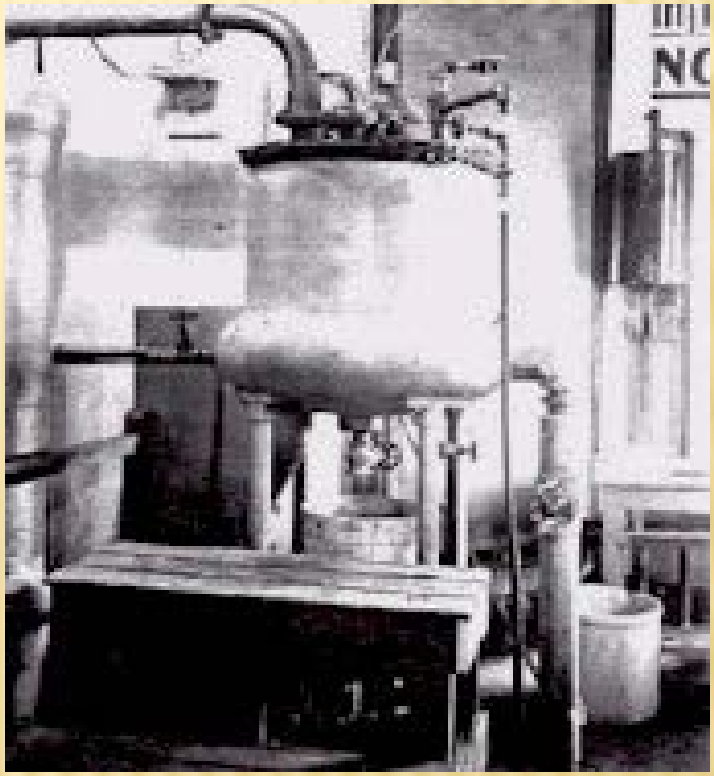
Insulins

CLASS OBJECTIVES

- Describe the history of insulin discovery
- List types of insulin
- Define indications and dosages
- Review case studies

INVENTION OF INSULIN 1921

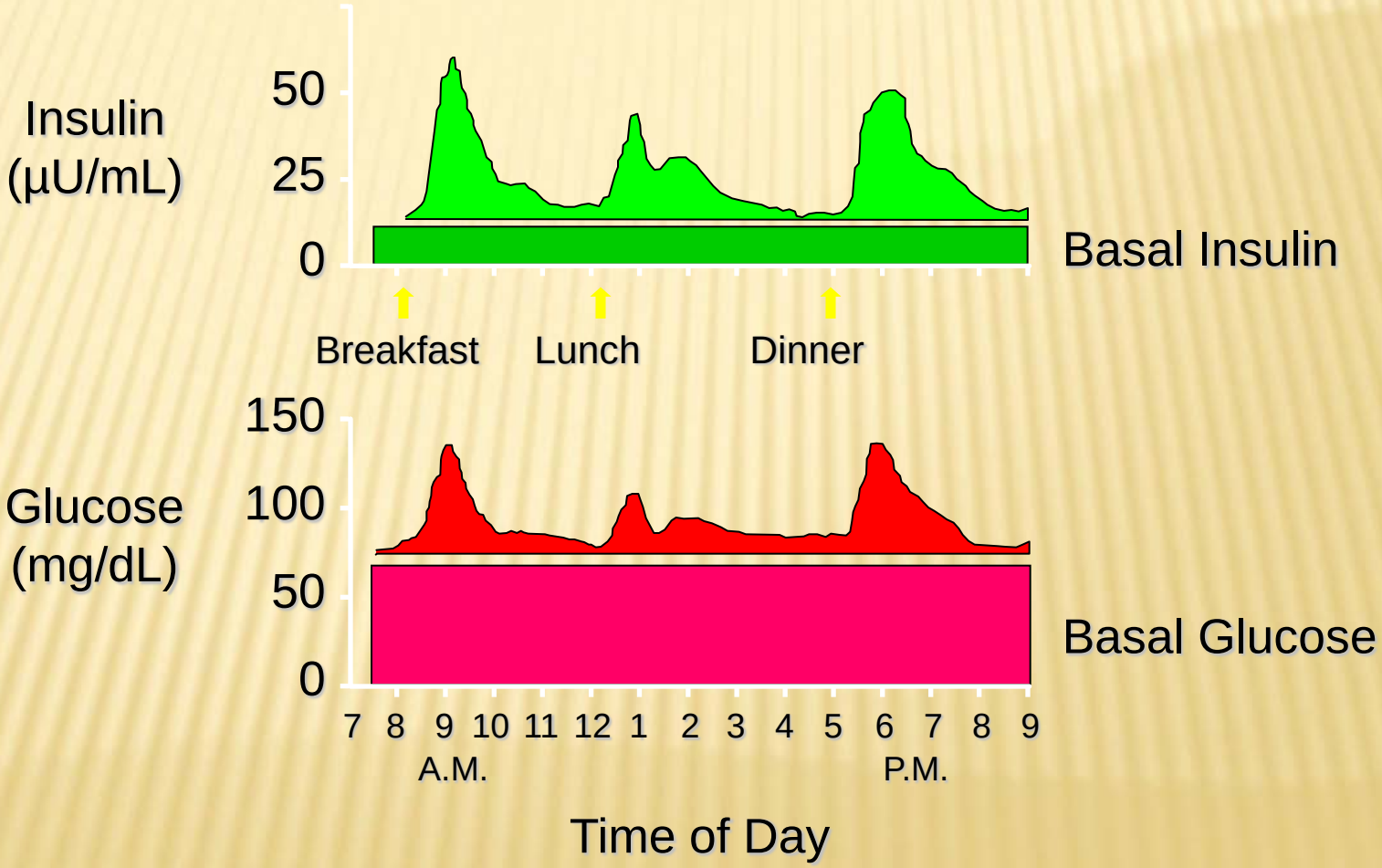


The first stills used to make insulin (early-mid 1920's).

Patient — J.L.


OMEGA
USA

PHYSIOLOGIC INSULIN SECRETION: 24-HOUR PROFILE



INSULINS

- Function as substitute for endogenous hormone
- Effects are same as normal endogenous insulin
- Human insulin
  - Derived using recombinant DNA technologies
  - Recombinant insulin produced by bacteria and yeast
- Restores the diabetic patient's ability to:
  - Metabolize carbohydrates, fats, and proteins
  - Store glucose in the liver
  - Convert glycogen to fat stores

INSULIN THERAPY

Short-term use:

- Acute illness, surgery, stress and emergencies
- Pregnancy
- Breast-feeding
- Used as initial therapy in type 2 DM in marked hyperglycaemia
- Severe metabolic decompensation
  - diabetic ketoacidosis, hyperosmolar nonketotic coma, lactic acidosis, severe hypertriglyceridaemia

Long-term use:

- If targets haven't been reached after optimal dose of combo therapy
- Start with bedtime Lantus therapy
- Consider change to multi-dose insulin therapy when A1c goal not achieved.
- With insulin therapy, insulin secretagogues should be stopped and insulin sensitisers e.g. Metformin or TZDs, can be continued.

INSULINS

- Rapid-acting
  - Most rapid onset of action (5 to 15 minutes)
  - Shorter duration
  - Patient must eat a meal after injection
  - Insulin lispro (Humalog)
    - Similar action to endogenous insulin
  - Insulin aspart (NovoLog)
  - Insulin glulisine (Apidra)
  - May be given subcutaneously or via continuous subcutaneous infusion pump (but not IV)

INSULINS

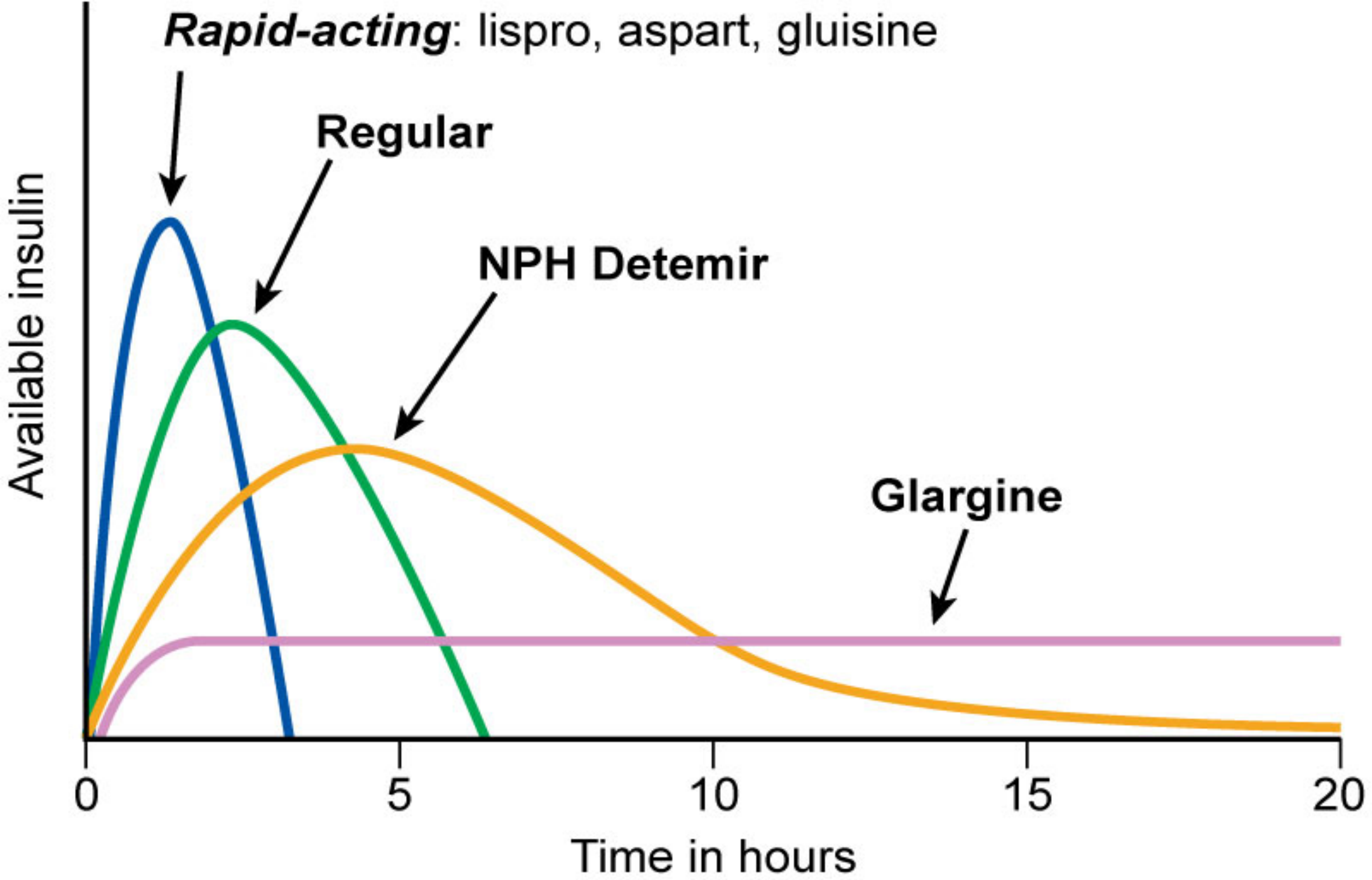
- Short-acting
  - Regular insulin (Humulin R)
  - Onset 30 to 60 minutes
    - The only insulin product that can be given by IV bolus, IV infusion, or even IM

INSULINS

- Intermediate-acting
  - Insulin isophane suspension (also called NPH)
    - Cloudy appearance
    - Slower in onset and more prolonged in duration than endogenous insulin

INSULINS

- Long-acting
  - glargine (Lantus), detemir (Levemir)
    - Clear, colorless solution
    - Usually dosed once daily
    - Referred to as *basal insulin*



From Messinger-Rapport BJ, Thomas DR, Gammack JK: Clinical update on nursing home medicine: 2008, *J Am Med Dir Assoc* 9(7):460-475, 2008.

COMBINATION INSULIN

Insulin Type	Onset	Peak
Humolog Mix 75/25	0.25-0.5 hr	1-12 hrs
75% NPL, 25% Lispro		
Humolog Mix 50/50		
NovoLog Mix 70/30		
70% Novolog protamine susp, 30% aspart		
Humalin or Novolin		
Combo 70%N / 30%R	0.5-1.0 hr	2-12 hrs
Combo 50%N / 50%R	0.5-1.0 hr	2-12 hrs

Considerations:

Premixed: difficult to fine tune therapy.

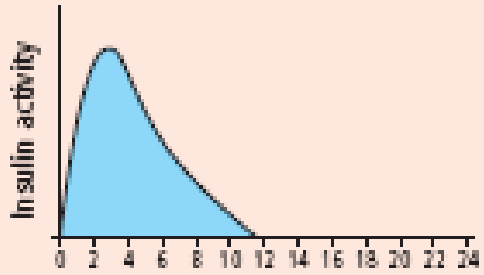
Types of insulin

Insulin type/action (appearance)	Brand names (generic name in brackets)	Basal/bolus	Dosing schedule
Rapid-acting analogue (clear) Onset: 10–15 minutes Peak: 60–90 minutes Duration: 4–5 hours	Humalog® (insulin lispro) NovoRapid® (insulin aspart)	Bolus	Usually taken right before eating or to lower high blood glucose
Short-acting (clear) Onset: 0.5–1 hour Peak: 2–4 hours Duration: 5–8 hours	Humulin®-R Novolin®ge Toronto	Bolus	Taken about 30 minutes before eating, or to lower high blood glucose
Intermediate-acting (cloudy) Onset: 1–3 hours Peak: 5–8 hours Duration: up to 18 hours	Humulin®-N Novolin®ge NPH	Basal	Often taken at bedtime, or twice a day (morning and bedtime)
Extended long-acting analogue (Clear and colourless) Onset: 90 minutes Peak: none Duration: 24 hours	Lantus® (insulin glargine) Levemir® (insulin detemir)	Basal	Usually taken once or twice a day
Premixed (cloudy) A single vial contains a fixed ratio of insulins (the numbers refer to the ratio of rapid- or fast-acting to intermediate-acting insulin in the vial)	Humalog® Mix 25™ Humulin® (20/80, 30/70) Novolin®ge (10/90, 20/80, 30/70, 40/60, 50/50)	Combination of basal and bolus insulins	Depends on the combination

OVERVIEW OF INSULIN AND ACTION

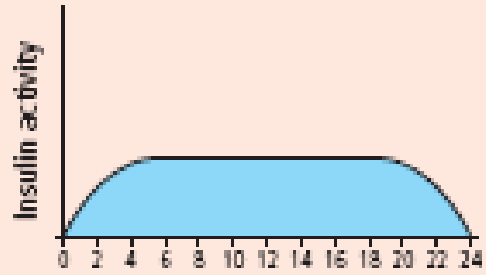
Soluble Human Insulin: Actrapid, Humulin S

Onset: 30 mins
Peak: 2-4 hours
Duration: 6-8 hours



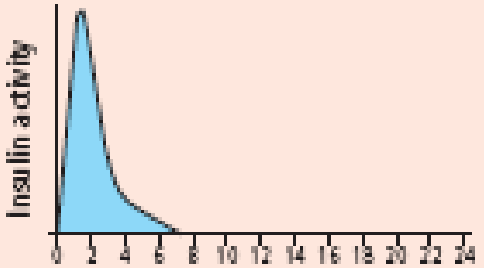
Long Acting Basal Analogues: Glargine (Lantus), Detemir (Levemir)

Onset: ~ 2 hours
Peak: None
Duration: 18-24 hours



Rapid Acting Insulin Analogue: Novorapid Aspart, Humalog Lispro, Apidra

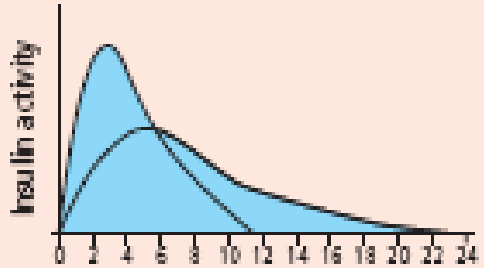
Onset: 0-15 mins
Peak: 1-2 hours
Duration: 3-5 hours



Pre-mixed Human Soluble/Isophane: Mixtard 30, Humulin M3 etc

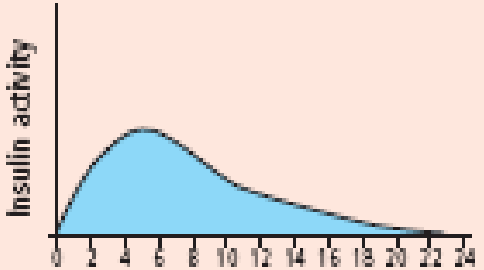
Onset: See above
Peak: See above
Duration: See above

Mixtard 30, M3 refers to % of soluble insulin ie. 30% Soluble 70% Isophane



Intermediate Human Isophane Insulin's: Insulatard, Humulin I

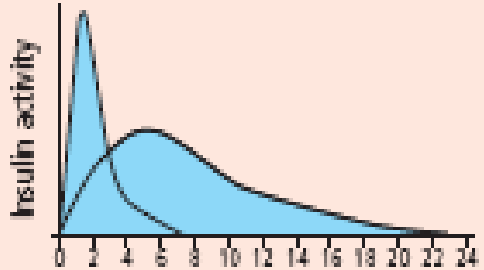
Onset: -
Peak: 4-8 hours
Duration: 14-16 hours



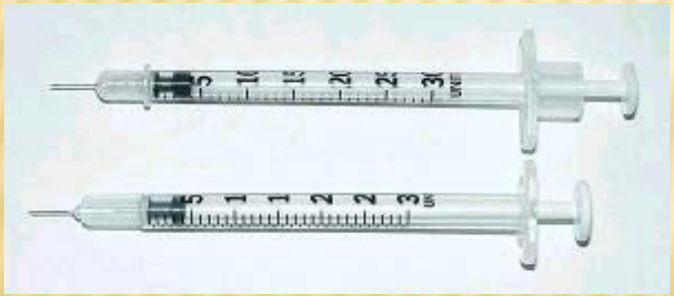
Pre-mixed Analogues/Isophane: Novo Mix 30, Humalog Mix50, Mix25

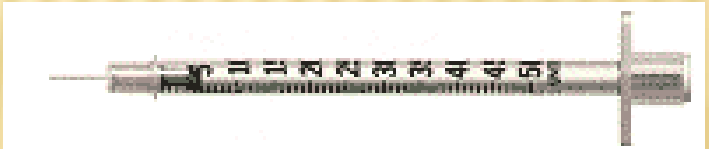
Onset: See above
Peak: See above
Duration: See above

Novo Mix 30, Humalog Mix50/ Mix25 refers to % of rapid acting analogue insulin

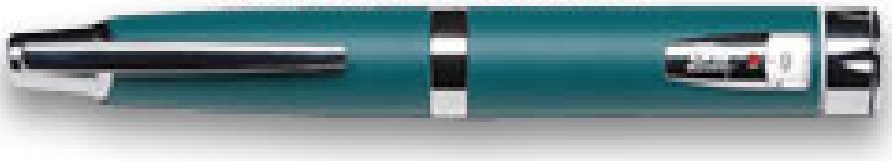


INSULIN NEEDLES AND PENS





HumaPen® LUXURA™ HD



Dosing in half-unit increments from 1 to 30 units

Original Prefilled Pen

Humalog® KwikPen™

A light and portable prefilled pen

HumaPen® MEMOIR™

The insulin pen with a memory

INSULIN REGIMENS

- Once-daily injection of an intermediate or long acting preparation may **be effectively used in some patients.**
- Split mixed, twice-daily mixtures of short/intermediate-acting insulin is a commonly used regimen.
- **Mixture of short/intermediate-acting insulin may be given in** the morning. Short-acting insulin are given before evening meal and an intermediate-acting insulin is given at bedtime.
- A regimen of multiple injections of rapid-acting insulin before the main meals, with an appropriate dose of a before breakfast and before dinner intermediate acting insulin.

BASAL-BOLUS INSULIN DOSING

- Preferred method of treatment
- Mimics a healthy pancreas by delivering basal insulin constantly as a basal
- Basal insulin is a long-acting insulin (insulin glargine)
- Bolus insulin covers the meals
- Bolus insulin (insulin lispro or insulin aspart)

HOW TO INITIATE INSULIN?

- Wt in kg. divide by 0.5= TDD
- 50% TDD= basal
- Titer dosage till FBS is target 110-120 mg/dl
- 50% TDD= bolus
- Bolus divide by 3. Administer AC meals

INSULIN SENSITIVITY FACTOR

- Refers to number of points 1 unit of rapid acting insulin lowers blood glucose.
- Goal of ISF, is to bring blood glu level to target if elevated.
- If ISF is set correctly, bld glu should ↓ into target range 3-4 hours after the correction bolus is given.
- ISF is determined by using the “1800 Rule.”
  - Determine average total daily insulin dose (TDD)
  - Divide 1800 by TDD

EXAMPLE:

- Humalog insulin at ratio 1 unit/15 gm of CHO with each meal and snack. 36 units of Lantus insulin at bedtime.
- Below is the calculation of his estimated TDD.
- Breakfast: 8 units Humalog Lunch: 5 units Humalog
- Snack: 3 units Humalog Dinner: 8 units Humalog
- Bedtime: 36 units Lantus **TDD: 60 unit**
- **ISF 1800/60=30. 1 unit of insulin will lower bld glu by30**
- Before dinner today bld glu 250. Target is 120
- 130 above target. 130/30=4.3. 4 units needed to correct

SLIDING-SCALE INSULIN DOSING

- Subcutaneous short-acting or regular insulin doses adjusted according to blood glucose test results
- Typically used in hospitalized diabetic patients or those on total parenteral nutrition (TPN) or enteral tube feedings
- SQ insulin is ordered in amt that ↑ as the bld glu ↑
- Disadvantage: delays insulin administration until hyperglycemia occurs; results in large swings in glucose control

GLUCAGON INJECTION

- Used to treat very low blood sugar which may occur in people who take insulin.
- Given if the person is unconscious, is having seizure or is disoriented and unable to eat sugar of sugar-sweetened products
- One vial contains 1 mg (1 unit) GlucaGen and 1 ml sterile water for reconstitution
- Injected: IV, IM or SQ

GLUCAGON INJECTION