1) Symptoms that preceded the diagnosis of diabetes i.e

- 3ps (polyuria , polydipsia, polyphagia)
- Skin dryness, blurred vision, weight loss, vaginal itching and non healing ulcer
-

2) Physical factors -that may impair ability to learn or perform self-care skills, or result in complications such as

- Visual deficit
- Deficits in motor coordinator (patient is observed eating or performing other tasks)
- Neurological defect- assessed for aphasia, mental status, sensation in feet

3) Social situation -that may influence the diabetes treatment and educational plan

- Decreased literacy
- Limited financial resource /lack of health insurance
- Presence or absence of family support
- Typical daily schedule

4) Emotional status **-i**s assessed through observation of

General demeanor- anxiety, withdrawn

Body language - avoid eye contact

Collaborative problem /potential complications

- Fluid over load, pulmonary edema congestive heart failure
- Hypokalemia
- Hyperglycemia and ketoacidosis
- Hypoglycemia
- Cerebral edema

Nursing care Plan

- Attainment of fluid and electrolyte balance
- Optimal control of blood glucose
- Improving nutritional intake and regaining weight loss
- Ability to perform basic diabetic skills and self care activity
- Reduction in anxiety
- Absence of complications

Nursing Interventions

1. Maintaining fluid and electrolyte balance

- Measuring Intake and output
- Administering I/v fluid and electrolytes as ordered
- Encouraging oral fluid intake
- Monitor lab values of serum electrolyte ( esp, Na and k)
- Vital sign monitoring

2. Improving nutritional intake

- Diet is planned for the control of glucose
    - Take in to consideration the patients life style, cultural back ground, activity level and food preference
- Patient is encouraged to eat full meals and snack as based on the kcal need.
- Arrangement are made with the dietitian for an extra snack before increased physical activities

3. Improving self care

- Patient teaching to prepare for self care
- Special equipment is used for instruction on diabetic injection skill
- Low literacy information is used
- Families are instructed to enable them to assist in diabetic management
    - Á to profile syringe
    - Á to monitor blood glucose
- Follow up education is arranged
- Consideration is given for financial limitation or physical limitation (such as center for visually impaired)

Other members of the health care team are informed about variation in the timing of meal and the work schedule (e.g. if pt works at night or in the evening and sleeps during the day / so that the diabetes treatment regimen can be adjusted accordingly.

4. Reducing Anxiety

- Nurse provide emotional support and gives time for client
- Patient and family are assisted to focus on learning self care behavior
- Encouraged to perform the skills that are most feared and reassured and self injection and puncturing a finger for glucose monitoring

B. Treatment modalities

- Simple patho physiology
- Treatment modalities (diet, insulin administration, monitoring BG, Urine ketone)

C. Recognition, treatment, and prevention of acute complications

- Hypoglycemia
- Hyperglycemia

D. Pragmatic information

- Where to buy and store insulin, syringes, glucose monitoring supplies when to call the Nurse or physician.
- When and how to reach to health unit

In depth / continuing education during follow up

Preventive measures for the avoidance of long-term complications

- Foot care
- Eye care
- General hygiene (of skin care oral hygiene)
- Risk factor management eg control of BP.

Monitoring and managing potential Complication

1. Fluid over load caused by administration of large volume at a rapid rate

- This risk is increased in elderly patient and in those with preexisting cardiac disease

Nursing care – Monitor the pt closely during treatment for

- ü Vital sign at frequent interval
- ü Intravenous (IV) in take and keep careful records of I/v and other fluid intake along with urine out put measurement

- Physical exam with focuses on cardiac rate, rhythm breath sound, venous distension skin torpor and urine output

2. Ortho static hypotension secondary to dehydration

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1. Achieve fluid and electrolyte balance

   a, Demonstrate I/o balance

   b, Exhibit  electrolyte values that are with in normal limit

   c, Vital signs remain stable

2. Achieves metabolic balance

   a, Avoid extremes of glucose level( Hpo/hyperglycemia

   b, Demonstrate rapid resolution of hypoglycemia episode

   c, Avoid further weight loss

3. Demonstrate verbalizes diabetic survival skill

   Simple pathophysiology

   a.  Define diabetes as a condition in with high blood glucose is present

   b.  State normal bloo(dlucose lerang )Tj-1.3extre.725 TD-0 [ (c)-38440(Idt  ifi asfactors at arcTJ15.5

d. Exhibit no manifestation of hypo or hyper glycemia
e. Mental status improved with out sign of cerebral edema
f. States measures to prevent occurrence of complications

**Keys for the pretest and post test questions for Nurses**

1. A
2. C
3. C
4. E
5. A
6. C
7. A
8. C
9. D
10. A- site of injection
    -Preparations of medication
    -Rotations
    -About syringe and needle
    -Some problems with insulin injections
    B)-Too much insulin
    -Too little food or
    -Excessive physical exercise
    -Delay of meal or omitting of snacks
    C) Sweating
    -Tremor
    -Tachypnea
    -Confusion
    -Seizure
    -Loss of consciousness

D) Having snack, not delaying the meal, right dose of medications, having Candies at hand

F)-assess foot daily for sensation, redness and broken skins

-Wash dry feet daily

- If skin is dry apply a thin coat of lubricating oil

-Tie shoes loosely but firmly

-If your feet perspire, change shoe and stocking during the day

-Wear shoe and stocking that gives room for the movement of the toe

Part-ii True or false

| | | |
|---|---|---|
| A.T | K. F | T.T |
| B. F | L. T | U.T |
| C. T | M.T | |
| D. T | N.F | |
| E. T | O.F | |
| F. F | P.T | |
| H.T | Q.F | |
| I. T | R.T | |
| J. T | S.T | |

**REFERENCES**

# 3.3 SATELLITE MODULE FOR MEDICAL LABORATORY TECHNOLOGISTS

## Introduction

## 1. Purpose of the module

Diabetes mellitus is a diverse group of hyper glycemic disorders with different etiologies and clinical pictures; there fore timely diagnosis and management based on true laboratory results are crucial.

This Satellite Module on Diabetes Mellitus is intended to resolve the critical shortage of clinical chemistry reference materials both for students and for other professionals of the same field working in different health institutions

## 1.1 Directions for using the satellite Module

- After completion of the Core Module, try to answer all pre- test questions and write the answers on a separate sheet of paper
- Read the rest of this Satellite Module
- Refer to the Core Module whenever necessary
- Answer the post- test questions
- Compare the results of the pre- test questions with the key given at the end.

## 2. Pre- test questions

**Instructions:** choose the appropriate answer from the alternatives given for each question and write the answers on a separate sheet of paper.

1. Why is there a discrepancy between the whole blood glucose concentration and the plasma glucose concentration?
    A. Because there is a different distribution of Glucose in whole blood and plasma
    B. Because there is a high amount of water in plasma
    C. Because the cellular component in whole blood use glucose frequently
    D. None
2. One of the following methods of Glucose determination does use enzymatic reaction
    A. Folin- MU copper Reduction method
    B. Alkaline ferric cyanide method
    C. Hexokinase n.v. method
    D. Somogyi-Nelson method
3. Which one of the following methods is highly specific for glucose determination
    A. Alkaline ferric cyanide method
    B. Copper Reduction method
    C. Glucose oxidase method
    D. O-Toluidine method
4. When does glucose appear in the urine?
    A. When the urine glucose level higher than blood glucose level
    B. When blood glucose level is between 60-110 mg/dl
    C. When the blood glucose level is greater than 180-200 mg/dl
    D. When a person is starved
5. One of the following methods for urinary glucose determination is highly specific
    A. Copper reduction method
    B. O-Toluidine method
    C. Reagent strip Tests
    D. A and B

6. Sodium fluoride additive used in a specimen collected for Glucose
    A. Inhibits glycolytic enzymes from destroying the glucose
    B. Precipitates the protein present in the sample
    C. Prevents non glucose reducing substances from interfering with the testing
    D. None of the above
7. During GGT test in a person with normal glucose metabolism, the blood glucose level usually increases rapidly after carbohydrates are ingested, but returns to a normal level after
    A. 30 minute
    B. 60 minute
    C. 90 minute
    D. 15 minute
8. Which one of the following organs uses glucose from digested carbohydrates and stored it as glycogen for later use as a source of immediate energy by the muscles?
    A. Kidneys
    B. Liver
    C. Pancreas
    D. Thyroid
9. Which one of the following samples good for Glucose determination
    A. Serum/ plasma
    B. Whole blood
    C. Urine
    D. All
10. To say the Oral Glucose Tolerance test is normal
    A. The fasting blood sugar level should be 60-110 mg/dl
    B. The fasting blood sugar level should be higher than 110 mg/dl
    C. The fasting blood sugar level should be normal or slightly elevated
    D. The fasting blood sugar level should be always less than the lower limit.

## 3. Learning objectives

After studying this satellite module the student will be able to:-

Ą

- Because there are several substances in blood (particularly in red cells) that interfere with tests for blood glucose either because they are measured as glucose or because they interfere in enzyme procedures.
- As indicated above, values based on whole blood tend to vary with the hematocrit.
- Glucose is more stable in plasma or serum than in whole blood, as many glycolytic enzymes are present in RBC.
- Plasma or serum is easier to handle, to pipette precisely and to store than is whole blood.

The blood specimen can be coll

### 4.2.3Capillary blood specimen

An advantage of using whole blood is the convenience of measuring glucose directly on capillary blood, such as:

- That taken from infants
- In mass screening programs for detection of diabetes mellitus, or
- In the home monitoring being done by so many diabetes patients.

In the fasting state the arterial (capillary) blood glucose concentration is 5 mg/dl higher than the venous concentration.

## 5. Preparation and preservation Samples for glucose determination

The following factors which affects the stability of glucose in body fluid must be take in to account, such as:

- Those glycolytic enzymes found particularly in the red cells, which under goes glycolysis at an average rate of approximately 10 mg/dl/hr in whole blood or 5 mg/dl/hr in sufficiently centrifuged plasma which still contain leukocytes

Keeping these considerations in mind, there are several ways to prevent or retard glycolysis in specimen to be analyzed. For example:

- Sample for glucose analysis should be delivered to the laboratory as soon as possible after being drowned from the patient.
- Refrigeration or addition of small amount of sodium fluoride to the fluid may retard glycolysis for a few hours
- If plasma or serum is to be used for the glucose determination, it must be separated from the cells or it will clot with in 30 minutes after the blood is drown unless a specific additive is used.

***Note*** *When certain enzymatic glucose methods are used, fluoride anticoagulated blood should not be used, as the fluoride might inhibit the enzyme. Use of serum separator gel tubes, processed as quickly as possible with in thirty minutes if possible- is preformed for these methods.*

## 6. Diagnostic criteria of DM

dehydrogenase oxidizes glucose 6-phosphate in the presence of hydrogen acceptor $NADP^+$. Proportionally $NADP^+$ is reduced to NADPH. The amount of formed NADPH is directly proportional to the amount of glucose present in the sample. The absorbance due to NADPH is read at 340nm every minute and change in absorbance of the test is compared with that of the standard.

1. Glucose + ATP $\xrightarrow{hexokinase}$ Glucose – 6- phosphate + $ADP^+$

2. Glucose-6- phosphate +$NADP^+$ $\xrightarrow{G_6PDH}$ $NADPHH^+$

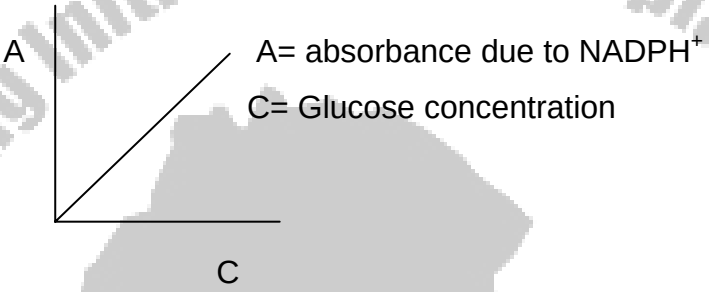


Fig 1. The relation ship between absorbance and concentration

### 7.2 Oxidation- Reduction Methods

Oxidation methods for blood glucose depend on the fact that glucose contains an aldehyde group as part of its chemical structure. The presence of this aldehyde gives glucose its reducing properties. Other substances in blood also have reducing properties. Some of these non glucose reducing substances are other sugars and metabolic compounds and materials such as uric acid, creatinine, ascorbic acid, certain amino acids, creatine, and phenol. The oxidation- reduction methods for determining blood glucose differ primarily in the way they handle the non-glucose reduction substances. When the non-glucose reducing substances are removed as part of a glucose determination, the resulting value is called the true glucose value.

#### 7.2.1 Alkaline ferric cyanide method

**Sample:** serum, plasma, and whole blood

**Principle:** In hot alkaline solution ferric cyani

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### 7.2.3.b. Somogyi- Nelson Method

| |
|---|
| 1. Zinc sulfate solution |
| Á $ZnSo_4 .7H_2O$ …….. 50 gm<br>Á Water to …….. 1000ml |
| 2. Barium hydroxide solution (0.3N)<br>Á $Ba(OH)_2. 8H_2O$…….. 50 gm<br>Á Water to …… 1000ml |
| After 3 days filter and keep in poly ethylene bottle |
| 3. Copper sulfate solution<br>- $Na_2HPO_4$ …… .29 gm<br>- K-Na-$C_4H_4O_6.4H_2O$…… 4ogm<br>- Water to …….. 700ml<br>- 1 N NaOH…… 100ml<br>- 10% W/V $cuso_4.5H_2O$…….. . 80 ml |
| $cuso_4$ is added with stirring |
| - $Na_2SO_4$……180 gm<br>- Water to……1000ml |
| Let stand for two days and filter and precipitate. Keep at 20-25$^0$C |
| 4. Arsenomolybdic soltuon |
| 5. Water…….. 900ml |
| 6. Conc. $H_2SO_4$ …… 42ml |
| 7. Ammonium molybdate …… 50 gm |
| 8. 12 gm% W/V sodium arsenate ... 50ml |

Mix and incubate at 37$^0$C for 48 hours. Store in a brown bottle

## Procedure

| | |
|---|---|
| - Blood, serum or CSF | 0.5ml |
| - Water | 7.5ml |
| - $Ba(OH)_2$ | 1ml |
| - Mix and let stand for 1 minute | |
| - $ZnSO_4$ | 1ml |
| - Mix and let stand for 2 minutes | |

Separate the protein free filtrate from the precipitate. Arrange 3 folin- Mutubes labeled

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***Reagent***

| |
|---|
| 1. O- Toludin reagent<br>Thiourea …….. 1.5gm<br>Aceticacid (pure)…… 940ml<br>O-Toluidine…….. 60ml |
| Mix well and keep the solution in brown bottle in the dark at $20^0$C stable for two months |
| 2. Glucose standard (stock)<br>Glucose powder ……..……20gm<br>1gm% W/V benzoic acid to…… 1000ml<br>Stable for one year if kept at 4-$10^0$C |
| 3. Glucose working standard<br>Glucose stock standard…….5ml<br>1gm% benzoic acid to…….. 100ml |

Stable for Six months if kept at 4-$10^0$C. Both stock and working glucose standards should be stored (kept) at 4-$10^0$C

***Procedure***

| | B | St | T |
|---|---|---|---|
| Distilled water (ml) | 0.1 | - | - |
| Glucose standard (ml) | - | 0.1 | - |
| Serum (ml) | - | - | 0.1 |
| O-Toluidine reagent (ml) | 7 | 7 | 7 |

Mix well and incubate at $100^0$

$$C_T = \frac{A_T x C_{S_T}}{A_{S_T}}$$

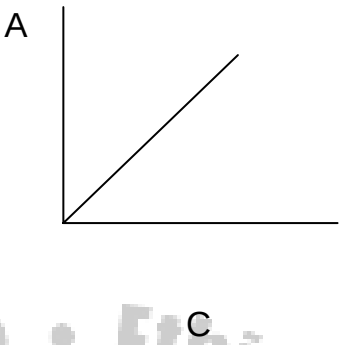



***Fig 2.*** The relation ship between Abso

In the detection and treatment of diabetes it is sometimes necessary to have more information than can be obtained from only testing the fasting specimen for glucose. There fore the GTT is usually performed:

- When a person has been found to have a fasting serum or plasma glucose concentration above that of most non diabetic persons (about 110 mg/dl)
- To identify hypoglycemia, an abnormal response to a glucose load that results in a serum or plasma glucose concentration much below the normally accepted range

Since early detection and management of diabetes are important to avoid the many complications of the disease, it is desirable to detect these early cases of diabetes or pre diabetes. For these reasons, the physician may request a glucose tolerance test.

**a. Oral glucose Tolerance Test.**

To conduct oral glucose tolerance test on a subject, first blood and urine samples are taken in fasting state, and. the blood glucose level is determined. The urine sample is qualitatively tested for glucose. If blood glucose level is normal and urine sample is negative the individual will be loaded with 75 gm glucose dissolved in 300 ml of water. Blood and urine samples are collected every 30 minutes four times for a period of 3 hours. The blood sample are analyzed for glucose concentration and the urine samples are qualitatively tested for glucose.

***Note:-*** In malabsorption of carbohydrate the fasting blood glucose level is always less than the lower limit of the normal rang. During GTT, blood glucose level will not rise even with in 2 hours, above the normal range. Most probably slight elevation may be observed after 3 hours then falls down below the normal range with in one or one half hours

**b. Intravenous Glucose Tolerance Test:** this method is less commonly used, although it eliminates the variable factors involved in the rate of intestinal absorption in different individuals. 0.5g. Glucose is given per kg body weight by infusing 20gm% W/V glucose solution and the infusion will be completed with in half an hour. In normal individuals the blood glucose concentration does not rise to more than 250 mg% at the end of infusion and falls below the fasting level with in 2 hours. In case of latent and severe diabetes mellitus glucose concentration pattern will be as in oral GTT.

**Factors affecting (altering) carbohydrate tolerance**

1. Quantity of glucose administered: The peak level doesn't increase if the quantity of glucose administered is greater than 50 gm, since glucose is absorbed at a steady rate by the intestine and it may take a longer time to return to fasting level even in normal GTT.
2. The rate of absorption may be low in conditions of mal absorption and high in hyperthyroidism. This m.o20005 Tc0.w [ 3D0.ills

## 8. Self- Monitoring of glucose

Many patients (especially those with type 1(insulin- dependent diabetes mellitus)) now regularly monitor their own blood glucose concentrations on the advice of their health care provider, using reagent test strips and reflectance meter. Several companies manufacture reagent test strips for monitoring blood glucose, and most of these companies make reflectance meters to be used to electronically read the test result. Instruments include one Touch,* Accu- chek Easy, and Glucometer Elite. The strips used for these tests are impregnated with the enzyme glucose oxidase, enzyme peroxidase and an indicator to give a color change that is detectable. The color change can be read in a reflectance meter on which the result (in mg/dl) is visualized. Although blood is tested, results are converted to plasma glucose values by the instrument.

Eg. Glucose oxidase reaction (Vitros Method)

Ex β- D- glucose + $H_2O$ $\xrightarrow{glucose\ oxidase}$ D- gluconic acid + $H_2O_2$

$2H_2O_2$ + 4 aminopyrine + 1,7- dehydroxynapthylene $\xrightarrow{peroxidase}$ $H_2O$ + a red dye

## 9. Urine Glucose determinations

Chemical screening tests for glucose (dextrose) are generally included in every routine urinalysis. The occurrence of glucose in the urine indicates that the metabolic disorder diabetes mellitus should be suspected, although several other conditions result in glycosuria (glucosuria).

The lowest blood glucose concentration that will result in glycosuria is termed the renal threshold (180-200 mg/dl). Icosur82ad

## 9.1 Enzymatic technique

### 9.1.1 Reagent strip (Glucose oxidase) Tests

**Principle and specificity**

Since the reagent strip tests for urinary sugar use glucose oxidase which only react in the presence of glucose they are highly specific. Reagent strip tests for urine glucose are double sequential enzyme reactions. Glucose oxidase will oxidize glucose to gluconic acid and at the same time reduce atmospheric oxygen to $H_2O_2$. The hydrogen peroxide formed will, in the presence of the oxidized form, which is indicated by the color change of an oxidation- reduction indicator.

**Step 1:**

$$\text{Glucose (In urine)} + O_2 \xrightarrow[\textit{oxidase}]{\textit{Glucose}} \text{Gluconic acid} + H_2O_2$$

**Step 2**

$$H_2O_2 + \text{Reduced Form of dye} \xrightarrow{\textit{Proxidase}} \text{oxidized form of dye} + H_2O$$

**Note*:*** The glucose oxidase, peroxidase and the reduced form of the Oxidation-Reduction indicator are all impregnated on to a dry reagent strip. There are different kinds of reagent strips and they all contain Gluocse oxidase and peroxidase.

#### 9.1.1.1 Procedure

1. Collect the urine sample with a clean, dry, free from any antiseptic and wide mouth container
2. Transfer the urine into a conical test tube
3. Take one strip from the reagent strip container
4. Immerse the strip into the urine in a conical test tube
5. Immediately pull it out and let it stand for one minute. So as to have time for reaction and color change to occur on the strip

6. After one minute read the result by matching the color on the strip with the color on the reagent strip container
7. Report the result

#### 9.1.1.2 Interferences

False – positive results can occur due to:

Contamination by bleach or other strong oxidizing agents

Trace values may be seen in very dilute urine specimens, because of increased sensitivity at low specific gravity

When the strip is exposed to air

False- negative or delayed results

- Large urinary concentration of ascorbic acid
- Sodium fluoride is an enzyme inhibitor
- Refrigerated specimens, because of decreased enzyme activity

### 9.2 Oxidation reduction technique

The reaction is essentially Benedict's qualitative test for urine sugar in a solid form. The tablet combines: -

Copper sulfate

Anhydrous sodium hydroxide

Citric acid and

Sodium carbonate in an effervescent tablet

The interaction of sodium hydroxide with citric acid and water results in moderate boiling, making an external boiling water bath unnecessary.

#### 9.2.1.1 Procedure for clinitest Tablet test

- Place five drops of urine in a 15x85 mm test tube and add ten drops of water
- Add one clinitest tablet
- Watch while boiling takes, but do not shake

#### 9.2.1.2 Interferences

False positive results occurs:

- Since it is reducing substance, the presence of extremely large amount of ascorbic acid
- Specimens that have a low specific gravity and contain glucose may give slightly elevated result
- Large quantities of nalidixic acid, cephalosporins and probenacid.

False negative results

- Mixing the test tube before the 15 second wait after boiling stops, due to reoxidation of the cuprous ions to cupric ions by atmospheric oxygen

## 10. Determination of ketone bodies in urine

ketone bodies are a group of three related substances: acetone, aceto acetic acid, and β – hydroxyl butyric acid. When ever fat (rather than carbohydrate) is used as the major source of energy, ketosis and ketonuria may result. The two out standing causes of ketone accumulation are diabetes mellitus and starvation In diabetes mellitus, the body is unable to use carbohydrate as an energy source and attempts to compensate by resorting to fat catabolism, which results accumulation of ketone more than normal, that the body is unable to utilize it. The clinical result is an increased concentration of ketones in the blood (ketonemia) and in the urine (ketonuria.) Since the presence of ketone bodies in urine is an early indication of lack of adequate insulin control, reagent strips that combine tests for glucose and ketone are often used.

### 10.1 Dipstick test

**Principle:** the reagent strip tests for ketone bodies are based on legal's (Rothera's) test, a color reaction with sodium nitroprusside (nitro ferricyanide). Acetic acid will react with sodium nitro prusside in an alkaline medium to form a purple color.

### 10.1.1 Procedure

1. After collecting the urine sample from the patients, transfer into a clean, dry and free of disinfectant test tube
2. Then immerse the dipstick into the urine
3. Then drain and let it stand for certain seconds for the reaction to take place
4. Read the result by comparing the color produced with the standard on the strip container

***Note*** acetone and aceto acetic acid can be detec

desirable, as better control of blood glucose levels may delay the progression of renal disease

### 11.1 Methods of measurement

Test for urinary protein are of two major types:

a. Tests that are based on the use of the protein error of PH indicators

- This is the methodology employed in the various reagent strip tests
- They are more sensitive to the presence of albumin than to other proteins.

b. Tests that are based on the precipitation of protein by chemical or coagulation by heat

- This test will detect all proteins, including albumin, glycoproteins, globulins, Bence Jones protein & hemoglobin

#### 11.1. a Reagent strip test

Principle: Reagent strip tests for urinary protein involves the use of PH indicators substances that have characteristic colors at specific PH values. The phenomenon of showing different color at different PH is called. “The protein error of indicators” The PH of the urine is held constant by means of buffer, so that any change of color of the indicator will indicate the presence of protein.

#### 11. 1.a. 1 Procedure

It is the similar with other reagent strip test procedure. (But the reading time can vary manufacture to manufacturer instruction on the leaf late)

**Specificity**

The reagent strip tests for urinary protein are more sensitive to the presence of albumin than they are to other proteins

**Sensitivity (minimum Detectable level:)**

Manufacturer's value

- Multistrx /Albustix……..15 to 30 mg/dl albumin
- Chemstrip……. 6 mg/dl albumin
- Etc

### 11.10.2 Interferences

- If the urine is strongly pigmented, there may interference with the color reaction.

False- positive results

- if the urine is exposed to the reagent strip for too long, the buffere may be washed out of the strip, resulting in the formation of blue color whether protein is present or not
- If a urine specimen is exceptionally alkaline or highly buffered, the reagent strip tests may give a positive result in the absence of protein

False – Negative results

- When proteins other than albumin are present, the reagent strip will give a negative result in the presence of protein

### 11.1. b. Confirmatory tests (sulfosalicylic acid (SSA) test

SSA test or another protein precipitation method may be used to confirm the presence of protein when reactions indicating a trace or more are obtained or when reagent strip results are in doubt.

SSA test

**Principle:** This test is based on the cold precipitation of protein with a strong acid, namely sulfosalicylic acid.

### 11.1b.1 procedure for SSA test for urine protein

- Centrifuge a 12 ml aliquot urine

- Decant 11 ml of the supernatant urine into a 16x125 mm test tube. Note the clarity of the centrifuge urine
- Add 3 ml of 7g/dl sulfosalicylic acid reagent
- Stopper the tube and mix by inverting twice
- Let stand exactly 10 minutes
- Invert tube twice
- Observe the degree of precipitation and grade the results
- To observe the degree of precipitation, tilt the test tube while simult ancously viewing the quality and quantity of precipitate in the mirror

**Table shows SSA protein test result**

| **SSA result** | **Description** | **Approximate protein concentration in mg/dl** |
|---|---|---|

False- Negative results

- The occurrence of highly buffered alkaline urine if the buffer is sufficient to neutralize the acid in SSA.

## 12. Determination of creatinine and BUN

Diabetes mellitus can have profound effects on the renal system. In insulin- dependent diabetes mellitus (IDDM, type I) patients suffer from a deficit of insulin activity. Approximately 40% to 50% of these patients will develop progressive deterioration of kidney function (diabetic nephropathy) with in 15 to 20 years after their diagnosis.

The lesions are primarily glomerular, but they may affect all other kidney structures as well, they are theorized to be caused by the abnormally hyper glycemic environment than constantly bathes the vascular system. In this case we will do a renal function tests, such as

- Determination of blood and urine creatinine
- Determination of Blood urea nitrogen & urea

### 12.1 Determination of blood urea nitrogen and urea

It is customary, in most laboratories, to express urea as BUN, but urea is quit different from BUN. The structure of urea is $NH_2$-CO-$NH_2$ having a molecular weight of 60. the two nitrogen atoms represent 28. There fore urea represents 28 gm urea nitrogen (BUN), or 2.14 gm urea stands for 1gm BUN. BUN is converted to urea by multiplying the value of BUN by 2.14 and urea is converted to BUN by dividing the value of urea by 2.14

#### 12.1.1 Determination of urea

There are two methods, such as:-

##### 12.1.1.1 colorimetric methods for urea determination

eg. Bertholet method

##### 12.1.1.2 U.V enzymatic method in urea determination

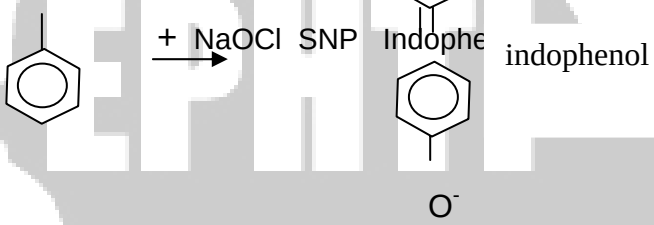
**Bertholet method**

**Specimen:** serum, plasma, urine and other body fluid

**Principle:-** urea is hydrolyzed to $NH_4HCO_3$ by urease enzyme at $37^0C$. The released $NH_4HCO_3$ is converted to $NH_3$, $CO_2$ and $H_2O$ by making the reaction mixture alkaline. This $NH_3$ reacts with phenol in the presence of sodium hypochloride and sodium nitropreside SNP (catalyst). The reaction product is a blue colored derivative indophenol. The intensity of blue color is directly proportional to the concentration of urea present in the sample and the absorbance is read it 560 nm and compared with the standard.

1. $NH_2\text{-}C\text{-}NH_2 + 2H_2O \xrightarrow[37^0C]{\text{urease}} (NH_4)_2CO_3 + H^+$

2. $2NH_4^+ \xrightarrow{NaOH} 2NH_3 + H_2O$

3. $NH_3 + 2$  $\xrightarrow{+ NaOCl\ SNP}$ Indophe indophenol

SNP= sodium nitropruside

## Reagents

| | |
|---|---|
| **1. Urease buffer, $p_H$ 6.5** | |
| Urease powder 300,000 IU | 15 mg |
| EDTA powder | 100 mg |
| Water to | 100 ml |
| Before making the volume to 100 ml adjust the $p_H$ to 6.5 The reagent is stable for six months at 4-$10^0C$ | |
| **2. Phenol reagent** | |
| Phenol | 50 g |
| Sodium nitropruside | 250 mg |
| Distilled water to | 1000 ml |

| | |
|---|---|
| If it is stored in brown bottles at 4-10$^0$C the reagent is stable for two months. | |
| **3. Alkaline hypochlorite reagent,** | |
| NaOH pellets | 25g |
| Sodium hypochlorite (NaOCl) or | 2mg |
| Purex bleach | 20 ml |
| Distilled water to | 1000 ml |

N.B If NaOCl is not available use 20 ml purex bleach (10%)

## Urea standard

Stock standard- Dissolve 1.0717 gm pure urea in about 50 ml of distilled water in 100 ml volumetric flask. Add 0.1 gm sodium azide as preservative. Make the volume to 100 ml with ammonia free distilled water. This stock standard provides you 500 mg BUN per 100 ml and 1.072 gm urea/ 100 ml.

Working standard- 50mg/100 ml BUN or 107.2 mg/100ml Urea. Dilute 10ml of stock standard to 100ml using ammonia free water.

## Procedure

| | **B** | **S** | **T** |
|---|---|---|---|
| Urea Buffer (ml) | 0.2 | 0.2 | 0.2 |
| Distilled water (µl) | 20 | - | - |
| Urea working standard (µl) | - | 20 | - |
| Serum /plasma (µl) | - | - | 20 |
| Mix well and incubate at 37$^0$ C for 15 min | | | |
| Phenol reagent (ml) | 5 | 5 | 5 |
| Alkaline hypochlorite (ml) | 5 | 5 | 5 |

If the reagent is stored at 4-10$^0$C in brown bottles it is stable for two months. Mix well and incubate at 37$^0$C for 15 minute. Read the absorbance of the tests and standard at 560 nm against reagent blank

**Calculation**

a. For serum

$CT = \frac{C_{st} x A_T}{A_{st}} = mg/100ml$

b. For 24 hour urine volume in ml

V= 24 hrs. urine

$C_T = \frac{C_{st}\ x A_T}{A_{st}} \times \frac{\text{dilution factor}}{100{,}000} \times v = gm/s4\ hrs$

**Normal values for both sexes**

| | |
|---|---|
| a. Serum/ plasma | |
| BUN | 7.18 mg/100ml |
| Urea | 13-45 mg/100ml |
| b. 24 hours urine | |
| BUN | 12-20 gm/24 hrs |
| Urea | 25-58 gm/24 hrs |

**12.1.1.2 U.V enzymatic method**

**Sample:** serum, plasma, urine

**Principle:** urea present in the sample is hydrolyzed to $NH_4^+$ and $CO_2$ by catalytic activity of urease enzyme at $37^0C$. The released $NH_4^+$ is coupled with α–ketoglutarate, in the presence of co- enzyme NADH, which is catalyzed by an enzyme glutamate dehdrogenase (GLDH). The reaction products are glutamate, $NAD^+$ and $H_2O$.

1. $Urea + H_2O \xrightarrow{Urease} 2\ NH_3 + CO_2$

2. $2\ NH_3 +$ α – ketoglutarate + NADH

glutamate dehydrogenase

$2\ Glutamate + 2H_2O + 2NAD^+$

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V= Total 24 hours urine volume

## Normal ranges

| | Male | Female |
|---|---|---|
| Serum- Creatinine | 0.7-1.6mg% | 0.4-1.2 mg% |
| Serum creatine | 0.2 - 0.5 mg% | 0.4-0.9 mg% |
| Urine – Creatinine | 1.0-2.0 gm/day | 0.5-1.8gm/day |
| Urine - Creatine | 0-40mg/ day | 0-0.8 mg/day |

**Reagents**

1. Picric acid ($C_6H_3N_3O_7$)- 0.04 mole/L
2. NaOH-0.75 mole/L or 30g/L
3. Creatinine standard
    a. Stock: Dissolve 100 mg of pure creatinine in 100 ml of 0.1 N HCL which gives 100 mg/dl
    b. Working- Dilute 2 ml of stock standard to 100 ml of solution using 0.1N HCL to get 2 mg/dl creatinine
4. $H_2SO_4$ …… 0.33 mole/L
5. Sodium tungstate…… 5.0 gm/100 ml

Dissolve 50 gm $Na_2WO4.2H_2O$ in 700 ml of water and dilute to 1000 ml with water

*Procedure*

Transfer 1 ml of sodium tungstate, 1 ml of 0.33M $H_2SO_4$., and 1 ml of water to 1 ml of serum (or plasma). Mix well and centrifuge. Urine is diluted to 1:400. If there is proteinuria treat urine samples as in case of serum and dilute the protein free filtrate (PFF) 1:100. Separate the PFF and arrange the test tubes as follows:

| | Blank | Test | Standard |
|---|---|---|---|
| Distilled water (ml) | 4 | 2 | 3.5 |
| Creatinine working standard (ml) | - | - | 0.5 |
| Protein free filtrate of diluted urine (ml) | | | |

A. Patient preparation
B. Sample collection
C. Sample handling and storage

A. Patient preparation- during this time a lot of things can be done for example. The patient should be asked about his nutritional status, a recent mead. Alcohol, drugs etc. Which all affect the value of the anlyte.
B. Sample collection:- During sample collection the laboratory personnel should be a ware of the type of sample, time of collection, area of collection (ream or capillary) , etc.
C. Sample handling and storage here the type of test tube, anti coagulants and storage temperature with respect to the type of sample should be considered.

**2. Analytical factors**

The laboratory is more able to control the analytical factors, which depend heavily on instrumentation and reagents

A. Instrumentation

- Instrument function checks that are to be routinely performed should be detailed in procedure manual and their performance should be documented

B. Reagents and kits

Reagents and kits should be dated when received and also when opened. New lots of reagents should be run in parallel with old reagent lots before being used for analysis.

**3. Post analytical factors**

The post analytical factors consist of the recording and reporting of patient data to the physician with in the appropriate time interval

*Post test*

***Go back to the pretest questions & do them carefully***

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Identification of an environmental trigger has been difficult because the event may precede the onset of DM by several years. Though this is the case, it is strongly believed that there are environmental factors which have a link with DM like, chemical compounds (Rodenticides, heavy metals virus, rarely exposure to bovine milk proteins), physical factors (penetrative short- wave length rays) etc.

## 4. Why the pattern of prevalence of DM has changed across the globe?

For this new change of the pattern of prevalence of diabetes many factors were considered as the culprit. Among the factors that aid the increment of the prevalence diabetes even in the developing, countries the following are some:

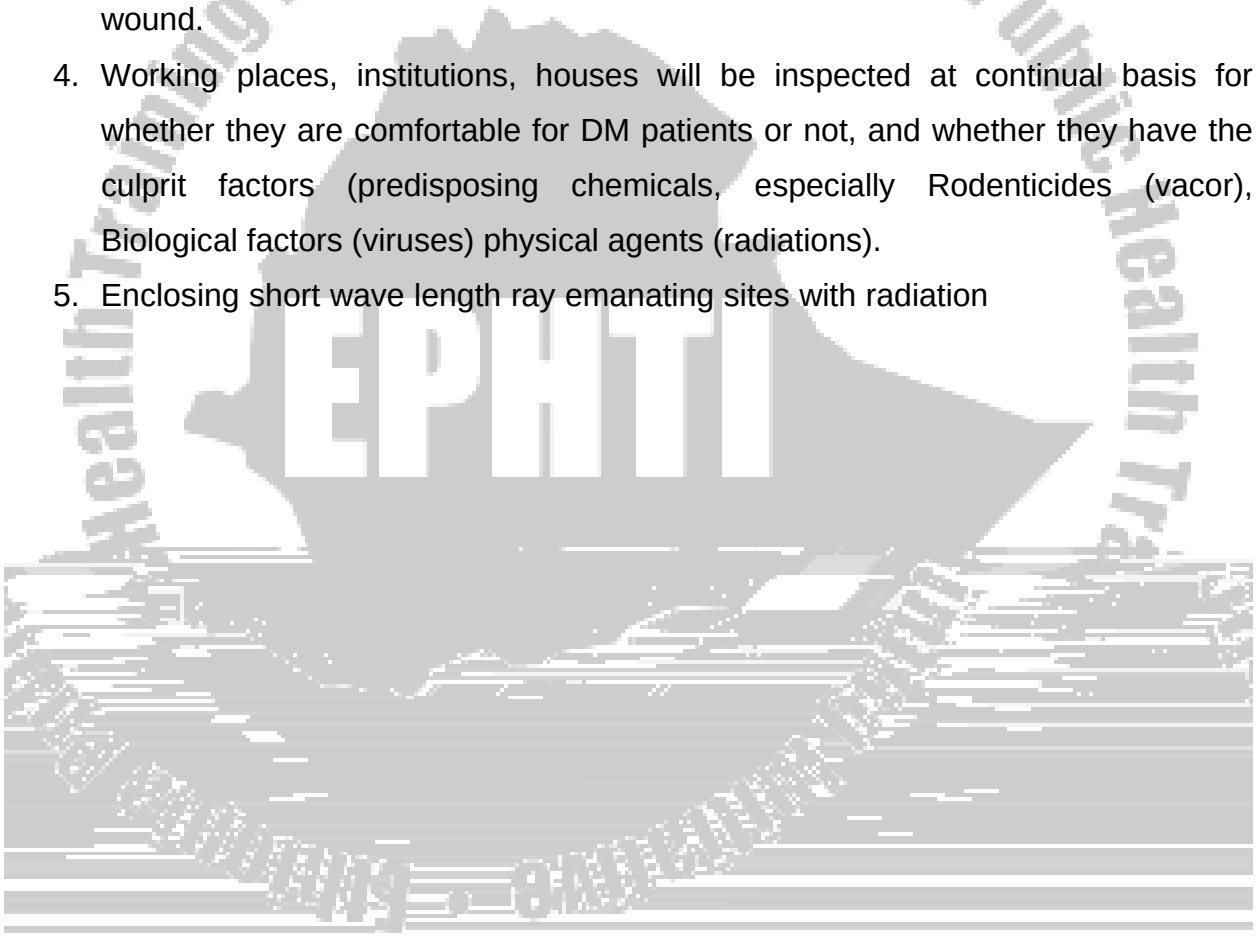
1. Most people are living in very hectic environment where by the housing condition is predominated with substandard housing condition that doesn't usually meet the physiological and psychological requirement of the dwellers. And this leads the people to live or to expend much of their time in very stressful environment.
2. People are more ignorant about the healthy style of nutrition at the family and community level in particular and at large respectively. In an area where there is no good understanding about the malnourishment consequences, especially obesity, the high prevalence occurrence of DM in that specific community will be highly inevitable.
3. Long term exposure to some specific type of organic and inorganic chemicals, recently it came to understand that they will cause DM by affecting the pancreas and they interfere with the right physiological secretion of insulin.
4. Exposure to some biological factor (coxsakie and rubella most prominently) cause DM by trigger the autoimmune system so that the destruction of β -cell of the pancreas will occur.
5. IN rarest case, DM may happen because of the destruction β – cell s of the pancreas by trauma, accidents, chronic inflammation.

6. Many jobs are becoming sedentary rather than exercise/movement demanding and in turn these furnish the ground for the people to become more obese.
7. Physical exercise is not taken as a routine life activity among the people especially living in developing country where the living places are not comfortable to make exercises at continual basis.

## 5. Environmental factors linked to DM

Putative environmental triggers include viruses (coxsackie and rubella most prominently) early exposure to bovine m

2. Construction of standard housing with local materials will be advocated and technically commented and regularly inspected by environmental Health officers. Thus the requirements of physiological and psychological health of the dwellers will be met and this consequently will alleviate the potential stressful environment.
3. Environmental health officers technically suggest comments and follow its implementation to make the working places more comfortable. E.g. a DM patient working in steel processing industry is often time advised to wear very thick and laceration proof gloves at any time of working to avoid the incidence of lacerated wound.
4. Working places, institutions, houses will be inspected at continual basis for whether they are comfortable for DM patients or not, and whether they have the culprit factors (predisposing chemicals, especially Rodenticides (vacor), Biological factors (viruses) physical agents (radiations).
5. Enclosing short wave length ray emanating sites with radiation



11. The EHOs are expected to be involved in research activities, to examine and analyze the environment for its physical, chemical and biological qualities that will help in modifying the environment to make ideal for DM cases.
12. Give refresher trainings on DM for environmental health technicians and health extension workers from environmental health point of view.

## Post – test

First try to look and do the pretest again, then keep on attempting the following questions.

1. What situation makes difficult the study of causation of environmental factors and to link conclusively with DM?
2. Why diabetes mellitus patients are most susceptible for different kinds of skin infections?
3. What is the basic reason for the fact that E.H.Os are supposed to be highly concerned to make the working places free of any possible causalities for DM patients?
4. What are the known environmental factors that are thought to cause DM?
5. What parcel of Health information is highly beneficial for the family or community with strong DM history?

**Multiple Questions**

1. DM can be transmitted through the following ways **except**
   - A. Feco-oral route
   - B. Aerosol respiration
   - C. contact
   - D. Unsafe sexual activity
   - E. None of the above
2. DM can be caused by one of the following factor **except**
   - A. β- cell affection by autoimmune system
   - B. Chemicals

C. Biological agents

D. taking high amount of sugar in the diet

E. None of the above

3. From the following alternatives one can be identified as one risk group to develop Dm **except**

A. Obese person

B. a person with strong DM family history

C. a person that had > 4 kg body weight during delivery

D. a person who has married Dm patient

E. none of the above

4. From the following set of types of rays one possibly could not cause DM compared with others

A. IR rays

B. Gamma rays

C. Beta rays

D. Radioactive rays

E. none of the above

5. The main causative agent of DM is

A. Bacteria

B. Viruses

C. Fungus

D. Parasites

E. none of the above

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- Having gone through the module, try to attempt the presented questions.
- Study the task analysis for the health center team members in comparison with that of your own.

## Objectives

### 2.3 Learning Objectives

After reading the module, one will be able to

- Explain the importance of diabetes mellitus as a public health problem
- Describe diabetes mellitus, its classification and clinical presentation.
- Outline the diagnostic tests for diabetes mellitus.
- Describe the logic behind appropriately employed treatment.
- Describe the role played by each member of the health center team.
- Describe the overall principles of management.

## Diabetes mellitus

## Definition

Diabetes Mellitus is a clinical syndrome comprising a heterogeneous group of metabolic diseases that are characterized by chronic hyperglycemia and disturbances in carbohydrate, fat and protein metabolism secondary to defects in insulin secretion, insulin action or both

## Types

**Type 1And type 2**

**CLINICAL FEATURES**

Classical symptoms

- Thirst
- Polyuria
- Nocturia

- Rapid weight loss
- Increased susceptibility to infection in patients with uncontrolled diabetes
- Chronic fatigue and malaise

Signs

- Signs related to acute and chronic complications

**Possible laboratory tests at Health center & Health post level for the investigation of Diabetics Mellitus**

**1. Self- Monitoring of glucose**

Many patients (especially those with type 1(

The lowest blood glucose concentration that will result in glycosuria is termed the renal threshold (180-200 mg/dl). It is possible to use both enzymatic technique and oxidation-reduction technique to determine urine glucose

## 2.1 Enzymatic technique

### 2.1.1 Reagent strip (Glucose oxidase) Tests

**Principle and specificity**

Since the reagent strip tests for urinary sugar use glucose oxidase which only react in the presence of glucose they are highly specific. Reagent strip tests for urine glucose are double sequential enzyme reactions. Glucose oxidase will oxidize glucose to gluconic acid and at the same time reduce atmospheric oxygen to $H_2O_2$. The hydrogen peroxide formed will, in the presence of the oxidized form, which is indicated by the color change of an oxidation- reduction indicator.

***Note:*** The glucose oxidase, peroxidase and the reduced form of the Oxidation-Reduction indicator are all impregnated on to a dry reagent strip. There are different kinds of reagent strips and they all contain Gluocse oxidase and peroxidase.

#### 2.1.1.1 Procedure

1. Collect the urine sample with a clean, dry, free from any antiseptic and wide mouth container
2. Transfer the urine into a conical test tube
3. Take one strip from the reagent strip container
4. Immerse the strip into the urine in a conical test tube
5. Immediately pull it out and let it stand for one minute. So as to have time for reaction and color change to occur on the strip
6. After one minute read the result by matching the color on the strip with the color on the reagent strip container
7. Report the result

**3. Determination of ketone bodies in urine**

ketone bodies are a group of three related substances: acetone, aceto acetic acid, and β – hydroxyl butyric acid.

When ever fat (rather than carbohydrate) is used as the major source of energy, ketosis and ketonuria may result.

The two out standing causes of ketone accumulation are diabetes mellitus and starvation

In diabetes mellitus, the body is unable to use carbohydrate as an energy source and attempts to compensate by resorting to fat catabolism, which results accumulation of ketone more than normal, that the body is unable to utilize it.

The clinical result is an increased concentration of ketones in the blood (ketonemia) and in the urine (ketonuria.)

Since the presence of ketone bodies in urine is an early indication of lack of adequate insulin control, reagent strips that combine tests for glucose and ketone are often used.

**3.1 dipstick test**

**Principle:** the reagent strip tests for ketone bodies are based on legal's (Rothera's) test, a color reaction with sodium nitroprusside (nitro ferricyanide). Acetic acid will react with sodium nitro prusside in an alkaline medium to form a purple color.

**3.1.1 Procedure**

1. After collecting the urine sample from the patients, transfer into a clean, dry and free of disinfectant test tube
2. Then immerse the dipstick into the urine
3. Then drain and let it stand for certain seconds for the reaction to take place
4. Read the result by comparing the color produced with the standard on the strip container

***Note*** acetone and aceto acetic acid can be detected by different dip stick tests, but there is no reagent strip test for β - hydroxyl butyric acid

## 4. Determination of urine protein

**Microalbuminuria**

- Diabetes mellitus causes progressive changes to the kidneys and ultimately results in diabetic renal nephropathy. This complication progresses over a period of years and may be delayed by aggressive glycemic control
- An early sign that nephropathy is occurring is an increase in urinary albumin
- It is thought that the early development of renal complications can be predicted by the early detection of consistent micro albuminuria. And this early detection is desirable, as better control of blood glucose levels may delay the progression of renal disease

### 4.1 Methods of measurement

Test for urinary protein are of two major types:

a. Tests that are based on the use of the protein error of PH indicators

- This is the methodology employed in the various reagent strip tests
- They are more sensitive to the presence of albumin than to other proteins.

b. Tests that are based on the precipitation of pr

**Complications**

- Classified into acute and chronic complications
- Acute complications are
    - Diabetic ketoacidois
    - Nonketotic hyperosmolar state
    - Hypoglycemia
- Chronic complications
    - Affect many organ systems
    - Are responsible for the majority of morbidity and mortality associated with the disease
    - Can be subdivided into **vascular** and **non-vascular** complications
    - The vascular complications are further subdivided into
        - Microvascular complications that includes
            - Diabetic retinopathy
            - Diabetic nephropathy
            - Diabetic neuropathy
        - Macrovascular complications
            - Coronary artery disease
            - Peripheral vascular disease
            - Cerebrovascular disease
    - The non-vascular complications are
        - Gastroparesis
        - Sexual dysfunction
        - Skin changes

## Therapeutic approach

There are four components of management for diabetes, which is carried by the health extension workers: -

- Diet
- Exercise
- Monitoring

- Education

**I. Dietary Management**

Goal: - provision of all the essential food constitutes (eg, vitamins, minerals)

- Achievement and maintenance of reasonable weight
- Meeting energy needs
- Prevention of wide daily fluctuations in blood glucose levels with BGL as close to normal as is safe & practical
- Decrease of blood lipid levels, if elevated

**A. Calories**

The most important objective in dietary management of DM is control of total calorie intake to attain or maintain a reasonable body weight & control of blood glucose levels.

**The general recommendation include consumption of a balanced health diet composed of the following**

- 50% to 60% of calories be derived from carbohydrates
- Less than 30% from fat &
- The remaining 10% to 20% from protein

***Food which diabetic should avoid (rapidly absorbed carbohydrate**)

1) Sugar, honey, jam, marmalade &candy
2) Cakes & sweat biscuits
3) Soft drink (Fanta, cocacola etc)
4) Alcohol (Cognac, tej, arki, whisky)

There are alcohols, which are allowed in moderation, that is, less sweat drinks i.e light beer or dry wine (not more than 2drinks for men, 1 drink for females/day). Alcoholic beverage is equivalent to12 oz beer, 5 oz wine& 1.5 oz spirit. It should be always taken with food.

*__Foods which diabetic should take with restrictions__

A) Foods from grain eg injera, bread, kinche , dabo kolo, kita ,atemit
B) Foods prepared from peas, beans, and lentils
C) Potato, sweat potato, kocho, bulla
D) All fruits except lemons& grap fruit
E) Macaroni, pasta, rice

**Foods, which diabetics can take freely or with minimal restriction**

A) Lean meat &fish
B) Eggs and milk
C) Green leafy vegetables (kale, salad, cabbage D) Lemon, grape fruit
E) Tea, coffee, lemon juice with out sugar, ambo water, and other mineral water & clear soup
F) Spices pepper ,berberi
G) Tomato, pumpkin, carrot, onion and chilipeper

**II. Exercise**

- Is extremely important in the management of diabetes because of its effect on
  - Á lowering blood glucose and
  - Á reducing cardiovascular risk factors

-Lowers blood glucose level by increasing the uptake of glucose by body muscles and by improving insulin utilization

- Pre or post exercise snack may be required to prevent hypoglycemia after exercise
- Patients should be thought to do regular, moderate exercise at the same time (preferably when blood glucose level are at their peak) and in the same amount for at least 30 minutes each day.

-Patient is advised:- to use proper footwear and if appropriate other protective equipment

- avoid exercise in extreme heat or cold

Absorption is greatest in abdomen and decreases progressively in the arm, thigh, and hips

**Rotation**

- Rotation of injection site is required to prevent lipodystrophy, localized changes in fatty tissue,

Pt is instructed as: -

1. Do not use a site > once every 4 to 6 weeks
2. Sites should be 1 to 1 ½ inches apart
3. Use all sites in one geographic area, then move to the next area
4. Document site use

**Side effects of insulin injections**

1. Local allergic reactions.
   - in the form of redness, swelling , tenderness , and indurations or a 2 to 4 cm wheal may appear at the injection site 1to 2 hrs after injection
   - usually occur during the beginning stage of therapy and disappear with continued use of insulin
   - antihistamine will be given 1 hr before injection
   - if alcohol is used to clean the area the skin should be allowed to dry
2. Systemic allergic reaction
   - are rare
   - local skin reaction that gradually spreads in to generalized urticaria

   Treatment:- desensitization , gradually increasing the amount of insulin

3. Insulin lipodystrophy
   - Refers to a localized disturbance of fat metabolism in the form of loss of sc fat and appears as slight dimpling or more serious pitting of sc fat or is the development of fibrofatty masses at the injection site and is caused by the repeated use of injection site
   - if insulin is injected in to scarred areas the absorption may be delayed

   Treatment: Pt should avoid injection on t

## Table - Knowledge

| Learning Objectives | HO | Nurses | Medical Laboratory | Environmental Health |
|---|---|---|---|---|
| Describe DM | Define DM<br>study the pathogenesis and clinical manifestations | Define DM<br>study the pathogenesis and clinical manifestations | Define DM<br>study the pathogenesis and clinical manifestations | Define DM study the pathogenesis and clinical manifestations |
| Understand the diagnostic approach of DM | Study history and physical examination<br>Study diagnostic procedures | Study history and physical examination<br>Study diagnostic procedures | Study history and physical examination<br>Study diagnostic procedures | Study history and physical examination<br>Study diagnostic procedures<br>Study recording and reporting of results |
| Describe the global magnitude of the problem of DM and its importance in Ethiopia | Study the epidemiology<br>Study the risk factors | Study the epidemiology<br>Study the risk factors | Study the epidemiology<br>Study the risk factors | Study the epidemiology<br>Study the risk factors |
| Study the treatment strategies for DM | Study overall principles of management of DM<br>Study the therapeutic approach | Study overall principles of management of DM<br>Study the therapeutic approach | Study overall principles of management of DM<br>Study the therapeutic approach | Study overall principles of management of DM<br>Study the therapeutic approach |

# Table - Attitude

| Learning Objectives | HO | Nurses | Environmental | Laboratory |
|---|---|---|---|---|
| To believe that screening of high risk individuals for DM can reduce the occurrence of clinical DM | P | P | P | P |
| To believe that early detection and management reduces the | | | | |

## Table - Practice

| Learning Objectives | HO | Nurses | Environmental | Laboratory |
|---|---|---|---|---|
| Demonstrate methods and techniques of Diabetic patient examination | P | P | | |
| Label patients as high and low risk and follow them accordingly | P | P | P | P |
| Manage diabetics related complication | P | P | | P |
| Identify risk factors | P | P | P | P |
| Develop necessary skills on laboratory investigations | P | P | P | P |
| Follow the standard reporting and recoding technique | perform the appropriate laboratory tests<br>- Follow the scientific procedures to do the tests<br>- order routine lab investigations | performappropriate laboratory tests<br>- Follow the scientific procedures to do the tests<br>- order routine lab investigations | perform the appropriate laboratory tests<br>- Follow the scientific procedures to do the tests | perform the appropriate laboratory tests<br>- Follow the scientific procedures to do the tests |

**Keys for the pretest and post test questions for Nurses**

1. A
2. C
3. C
4. E
5. A
6. C
7. A
8. C
9. D
10. a- site of injection
    -preparations of medication
    -Rotations
    -about syringe and needle
    -some problems with insulin injections

    b) -too much insulin
    -too little food or
    -excessive physical exercise
    -delay of meal or omitting of snacks

    c) -sweating
    -tremor
    -tachypnea
    -confusion
    -seizure
    -loss of consciousness

    d) Having snack, not delaying the meal, right dose of medications, having candies at hand

    f)-assess foot daily for sensation, redness and broken skins
    -wash dry feet daily
    - If skin is dry apply a thin coat of lubricating oil

-tie shoes loosely but firmly

-If your feet perspire, change shoe and stocking during the day

-wear shoe and stocking that gives room for the movement of the toe

## Key For Laboratory Technology

1. B
2. C
3. C
4. C
5. C
6. A
7. C
8. B
9. A
10. A