Insulin Therapy

What is Insulin? (1)

- Polypeptide hormone
- Beta-cells of islets of Langerhans in pancreas
- Profound effects on
  - carbohydrate, fat & protein metabolism
  - To some extent on water & electrolyte balance

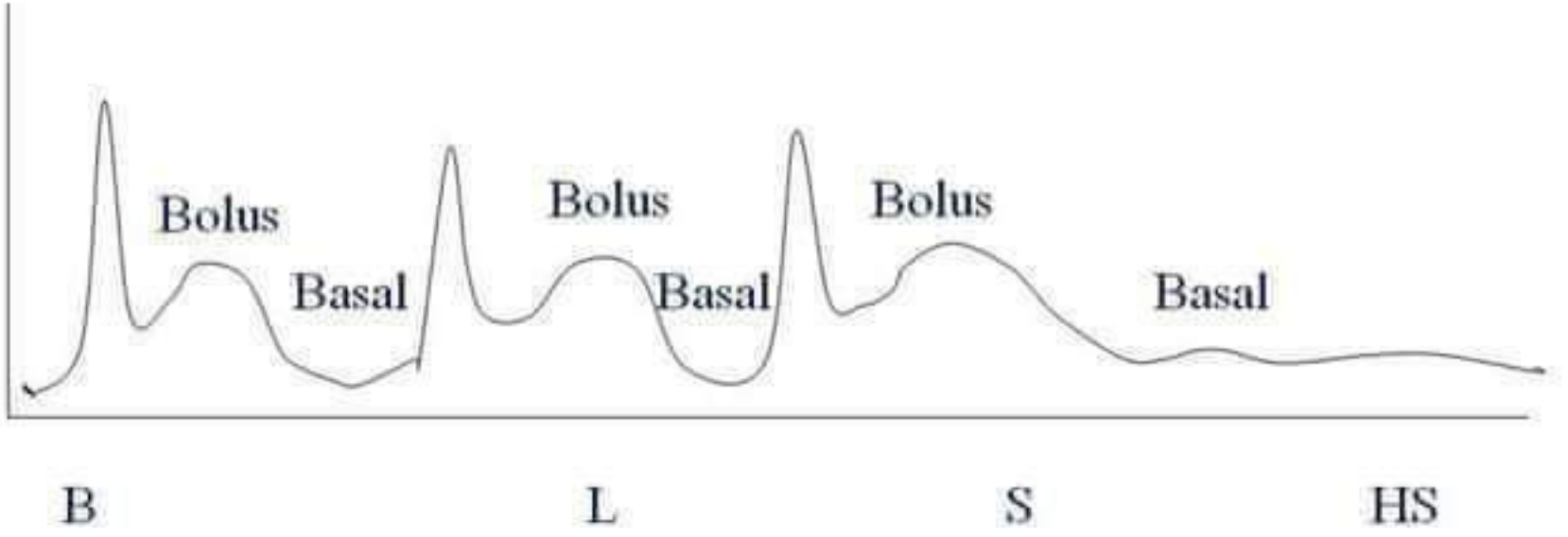
- 2 chains
- 2 bonds
- Secreted as basal & meal related (2)
- Meal related in 2 phases

What is Insulin? (2)

- Insulin deficiency results in
  - Elevated plasma glucose -*Hyperglycemia*
  - Elevated plasma lipid - *Hypertriglyceridemia*
  - Altered protein metabolism - *Metabolic & Immune defects*

- Insulin replacement in diabetes tends to restore normalcy

Insulin Secretion

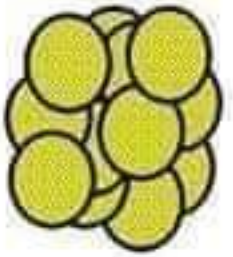


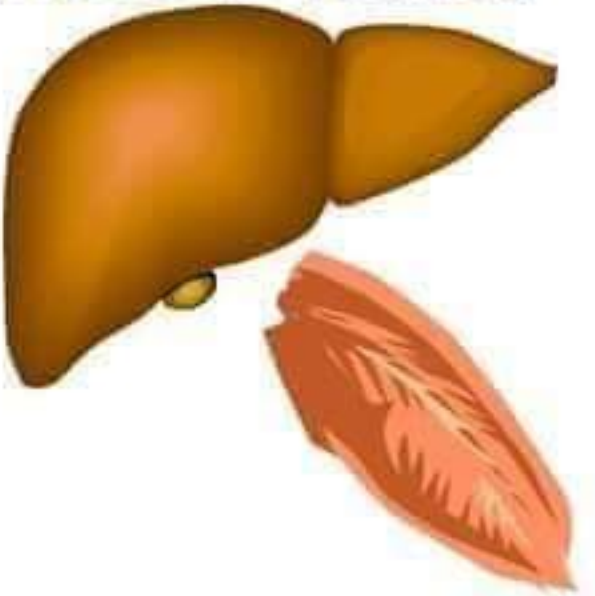
Normally secreted as basal (between meals & night time) & Meal-related peaks (1st & 2nd phase)

Actions of Insulin (1)

- Integrated action on carbohydrate, protein and fat metabolism

- Dominant effect on glucose homoeostasis predominantly exerted in 3 tissues
  - Liver
  - Skeletal muscle
  - Fat





Actions of Insulin (2)

In Liver

- Inhibition of glycogenolysis & gluconeogenesis
- Stimulation of glycogenesis & storage

In skeletal muscle & adipocytes

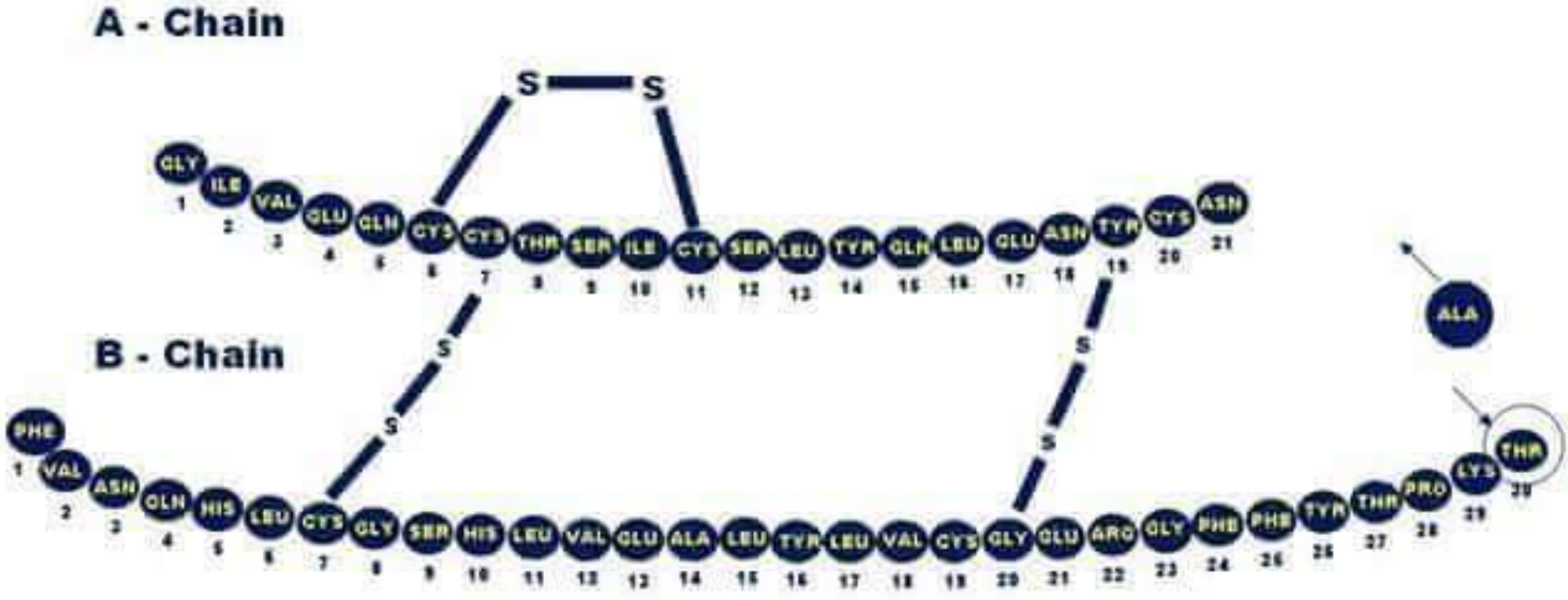
- Stimulation of glucose uptake, utilization & storage
- Increases glucose transport
- Activation/inactivation of enzymes responsible for storage & metabolism of glucose

Insulin:
The Definitive Therapy for Diabetes

- DM
  - Impaired insulin secretion (insulin deficiency)
  - Impaired insulin action (insulin resistance)
- Insulin can overcome both the defects
- Hence: Insulin-the definitive therapy for all types of diabetes

Insulin- a valuable therapeutic tool for early intervention, to attain and maintain target levels of blood glucose control.

Insulin Structure



Types of insulin

• Medrockets

Type of Insulin & Brand Names	Onset	Peak	Duration	Role in Blood Sugar Management
Rapid-Acting				
Lispro	15-30 min.	30-90 min	3-5 hours	Covers insulin needs for meals eaten at the same time as the injection.
Aspart	10-20 min.	40-50 min.	3-5 hours	
Glulisine	20-30 min.	30-90 min.	1-2½ hours	
Short-Acting				
Regular	30 min- 60 min	2-5 hours	5-8 hours	Covers insulin needs for meals eaten within 30-60 minutes
Intermediate-Acting				
NPH (N)	1-2 hours	4-12 hours	18-24 hours	Covers insulin needs for about half the day or overnight.

Types of insulin

• Medrockets

	Name of Insulin	Onset	Duration	Role in Blood Sugar Management
Long-Acting				
Long-acting insulin covers insulin needs for about one full day.	Degludec	30-90 min	No peak: insulin is delivered at a steady level.	Longer than 24 hours
	Glargine	30-90 min		Up to 24 hours
	Detemir	1-120 min		20-24 hours

Types of insulin

Type of Insulin	Onset	Peak	Duration	Role in Blood Sugar Management
Pre-Mixed*				
30/70	30 min.	2-4 hours	14-24 hours	These products are generally taken two or three times a day before mealtime.
50/50	30 min.	2-5 hours	18-24 hours	
25/75	15 min.	30 min -2½ hours	16-20 hours	
Inhaler				
Exubera	Banned			
Afrezza	With in min	12 to 15 min	2-3 hours	Post prandial effects.

*Premixed insulins are a combination of specific proportions of intermediate-acting and short-acting insulin in one bottle or insulin pen (the numbers the brand name indicate the percentage of each type of insulin).

Common Insulin Regimens (1)

Split Mix Regimens

- Two injections (intermediate + soluble) per day
  - * before breakfast & before bedtime
- Proportion/dosage of insulins titrated based on BG profile
- Drawback
  - Mixing insulins is tedious and problematic
  - Inaccuracy of dose

Not preferred –more problems for patients

Common Insulin Regimens (2)

Basal insulin

Usually given at night

- Proportion/dosage of insulin titrated based on FBG
- Drawback
  - Expensive
  - Fasting blood glucose is primary targeted
  - May be with sensitizer and or secretagogue

Common Insulin Regimens (3)
Basal Plus

- Basal insulin at night
- Any rapid acting insulin premeal.
- May be useful during early years of T2DM and in uncomplicated well motivated patients.
- May be needed to shifted to **Basal bolus regimen**

Not preferred –more problems for patients

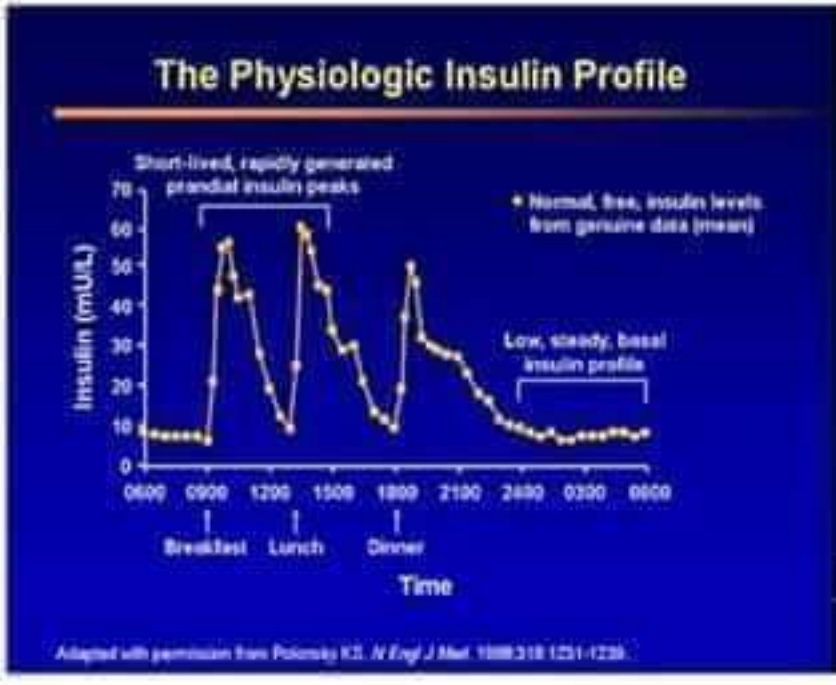
Common Insulin Regimens (4)

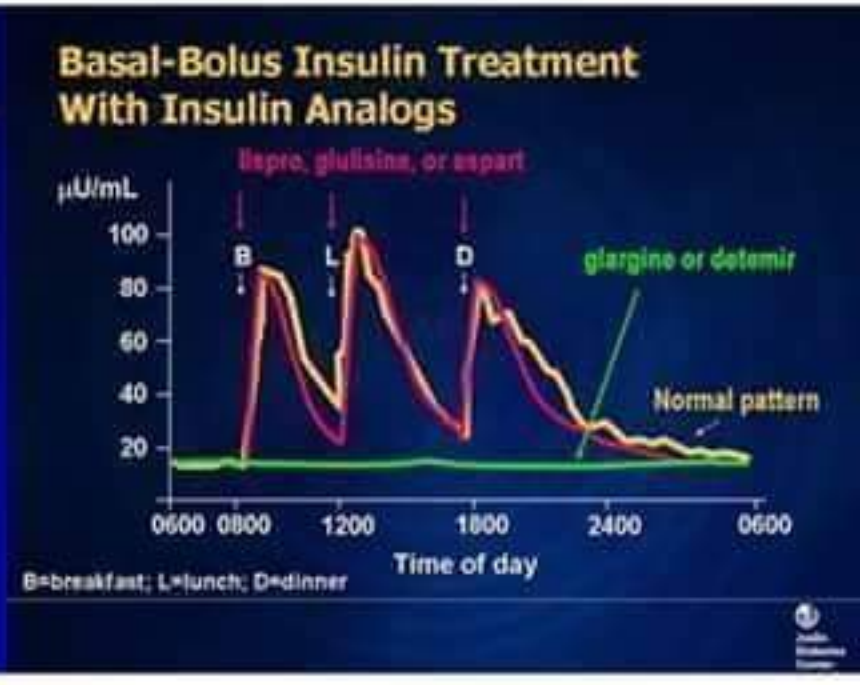
Basal Bolus

- Basal insulin at night and one rapid acting insulin immediately before each major meal (3 times).
- Basal insulin is titrated following FBG
- Rapid acting insulin is titrated by post meal BGs
- Drawback
  - Expensive
  - 4 times needle prick a day.

Most preferred –most fexible

Basal Bolus Insulin





Common Insulin Regimens (5)

Continuous subcutaneous insulin infusion (CSII):

Recommended for adults and children 12 years and older with T2DM provided:

- To achieve target HbA1c levels with MDIs result in the person experiencing disabling hypoglycaemia or
- HbA1c levels have remained high (8.5% or above) on MDI therapy despite a high level of care.

CSII sets


Quick-Set® (Paradigm®)
+
Medtronic Paradigm®
Reservoir
Quick-Set® (Luer Lock)
+
Fifty50 Luer Lock Reservoir

Indications of insulin

Continuous Use

* Type 1 Diabetes
* Type 2 Diabetes with OHA failure
  - Primary - Secondary

Intermittent Use

* Type 2 diabetes during
  - major surgery
  - pregnancy, labour and delivery
  - myocardial infarction
  - acute infections
  - Hypergycemic emergencies: DKA & HHS
* GDM

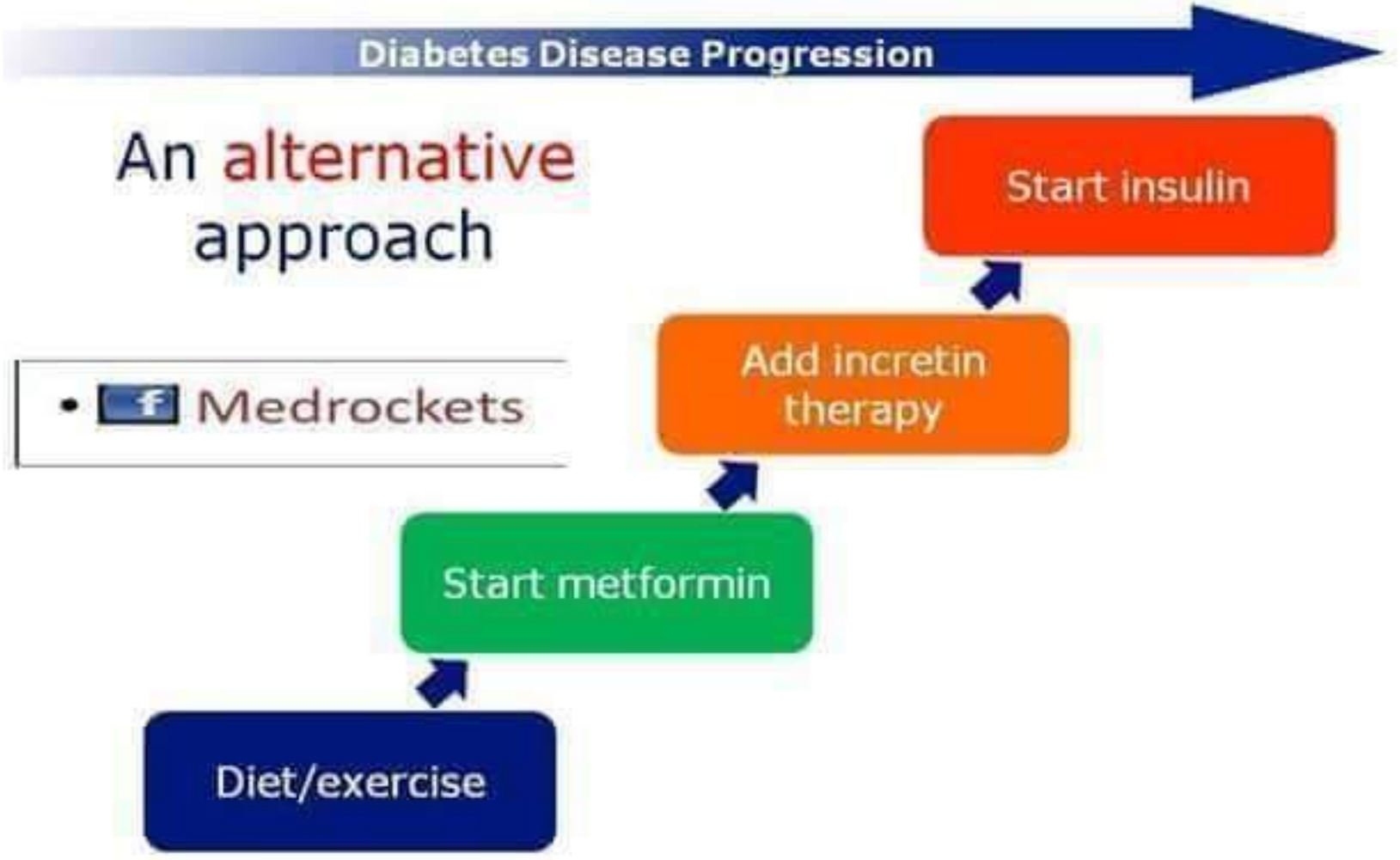
Starting dose of insulin

- T1DM: 1 -0.2-1 U/kg / day[1]
- T2DM: 0.2-0.3 U/kg / day

- In split mixed regimen- 2/3 as intermediate acting & 1/3 as short- acting [2]
- In basal bolus regimen: ½ basal at bed time and ½ bolus in 3 divided doses.
- Dosage is individualized and titrated soon

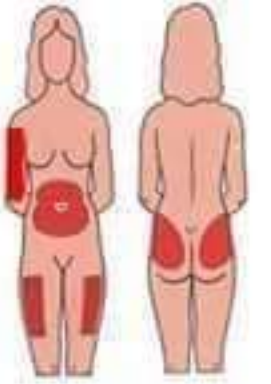
[1]Goodman & Gillman's The pharmacological basis of therapeutics ed. 9th .pg. 1501
[2]Harrison's Principles of Internal Medicine (15th Edition) pg. 2131

Current recommendations for the treatment of type 2 diabetes



Why Early insulin initiation?
Clinical & Pharmacological Reasons(4)

Insulin administration



Sites

- Abdomen (fastest absorption & most preferred)
- Buttocks
- Upper arm

(Intermediate)

- Thigh-lateral & anterior aspects (slowest)
- Rotate the site of injection around a selected area

Side effects of Insulin

5 Side effects

1. Hypoglycemia

2. Allergic Reactions –
   - Local redness, itching – self limiting, disappears with continuation of therapy
   - Systemic allergy – angioedema, anaphylaxis; rare, requires desensitization
3. Insulin lipoatrophy
4. Insulin lipohypertrophy
5. Insulin Edema & weight gain

Barriers to insulin therapy (2)

- Fear of hypoglycemia — DIPPAP 2 - 53%
- Inconvenient timing of injection
- Complicated regimen
  - to be taken 30 minutes before meal
  - lifestyle to fit therapy
  - Hyperglycemia immediately after meal
  - Hypoglycemia before next meal — Patient survey – ORG-MARG 2002 – 34%
- Fear of injection

DIPPAP 2 – 35%

Storage of Insulin (1)

- Vials, Penfills & Pens not in use
  stored between 2° & 8°C
- Storage in or near freezing compartment is to be avoided (more important-suspensions)
- Too high temp- gradual decrease in biological potency
- In use stored at room temperature (25°C) up to 6wks (Vials) & up to 4 wks (Penfills & Devices)
- Pens/ Penfills- in use- should not be kept in refrigerator