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- Diagnosis
- Treatment





INTRODUCTION

Definition:

- chronic metabolic disorder of multiple etiology in which the body can't metabolize carbohydrate, fats and proteins
- because of defects in insulin secretion and/or action.



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Classification of DM

I. Type 1 DM

- It is due to insulin deficiency and is formerly known as:
- Type I
- Insulin Dependent DM (IDDM)
- Juvenile onset DM

II. Type 2 DM

- It is a combined insulin resistance and relative deficiency in insulin secretion and is frequently known as:
- Type II
- Noninsulin Dependent DM (NIDDM)
- Adult onset DM

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Classification of DM

III. Gestational Diabetes Mellitus (GDM):

 Gestational Diabetes Mellitus (GDM) developing during some cases of pregnancy but usually disappears after pregnancy.

IV. Secondary DM:

- Results from another medical condition or due to the treatment of a medical condition that causes abnormal blood glucose levels
- Cushing syndrome (e.g. steroid administration)
- Hyperthyroidism

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Epidemiology

\square Type 1 DM:

- It is due to pancreatic islet β-cell destruction predominantly by an autoimmune process.
- Usually develops in childhood or early adulthood
- accounts for upto 10% of all DM cases
- Develops as a result of the exposure of a genetically susceptible individual to an environmental agent

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Epidemiology

☐ Type 2 DM:

- It results from insulin resistance with a defect in compensatory insulin secretion.
- Insulin may be low, normal or high!
- About 30% of the Type 2 DM patients are undiagnosed (they do not know that they have the disease) because symptoms are mild.
- accounts for up to 90% of all DM cases

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Etiology

☐ Etiology of Type 1 Diabetes:

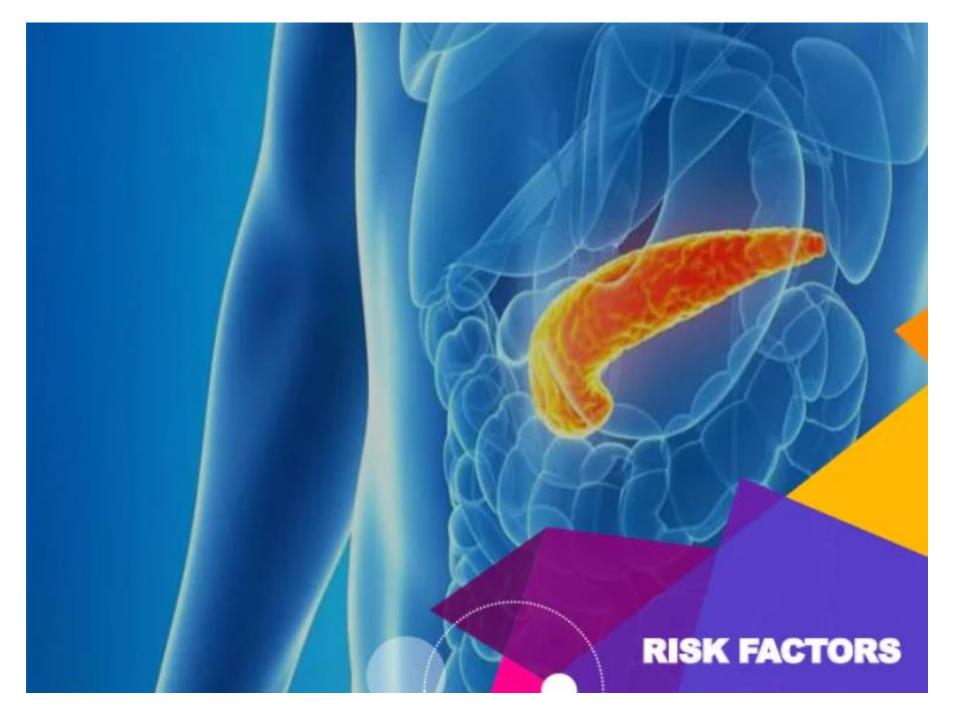
- Autoimmune disease
- Selective destruction of cells by T cells
- Several circulating antibodies against cells
- Cause of autoimmune attack: unknown
- Both genetic & environmental factors are important

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Etiology

☐ Etiology of Type 2 Diabetes:

- Response to insulin is decreased
- ∫ glucose uptake (muscle, fat)
- o † glucose production (liver)
- The mechanism of insulin resistance is unclear
- Both genetic & environmental factors are involved
- Post insulin receptor defects



Risk Factors

☐ For Type 1 DM

- Genetic predisposition
- In an individual with a genetic predisposition, an event such as virus or toxin triggers autoimmune destruction of β-cells probably over a period of several years.

Risk Factors

☐ For Type 2 DM

- Family History
- Obesity
- Habitual physical inactivity
- Previously identified impaired glucose tolerance (IGT) or impaired fasting glucose (IFG)
- Hypertension
- Hyperlipidemia



Clinical manifestations

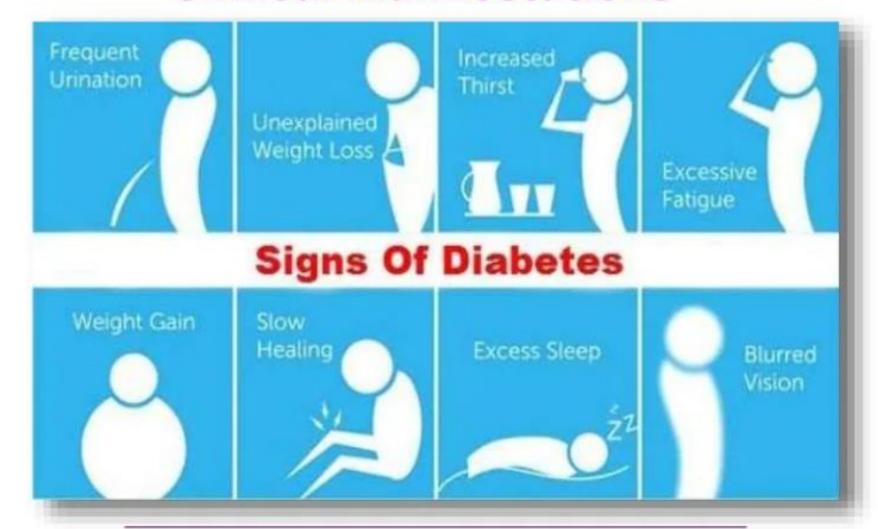
- **☐** Type 1 DM:
- Polyuria
- Polydipsia
- Polyphagia
- Weight loss
- Weakness
- Dry skin
- Ketoacidosis

Clinical manifestations

☐ Type 2 DM:

- Patients can be asymptomatic
- Polyuria
- Polydipsia
- Polyphagia
- Fatigue
- Weight loss
- Most patients are discovered while performing urine glucose screening

Clinical manifestations





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- Fasting blood glucose(FBG)
- Glucose blood concentration in samples obtained after at least 8 hours of the last meal
- Random Blood glucose
- Glucose blood concentration in samples obtained at any time regardless the time of the last meal

- Glucose tolerance test(OGTT)
- 75 gm of glucose are given to the patient with 300 ml of water after an overnight fast
- Blood samples are drawn 1, 2, and 3 hours after taking the glucose
- This is a more accurate test for glucose utilization if the fasting glucose is borderline

- Glycosylated hemoglobin (HbA1C)
- Normally it comprises 4-6% of the total hemoglobin.
- Increase in the glucose blood concentration increases the glycated hemoglobin fraction.
- HbA1C reflects the glycemic state during the preceding 8-12 weeks

- Glucosuria
- To detect glucose in urine by a paper strip
- Semi-quantitative
- Normal kidney threshold for glucose is essential
- > Ketonuria
- To detect ketonbodies in urine by a paper strip
- Semi-quantitative

Diagnostic criteria

	HbA1C	FBG (mg/dl)	OGTT (mg/dl)
Diabetes	≥6.5	≥126	≥200
Prediabetes	5.6-6.4	100-125	140-199
Normal	<5.6	≤99	≤139



DM - management

- ☐ Goals of therapy:
- Reduce symptoms
- Promote well-being
- Prevent acute complications
- Delay onset and progression of long-term complications

DM - management

- ☐ Lines of therapy:
- Non-pharmacological treatment
- Pharmacological treatment

Non-pharmacological treatment

- Nutritional therapy:
- Diet
- Exercise
- Stop smoking
- Avoid precipitating factors



- Overall goal of nutritional therapy
- Assist people to make changes in nutrition and exercise habits that will lead to improved metabolic control

- Type 1 DM
- Diet based on usual food intake, balanced with insulin and exercise patterns
- In most cases, high carbohydrate, low fat, and low cholesterol diet taken
- Type 2 DM
- Calorie reduction

- Food composition
- Meal plan developed with dietitian
- Nutritionally balanced
- Does not prohibit the consumption of any one type of food

- Exercise
- Essential part of diabetes management
- Increases insulin sensitivity
- Lowers blood glucose levels
- Decreases insulin resistance
- Take small carbohydrate snacks during exercise to prevent hypoglycemia
- Exercise after meals
- Monitor blood glucose levels before, during, and after exercise

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Pharmacological treatment

- Insulin (Type 1 and Type 2 DM)
- Sulfonylurea (Type 2 DM)
- Biguanides (Type 2 DM)
- Meglitinides (Type 2 DM)
- Thiazolidinediones Glitazones (Type 2 DM)
- α-Glucosidase inhibitors (Type 2 DM)
- Incretin mimetic (Type 2 DM)
- DPP4 inhibitors (Type 2 DM)
- Amylin analogs(Type 1 and Type 2 DM)
- SGLT2 Inhibitors(Type 2 DM)



Drug Therapy: Insulin

- > Exogenous insulin:
- Required for all patient with type 1 DM
- Prescribed for the patient with type 2
 DM who cannot control blood glucose by other means

Drug Therapy: Insulin

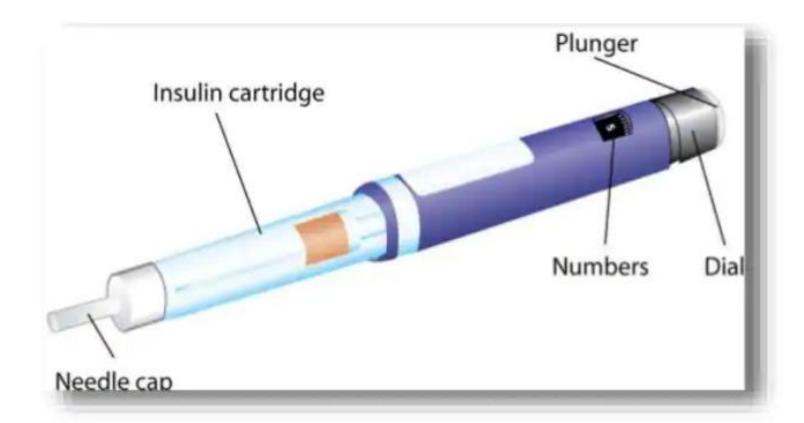
- Methods of Insulin Administration
- Cannot be taken orally
- Insulin delivery methods
- Ordinary SQ injection with syringes
- Insulin pen
- Insulin pump

Drug Therapy: Insulin

- > Administration of insulin
- Fastest absorption from abdomen, followed by arm, thigh, buttock
- Rotate injections within one particular site
- Do not inject in site to be exercised



Drug Therapy: Insulin



Drug Therapy: Insulin

- > Problems with insulin therapy
- Hypoglycemia:
- Due to too much insulin in relation to glucose availability
- Allergic reactions
- Local inflammatory reaction
- Lipodystrophy
- Hypertrophy or atrophy of SQ tissue due to frequent use of same injection site.

Drug Therapy: Insulin

- Drugs interfering with glucose tolerance
- Diazoxide
- Thiazide diuretics
- Corticosteroids
- Oral contraceptives
- Streptazocine
- Phenytoin
- All these drugs increase the blood glucose concentration.

Drug Therapy: Oral Agents

- Increase insulin production by pancreas
- Reduce glucose production by liver
- Enhance insulin sensitivity and glucose transport into cell
- Slow absorption of carbohydrate in intestine

Pharmacotherapy: Type 2 DM

☐ General considerations:

- Consider therapeutic life style changes (TLC) for all patients with Type 2 DM
- Initiation of therapy may depend on the level of HbA1C
- HbA1C < 7% may benefit from TLC
- HbA1C 8-9% may require one oral agent
- HbA1C > 9-10% my require more than one oral agent

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- **□** Obese Patients :
- Metformin or glitazone then if inadequate
- Add SU or short-acting insulin secretagogue then if inadequate
- Add Insulin or glitazone



Pharmacotherapy: Type 2 DM

□ Non-Obese Patients :

- Add SU or short-acting insulin secretagogue then if inadequate
- Add Metformin or glitazone then if inadequate
- Add Insulin

- **□** Early insulin resistance :
- Metformin or glitazone then if inadequate
- Add glitazone or metformin then if inadequate
- Add SU or short-acting insulin secretagogue or insulin

- The choice of therapy is simple
- All patients need Insulin
- The goal is:
- To balance the caloric intake with the glucose lowering processes (insulin and exercise), and allowing the patient to live as normal a life as possible

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- The insulin regimen has to mimic the physiological secretion of insulin
- With the availability of the SMBG and HbA1C tests adequacy of the insulin regimen can be assessed
- More intense insulin regimen require more intense monitoring

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Pharmacotherapy: Type 1 DM

- Example:
- Morning dose (before breakfast):

Regular + NPH or Lente

2) Before evening meal:

Regular + NPH or Lente

 Require strict adherence to the timing of meal and injections

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Pharmacotherapy: Type 1 DM

Modification

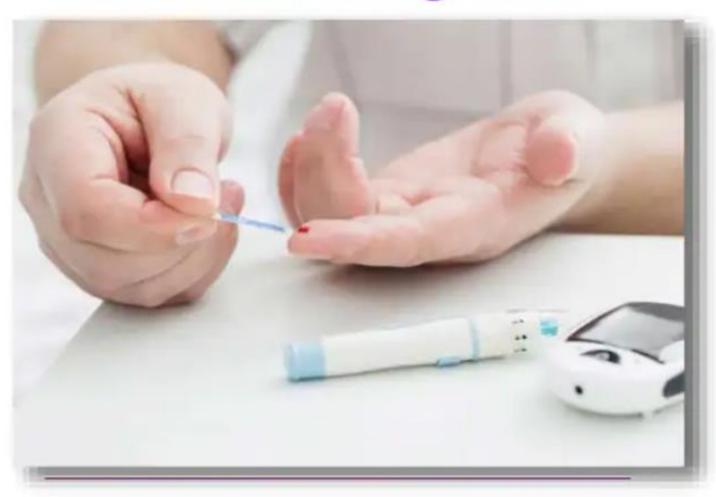
- NPH evening dose can be moved to bedtime
- Three injections of regular or rapid acting insulin before each meal + long acting insulin at bedtime (4 injections)
- The choice of the regimen will depend on the patient



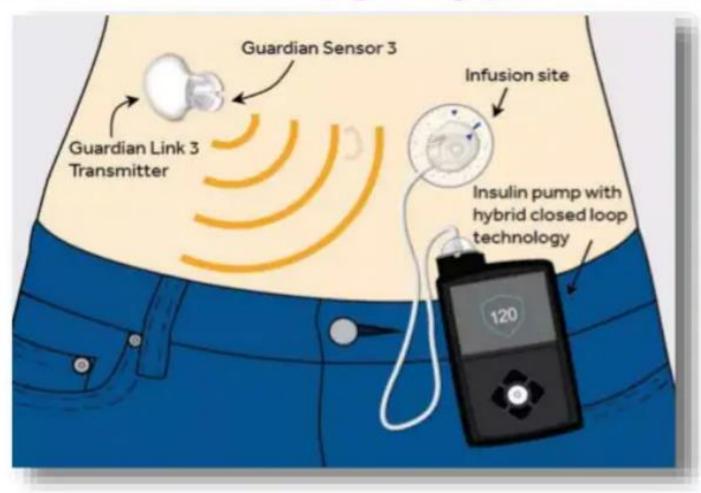
- ➤ How much insulin?
- A good starting dose is 0.6 U/kg/day
- The total dose should be divided to:
- 45% for basal insulin
- 55% for prandial insulin

- ☐ Self-monitoring of blood glucose(SMBG)
- Extremely useful for outpatient monitoring specially for patients who need tight control for their glycemic state.
- A portable battery operated device that measures the color intensity produced from adding a drop of blood to a glucose oxidase paper strip.
- e.g. One Touch, Accu-Chek, DEX, Prestige and Precision.

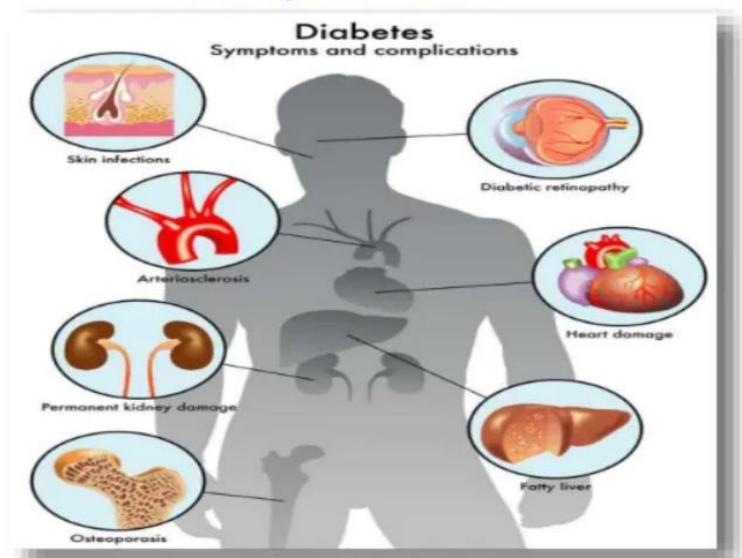
Self Monitoring Test



- ➤ Insulin Pump Therapy
- This involves continuous SC administration of short-acting insulin using a small pump
- The pump can be programmed to deliver basal insulin and spikes of insulin at the time of the meals
- Requires intense SMBG
- Requires highly motivated patients because failure to deliver insulin will have serious consequences



Complications



Complications

- Acute Complications
- Hypoglycemia
- Diabetic ketoacidosis
- Hyperosmolar hyperglycemic nonketotic syndrome

Complications

- Chronic Complications
- Macrovascular complications:
- Coronary heart disease, stroke and peripheral vascular disease
- Microvascular Complications:
- Retinopathy, nephropathy and neuropathy



Acute Complication: Hypoglycemia

- Hypoglycemia occurs due to too much insulin (or oral agents) in relation to glucose availability
- Brain requires constant glucose supply thus hypoglycemia affects mental function

Acute Complication: Hypoglycemia

- Clinical manifestations:
- Confusion, irritability
- anxiety, tachycardia, tremors
- Diaphoresis, tremor, hunger, weakness, visual disturbances
- If untreated → loss of consciousness, seizures, coma, death

Acute Complication: Hypoglycemia

- > Treatment for hypoglycemia
- Ingest simple CHO (fruit juice, soft drink), or commercial gel or tablet
- Avoid sweets with fat (slows sugar absorption)
- Then eat usual meal snack or meal and recheck
- if not alert enough to swallow
- ⊙ Glucagon 1m IM or SQ (glycogen → glucose)
- Then complex CHO when alert

Acute Complication: Diabetic Ketoacidosis (DKA)

- Usually in Type 1 diabetes; can occur in Type 2
- Causes:
- Infection
- Stressors (physiological, psychological)
- Stopping insulin
- Undiagnosed diabetes

Acute Complication: Diabetic Ketoacidosis (DKA)

- Clinical manifestations:
- Dehydration
- Deep difficult breathing (d/t metabolic acidosis)
- Fruity breath (d/t acetone)
- Abdominal pain, N & V, cardiac dysrhythmias

Acute Complication: Diabetic Ketoacidosis (DKA)

- > Treatment
- Replace fluid and electrolytes
- Insulin (First IV bolus, then infusion)
- correct precipitating cause (e.g., infection, etc.)

