Diabetes Management

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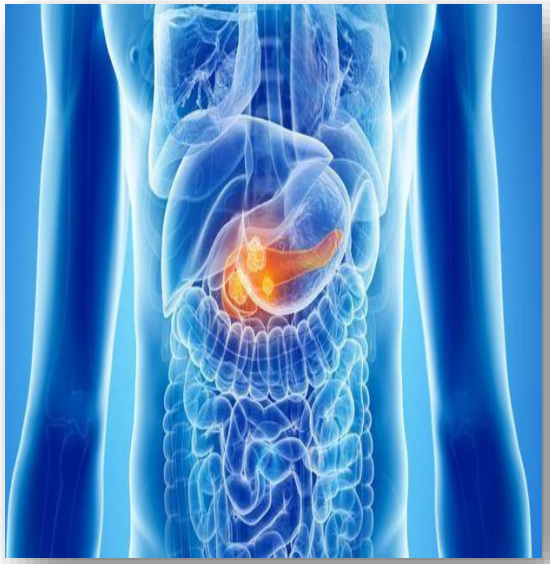


Diabetes Mellitus

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.

INTRODUCTION

- As of 2015, an estimated 415 million people had diabetes worldwide, with type 2 DM making up about 90% of the cases.
- From 2012 to 2015, approximately 1.5 to 5.0 million deaths each year resulted from diabetes.

Classification of DM

I. Type 1 DM

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

II. Type 2 DM

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

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

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

Etiology

❑ Etiology of Type 2 Diabetes:

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

Epidemiology

❑ 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

Epidemiology

❑ Type 2 DM:

- It results from insulin resistance with a defect in 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

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
- physical inactivity
- 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

Complications

➢ Acute Complications

- Hypoglycemia
- Diabetic ketoacidosis

Complications

➢ Chronic Complications

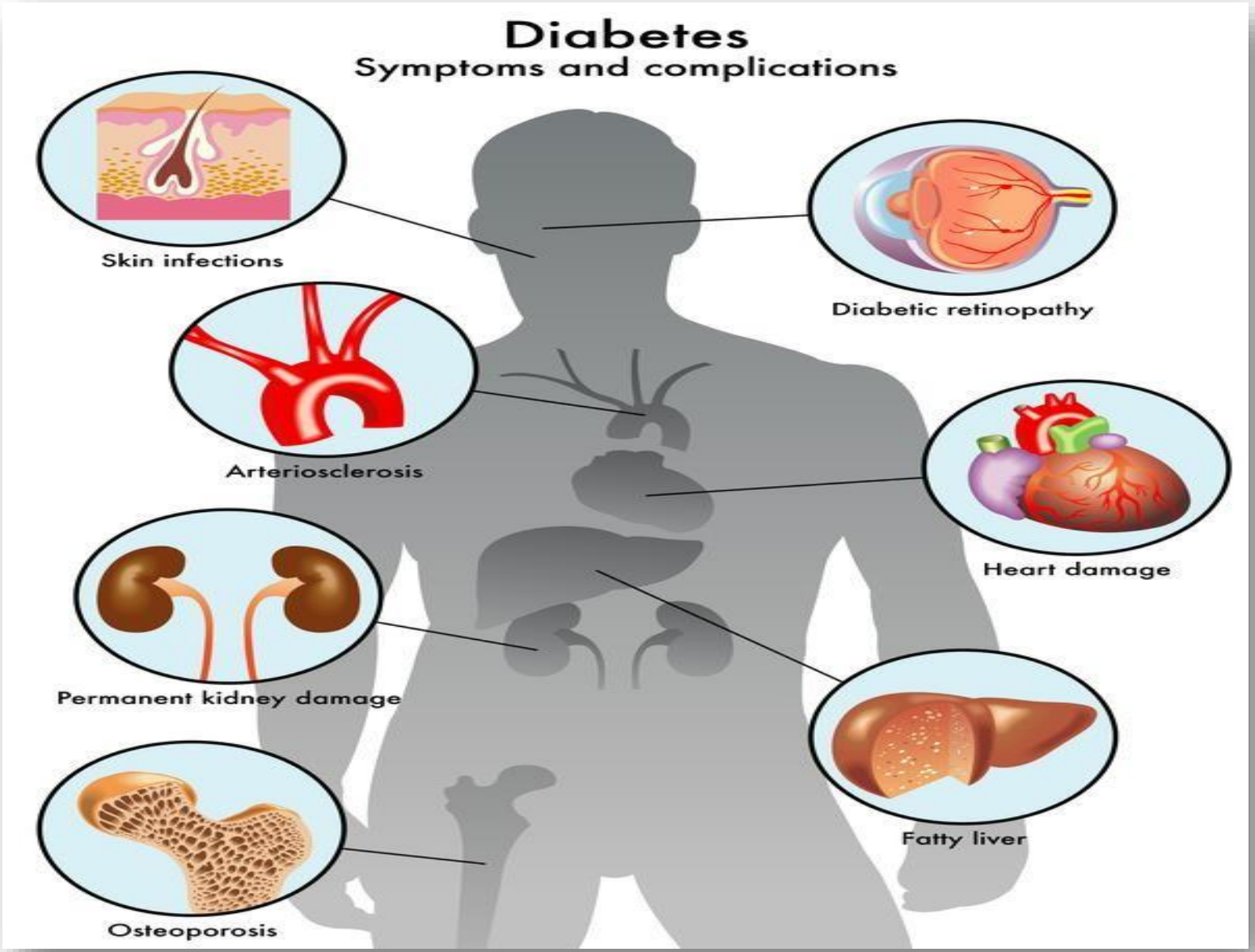
❑ Macrovascular complications:

- Coronary heart disease, stroke and peripheral vascular disease

❑ Microvascular Complications:

- Retinopathy, nephropathy and neuropathy

Complications



Laboratory examination

- **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.

Laboratory examination

➢ 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 1,٢ and 3 hours after taking the glucose
- This is a more accurate test for glucose utilization if the fasting glucose is borderline

Laboratory examination

- **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

Laboratory examination

- **Glucosuria**
  - To detect glucose in urine
  - Semi-quantitative
  - Normal kidney threshold for glucose is essential
- **Ketonuria**
  - To detect ketonbodies in urine
  - 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
- 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

Nutritional Therapy

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

Nutritional Therapy

- **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

Nutritional Therapy

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

Nutritional Therapy

- **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

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

- **Source of insulin**
- *Human insulin*
  - Most widely used type of insulin
  - Cost-effective & less allergic reaction
- Insulins differ in regard to start, peak action, and duration
- Different types of insulin may be used for combination therapy

Drug Therapy: Insulin

- **Types of insulin**
  - Regular insulins
  - Insulin analogs
  - Pre-mixed insulin

Drug Therapy: Insulin

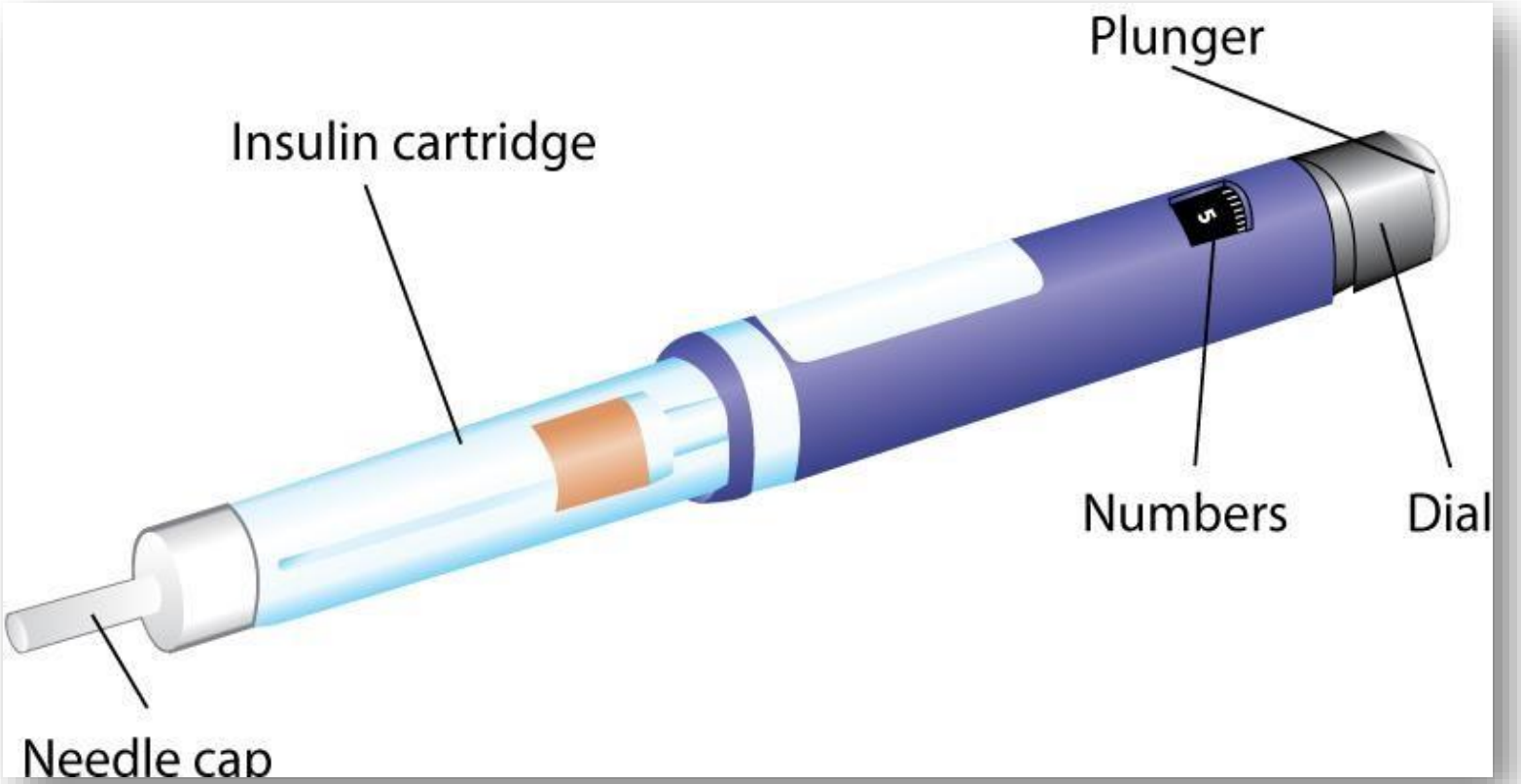
- **According to onset:**
  - Rapid-acting insulin e.g. Insulin lispro
    Short-acting insulin e.g. Regular insulin
  - Intermediate-acting insulin e.g. NPH and Lente insulin
  - Long-acting insulin e.g. Insulin Glargine
  - Mixture of insulin can provide glycemic control over extended period of time e.g. Humalin 70/30 (NPH + regular)

Drug Therapy: Insulin

➢ Methods of Insulin Administration

- Cannot be taken orally
- Insulin delivery methods
  - Injection with syringes
  - Insulin pen
  - Insulin pump

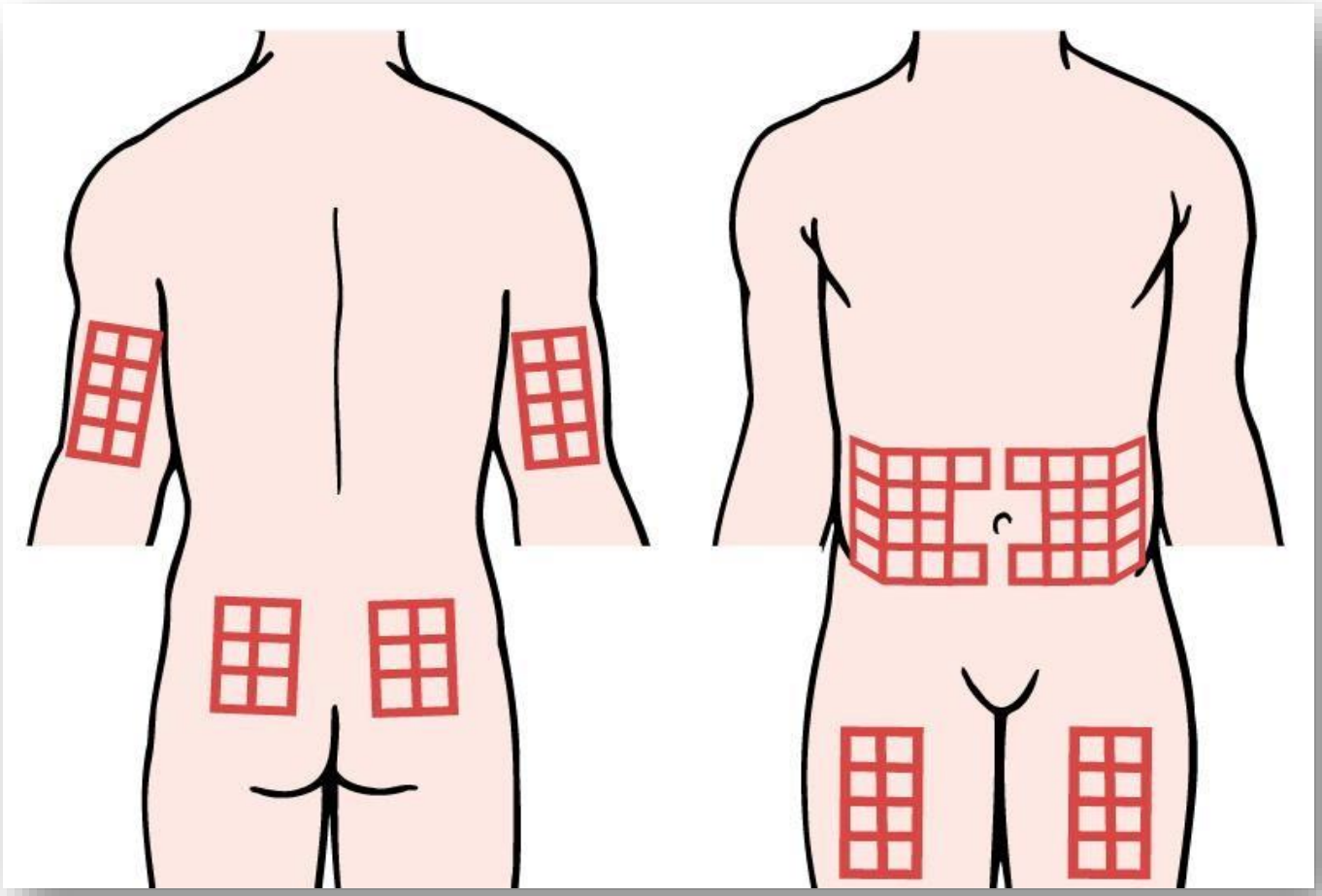
Drug Therapy: Insulin



Drug Therapy: Insulin

- **Administration of insulin**
- Fastest absorption from abdomen,
- 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 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

Sulfonylureas

- Stimulate the pancreatic secretion of insulin
- **Classifications:**

➢ *First generation*

- e.g. tolbutamide, chlorpropamide, and acetohexamide

➢ *Second generation*

- e.g. glimepiride, glipizide, and glyburide

Sulfonylureas

- **Side effects**
  - Hypoglycemia
  - Hypernatremia (↑Na)
  - Weight gain

Meglitinides

- E.g Repaglinide ,Nateglinide
- Stimulate the pancreatic secretion of insulin
- Should be given before meal or with the first bite of each meal.
- Should not be taken if meal skipped
- Lower incidence of hypoglycemia (0.3%)

Biguanides

- E.g Metformin
- Act by
  - Reduces hepatic glucose production
  - Increases peripheral glucose utilization
- Does not promote weight gain

➢ **Side effects**

- Nausea, vomiting, diarrhea, and anorexia
- lactic acidosis (rare)

Glitazones (PPARγ - Agonists)

- E.g Rosiglitazone - Pioglitazone
- Act by stimulation of peroxisome proliferator-activated receptor γ
  - Reduces insulin resistance in the periphery and possibly in the liver
- Most effective in those with insulin resistance
- Edema and weight gain are the most common side effects.

α-Glucosidase Inhibitors

- E.g Acarbose - Miglitol
- Act by
  - Slow down absorption of carbohydrate in small intestine
  - Prevent the breakdown of sucrose and complex carbohydrates
  - Th net result reduction of postprandial blood glucose rise

Amylin analog

- Indicated for type 1 and type 2 diabetics
- Administered subcutaneously (Thigh or abdomen)
- Slows gastric empyting, reduces postprandial glucagon secretion
- Example :Pramlintide

Incretin mimetic

- Synthetic peptide
- Given by subcutaneous injection
- Activates (glucagon like peptide) GLP-1 receptor
- This results in :
  - Stimulates release of insulin from β cells
  - Suppresses glucagon secretion
  - Reduces food intake
  - Slows gastric emptying
- Not to be used with insulin
- Example : Exenatide

DPP4-Inhibitors

- Inhibits (dipeptidyl peptidase 4 inhibitor) DPP-4
- This results in increase of Glucagon-like peptide-1 (GLP-1) action leading to improved pancreatic islet glucose sensing, increase glucose uptake
- Example : Sitagliptin - Linagliptin

SGLT-2 Inhibitors

- SGLT-2 :Sodium Dependent Glucose Transporters – 2
- Inhibit glucose reabsorption in renal proximal tubule
- Resultant glucosuria leads to a decline in plasma glucose & reversal of glucotoxicity
- This therapy is simple & nonspecific
- Even patients with refractory type 2 diabetes are likely to respond

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

Pharmacotherapy :Type 2 DM

❑ Obese Patients :

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

Pharmacotherapy :Type 2 DM

❑ Non-Obese Patients :

- Add SU or short-acting insulin
  then if inadequate

- Add Metformin or glitazone then if inadequate

- Add Insulin

Pharmacotherapy :Type 2 DM

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

Pharmacotherapy :Type 1 DM

- 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

Pharmacotherapy :Type 1 DM

- **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

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 أرتعاش
  - 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 (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
  - dysrhythmias

Acute Complication: Diabetic Ketoacidosis (DKA)

- **Treatment**
  - Replace fluid and electrolytes
  - Insulin