



Diabetes Mellitus Masterclass
Chapter 6

ADDING INSULIN



Tracy Tylee

INSULIN BASICS

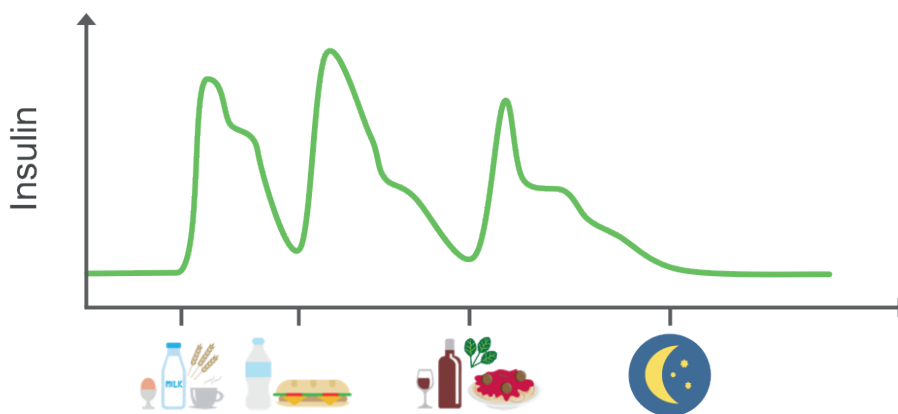
All patients with type 1 diabetes require insulin for survival.

Many patients with type 2 diabetes can be treated with oral medications. By ten years after diagnosis, up to 75% of patients, with type 2 diabetes, will require insulin therapy.

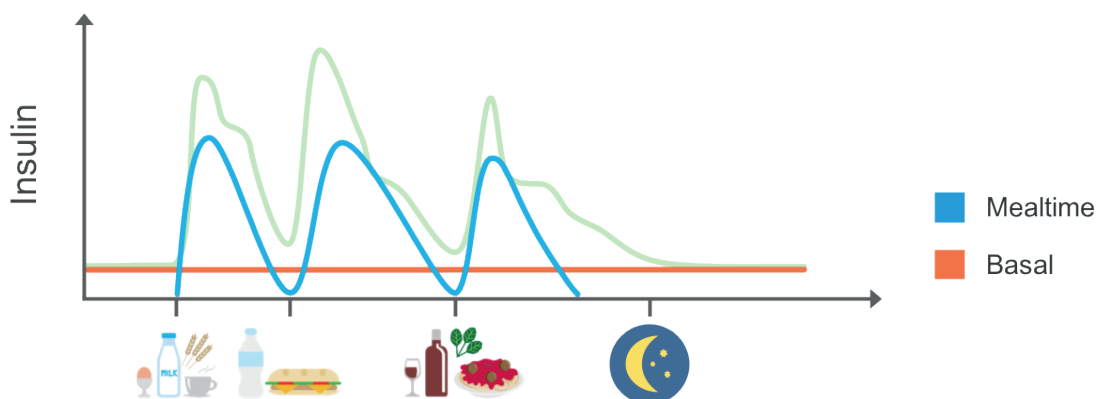
Insulin has two roles in controlling blood sugars

1. In the fasting state, insulin controls glucose release from the liver, maintaining normal fasting blood sugars.
2. After eating, increases in insulin levels help control post-meal increases in glucose levels.

Physiologic insulin levels are stable during fasting and between meals, with short term surges in insulin levels associated with meals.



Patients with type 1 diabetes have no insulin production, so exogenous insulin is used to recreate this profile as best as possible. This typically requires two different types of insulin, one to provide the long-acting basal coverage (red line below), and a second short-acting insulin to provide mealtime coverage (blue line below).



Patients with type 2 diabetes often need insulin to overcome their insulin resistance. These patients benefit from just long-acting basal insulin to provide coverage in the fasting state.

Types of insulin

There are several types of insulin available for clinical use.

Name	Time of onset	Time to peak	Duration of action	Dosing frequency
Basal insulin				
Glargine	60–90 min	No peak	20–24 hrs	Once daily
Detemir	60 min	No peak	16–24 hrs	Once or twice daily
Degludec	30 min	No peak	> 40 hrs	Once daily
NPH (neutral protamine Hagedorn)	30–60 min	4–6 hrs	10–16 hrs	Twice daily
Mealtime insulin				
Aspart, lispro, glulisine	15 min	1 hr	4–6 hrs	Before meals
Regular	30 min	4 hr	5–8 hrs	Before meals

BASAL INSULIN



Who needs basal insulin?

- All patients with type 1 diabetes
- Patients with type 2 diabetes who are not well controlled on three non-insulin agents
- Patients with type 2 diabetes who are symptomatic from their hyperglycemia
- Patients with type 2 diabetes who have an A1c over 10%

How do you choose which basal insulin to use?

All basal insulins work to lower the fasting blood sugars, so you can choose whichever insulin you are most familiar with, or whichever is most convenient for the patient.

NPH

- Requires twice daily dosing for 24 hour basal coverage
- Peak levels 4–6 hours after injection (may increase risk of hypoglycemia)

Glargine

- Once daily dosing without discernable peak
- May cause burning with injection due to lower pH

Detemir

- No peak (may require twice daily dosing for some patients)
- Less weight gain compared to glargine

Degludec

- No peak (lower risk of hypoglycemia)
- Dosing flexibility (good for patients with irregular schedules)

How to start basal insulin

- If A1c is < 9.0%—start 10 units at bedtime
- If A1c is > 9.0% or patient is symptomatic—start 0.2 units / kg / day
- Titrate dose based on fasting blood sugars
 - if fasting blood sugar is over 120 mg / dL for three days in a row—increase basal insulin by 1 unit
 - continue to increase basal insulin until fasting blood sugars are consistently < 120 mg / dL or insulin dose is 0.5 units / kg
- Continue oral medications

MEALTIME INSULIN



Mealtime insulin is necessary for all patients with type 1 diabetes, and for certain patients with type 2 diabetes.

When to consider mealtime insulin for patients with type 2 diabetes

- Normal fasting blood sugars but A1c still elevated
- Basal insulin dose is $> 0.5-1.0$ units / kg / day
- Blood sugars are dropping more than 50 mg / dL overnight

Analog versus regular insulin for type 2 diabetes

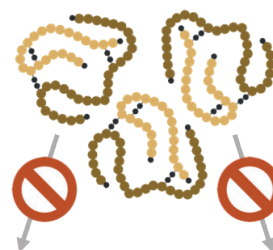
- No difference in efficacy
- No significant difference in hypoglycemia risk
- Analog insulins can be taken just before eating / regular insulin requires 30 minute lag time
- Analog insulins are significantly more expensive

Starting mealtime insulin

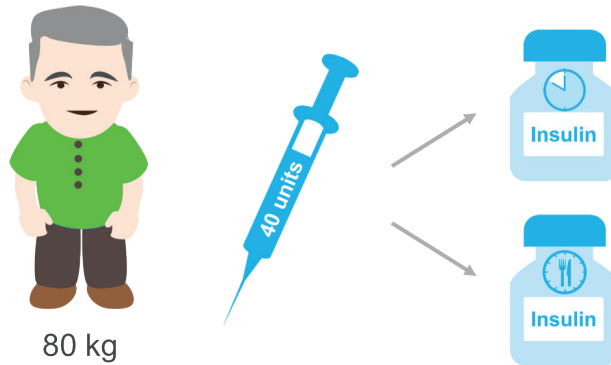
- Calculate patient's total daily insulin needs (type 2 diabetes: $0.3-0.5$ units / kg / day)
- Divide total daily dose into 50% basal and 50% mealtime
- Divide mealtime dose by three (three meals daily)
- Most patients can start with one mealtime dose before their largest meal of the day

Example

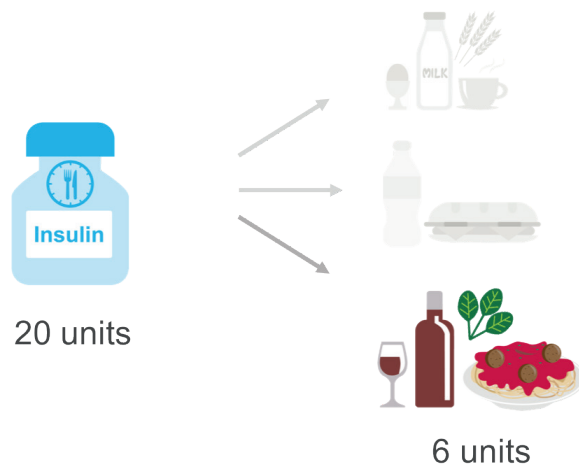
Mr. M has type 2 diabetes, is overweight, and has some signs of insulin resistance on exam.



He weighs 80 kg. You calculate his total daily insulin dose to be 40 units ($0.5 \text{ units / kg / day} \times 80 \text{ kg}$). This would be $(40 \text{ units} / 2)$ 20 units basal and 20 units mealtime, divided between three meals, which would be 6–7 units of insulin per meal ($20 \text{ units} / 3 \text{ meals}$).



Since his largest meal of the day is dinner, you ask him to start by taking 6 units of mealtime insulin before dinner.



ALTERNATIVE FORMS OF INSULIN

Concentrated insulin

There are multiple insulin concentrations available. Most are U-100, which means they contain 100 units per 1 mL. Others include

- U-100 (100 units / 1 mL)—glargine, detemir, degludec, NPH, regular, aspart, lispro, glulisine
- U-200 (200 units / 1 mL)—concentrated lispro, concentrated degludec
- U-300 (300 units / 1 mL)—concentrated glargine
- U-500 (500 units / 1 mL)—concentrated regular insulin

Benefits of concentrated insulin

- Smaller injection volume
 - improves patient comfort and insulin absorption
- Fewer injections per day
 - can improve patient compliance

U-200 and U-300 insulins can be used interchangeably with their U-100 counterparts without dose adjustment. U-500, however, has unique pharmacokinetics. It has a longer duration of action than U-100 regular insulin, so is able to provide both basal and mealtime coverage in a single injection.

Using U-500 insulin

- Calculate total daily insulin dose
- Start with 2/3 of dose before breakfast and 1/3 of dose before dinner
- If predinner blood sugar is elevated—increase breakfast dose by 10%
- If morning blood sugar is elevated—increase dinner dose by 10%

Inhaled insulin

Another alternative for mealtime insulin is inhaled insulin. This is a convenient option for patients who have difficulty giving themselves multiple daily injections, or have problems with taking insulin in public.



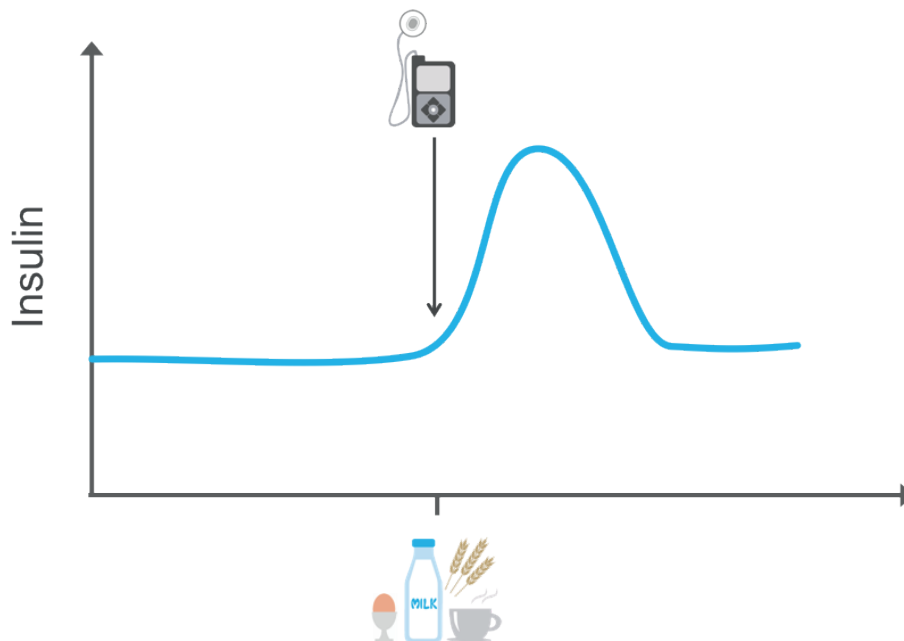
- This is only available as mealtime insulin
- Cartridges are only available in multiples of 4 units (4, 8, 12 units)—dose must be a multiple of four
- May require multiple inhalations for patients on high dose of mealtime insulin
- Contraindicated in lung disease

INSULIN PUMPS

Patients using the insulin pump insert a small catheter under their skin, connected to a pump with a reservoir containing three days worth of fast-acting insulin.



Fast-acting (aspart, lispro, glulisine) insulin is infused continuously to provide 24-hour basal coverage. When patients eat, they determine how much mealtime insulin they will need based on their blood sugar and what they are eating. They then enter this value into the pump, which delivers a bolus of fast-acting insulin to cover the meal.



The insulin pump does NOT automate insulin administration.

Who would benefit from an insulin pump?

- Motivated patients who check blood sugars more than four times daily and are compliant with treatment regimens / follow up visits
- Patients with type 1 or type 2 diabetes who are not at goal despite multiple daily injections
- Patients with type 1 diabetes who need greater dosing flexibility
 - e.g., higher basal needs in the early morning
 - e.g., lower basal needs with physical activity
- Patients with gastroparesis who need slower administration of mealtime insulin

Who is not a good insulin pump candidate?

- Patients with A1c >10%
- Patients with anxiety / depression or other mental illness that interferes with ability to manage diabetes
- Patients with a history of missed appointments and non-compliance

READING LIST

Pharmacologic therapy for type 1 and type 2 diabetes

American Diabetes Association. 2018. 8. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. *Diabetes Care*. **41**: S73–S85.

<https://www.ncbi.nlm.nih.gov/pubmed/29222379>

Review of U-500 insulin (including dosing guidelines)

Reutrakul, S, Wroblewski, K, and Brown, RL. 2012. Clinical use of U-500 regular insulin: review and meta-analysis.

J Diabetes Sci Technol. **6**: 412–420.

<https://www.ncbi.nlm.nih.gov/pubmed/22538155>

Insulin pump guidelines from the Endocrine Society

Peters, AL, Ahmann, AJ, Battelino, T, et al. 2016. Diabetes Technology-Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring in Adults: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. **101**: 3922–3937.

<https://www.ncbi.nlm.nih.gov/pubmed/27588440>