Group	Example	Feature
Rapid acting insulin analogs	- lispro - aspart	Given just before meal
Short acting insulin	Regular insulin	- Identical to human insulin - **Only one can be given IV**
Intermediate acting insulin	Isophane insulin (N.P.H.)	Made by adding protamine to insulin to increase the duration of action
Long-acting insulin	- glargine - detemir	- **Peakless** - Once daily
Premixed insulin (biphasic)	- Humalin 70/30 (NPH/Reg) - Mixtard	- Rapid onset - Long duration

Insulin

Sources

- **Traditional (animal) insulin**
- **Human insulin:**
  - Identical to human insulin (Made via recombinant DNA)
  - ↓ antigenicity & rare insulin resistance
- **Insulin analogs:** Modified human insulin → altered pharmacokinetics

Indications

- **Type 1 DM.**
- **Type 2 DM in some conditions:** After failure of oral drugs & Stress conditions (e.g. pregnancy).
- **Diabetic ketoacidosis (DKA) →** Use regular insulin I.V.

Administration

Standard concentration: 100 U/mL → Inject with U-100 syringe for accuracy.

Insulin requirement

Daily dose of 0.4 units/kg/d (then adjusted according to blood glucose)

Regimen

Basal-Bolus regimen	Twice-daily biphasic regimen
- Give **long-acting insulin (50% of total)** at bedtime + three daily injections of **short acting insulin (10-15 % each)** before each meal.	- Use biphasic insulin (**premixed**). - 2/3 of the dose in the morning & 1/3 at evening

Method of administration & follow up

Method of administration	Follow up
- S.C. injection (using insulin syringes). - Portable pen injector. - Pump.	- From **capillary** blood glucose level - Using portable glucometers - Self-Monitoring of Blood Glucose (**SMBG**)

S/E

- **Hypoglycemia** (TTT of DM part II)
- **Hypersensitivity:** Urticaria, angioedema or anaphylactic shock
- **Lipodystrophy:** Prevented by changing the injection site.

Insulin resistance (IR)

Def: Body cells fail to respond to endogenous/exogenous insulin → higher doses needed for effect

Causes: Metabolic syndrome, Obesity, Pregnancy Severe infection or stress, Drugs (corticosteroids)

TTT: Life-style modification & treat the cause

	Insulin secretagogue		Insulin Sensitizers	
	Sulfonylureas	**Glinides**	**Biguanides**	**Thiazolidinediones (TZD)**
E.g.	**Glimepiride (3rd gen)**	**Nate, Repa glinides**	**Metformin**	**Pioglitazone**
kinetics	➢ Well-absorbed ➢ **Food → ↓its absorption** ➢ High plasma protein binding (90%) ➢ Displaced by aspirin→ **↑Toxicity** ➢ Metabolized by liver ➢ Excreted by kidney	**Fast onset & short duration** → taken orally **just before meals** to control **postprandial** hyperglycemia.	➢ Well absorbed ➢ **Doesn't bind to plasma proteins** ➢ Short T½ ➢ Excreted unchanged in urine.	---
MOA	Block K^+ channels in β-cells → depolarization → ↑ Ca^{2+} influx → **↑ insulin secretion.**		➢ ❌hepatic gluconeogenesis **(most common) (activated AMPK)** ➢ **↑ insulin sensitivity & ↑ glucose** uptake in Sk. Ms. and adipose tissue ➢ ↑ Fatty acid oxidation ➢ ↓ glucose absorption from intestine ➢ **Doesn't cause insulin release** ➢ **↑ Anaerobic glycolysis**	**Act on nuclear PPAR-γ in muscle, adipose, & liver**: ○ ↑ glucose transporters → **↑ glucose uptake** ○ ↑ insulin sensitivity
Use	➢ T2DM ➢ Given 30 minutes before food	**patients allergic to sulfonylurea**	➢ T2DM ➢ **Obese patients** (↑weight loss).	T2DM (Improve resistance)
S/E	**1)** Hypoglycemia **(most common)** 2) Hepatotoxicity **3)** **Teratogenicity**		1) **GIT Upset (most common)** 2) **Lactic acidosis (most important):** Due to **↑ anaerobic glycolysis**, especially in severe renal, hepatic, or cardio-pulmonary diseases and **alcoholics**. 3) **Vitamin B12 deficiency**	➢ Hepatotoxicity ➢ **Salt & water retention** → peripheral edema & weight gain **(avoid in CHF patients)**
	Hypersensitivity	---		

	α-Glucosidase inhibitors	Dipeptidyl peptidase 4 inhibitors (Gliptins)
E.g.	**Acarbose**	**Sitagliptin**
MOA	❌**α- glucosidase**→ ↓ digestion & absorption of carbohydrates (starch blockers)	❌DPP-4 (the enzyme responsible for the proteolysis of the **incretins** [GLP-1])
Uses	T2DM	**T2DM (orally):** alone or in combination with metformin.
S/E	GIT Upset	Headache and nausea

	GLP-1 analogues			SGLT2 inhibitors
	Exenatide	**Liraglutide**	**Dulaglutide**	**Dapagliflozin**
MOA	➢ Synthetic ➢ ↑ insulin secretion ➢ ↓ glucagon secretion, ➢ ↓ gastric emptying and appetite	➢ **longer-acting** due to its tight binding to plasma proteins ➢ **T½> 12 hrs** ➢ Duration of action to > 24 hours	**very long acting**	➢ **SGLT-2 reabsorbs glucose** in PCT → inhibition → **glucosuria**, ↓blood glucose in T2DM ➢ **Causes weight loss** ➢ Once-daily dose → **24h effect**
Uses	T2DM (SC)	➢ T2DM (SC) **Once daily** ➢ **Obese patients**	T2DM (SC) **Once weekly**	➢ T2DM ➢ Reduce HbA1c but don't cause Hypoglycemia ➢ **Heart failure**
CI	---	---	---	**Renal insufficiency**
S/E	➢ Nausea & vomiting ➢ **Acute pancreatitis**	---	---	➢ Polyuria ➢ **UTI**

	Hypoglycemic coma	**Diabetic ketoacidosis (DKA)**
Cause	1) Large dose of insulin or sulfonylurea. 2) Missed meal while taking insulin or sulfonylureas.	↑↑ Glucose **(not utilized)** → ↑ Lipolysis → ↑ FFAs → **↑ Ketone bodies** → ↑ Acidosis
Management	1) **Conscious/semiconscious:** give sugar solution 2) **Deep coma:** ○ IV glucose ○ IM glucagon	1) **Fluids:** IV isotonic saline immediately 2) **Regular Insulin:** IV (0.1 U/kg/hr) → switch to SC when stable 3) **K^+:** replace as per serum level **as insulin ↑K+ Influx** 4) **HCO_3^-:** only if severe acidosis 5) **Treat cause** (e.g. antibiotics for infection)