

Diabetes: The Insulin Perspective

Kena K. Desai MS, MD

Clinical Diabetes Program at ANMC

Disclosures: None



Objectives:

1. Compare and contrast Type 1 Diabetes and Type 2 Diabetes.
2. Review the physiology of insulin release in the body and the goal of exogenous insulin replacement.
3. Review basal insulin regimens; injections vs. insulin pump.
4. Review bolus insulin regimens: injections vs insulin pump.
5. Discuss the dangers of “stacking” insulin by explaining the function of active insulin time.
6. Review hypoglycemia.

Case 1

- The patient is a 27 year old female, that presented with fatigue, body aches and difficulty sleeping.
- She has had these symptoms for 1-2 months.
- She has been training to be a professional body builder for the last 6 months.
- She has had an intentional weight loss of 8 kg , which she attributes to increased exercise and a high protein diet.

What additional questions do you have for the patient?

- Vital signs: Temp – 37.0, BP – 120/70 mmHg, HR – 95 beats/min, RR – 16 breaths/min, 98% on RA, weight – 88.0 kg / BMI – 29
- Exam: no concerning findings
- Labs:

CBC

	14.0	
8.0		210
	42.0	

BMP

140	110	20
4.0	24	0.9

GFR = 92

220

What is the diagnosis?

- Hyperglycemia
- Anabolic steroid induced diabetes
- Type 2 Diabetes
- Type I Diabetes
- Diabetes – etiology unknown

The patient is advised to refrain from exercise, rest and hydrate. She returns for follow-up of the hyperglycemia 7 days later.

Fasting finger-stick glucose: 200 mg/dl

HgBa1c: 8.7%

What is the diagnosis:

- a. Hyperglycemia
- b. Anabolic steroid induced diabetes
- c. Type 2 Diabetes
- d. Type I Diabetes
- e. Diabetes etiology unknown

Diagnostic Criteria for Diabetes:

- 1) HgBa1c \geq 6.5%
- 2) Fasting plasma glucose \geq 126 mg/dl
- 3) 2 hour plasma glucose \geq 200 mg/dl during a oral glucose tolerance test
- 4) In a patient with symptoms of hyperglycemia, a random plasma glucose \geq 200 mg/dl

- The patient was started on Metformin ER at 500 mg PO BID and advised to titrate up to 1000 mg PO BID in 3 weeks.
- At 3 month follow-up, she reported that she felt a little better but not back normal.
 - Fasting serum glucose = 165 mg/dl
 - HgBa1c – 7.8%

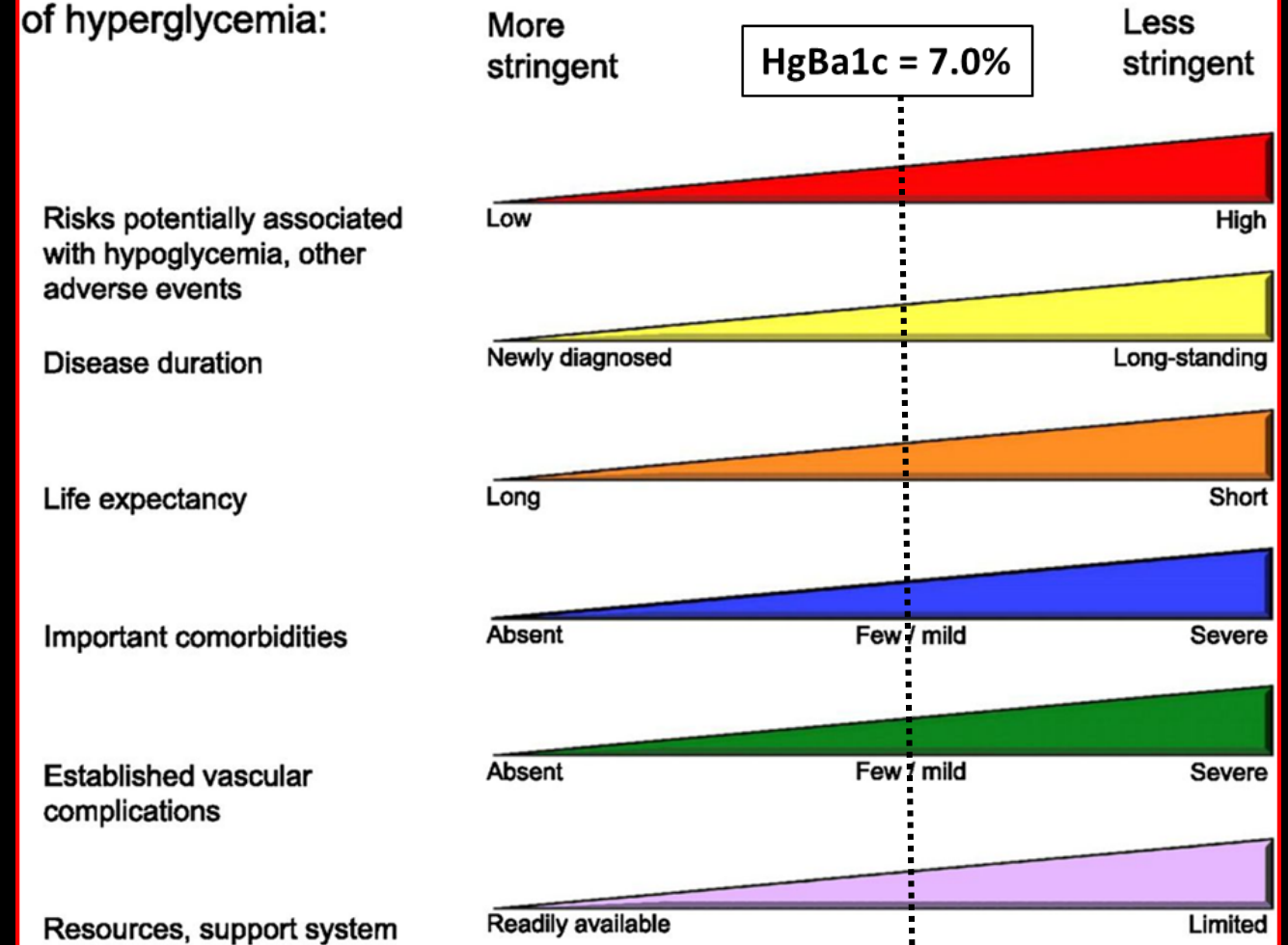
What is her glycemic goal?

- a. HgBa1c < 6.0%
- b. HgBa1c – 6.0 to 6.5%
- c. HgBa1c < 7.0%
- d. HgBa1c – 7.0 to 8.0%

Does she need a second diabetes medication added?

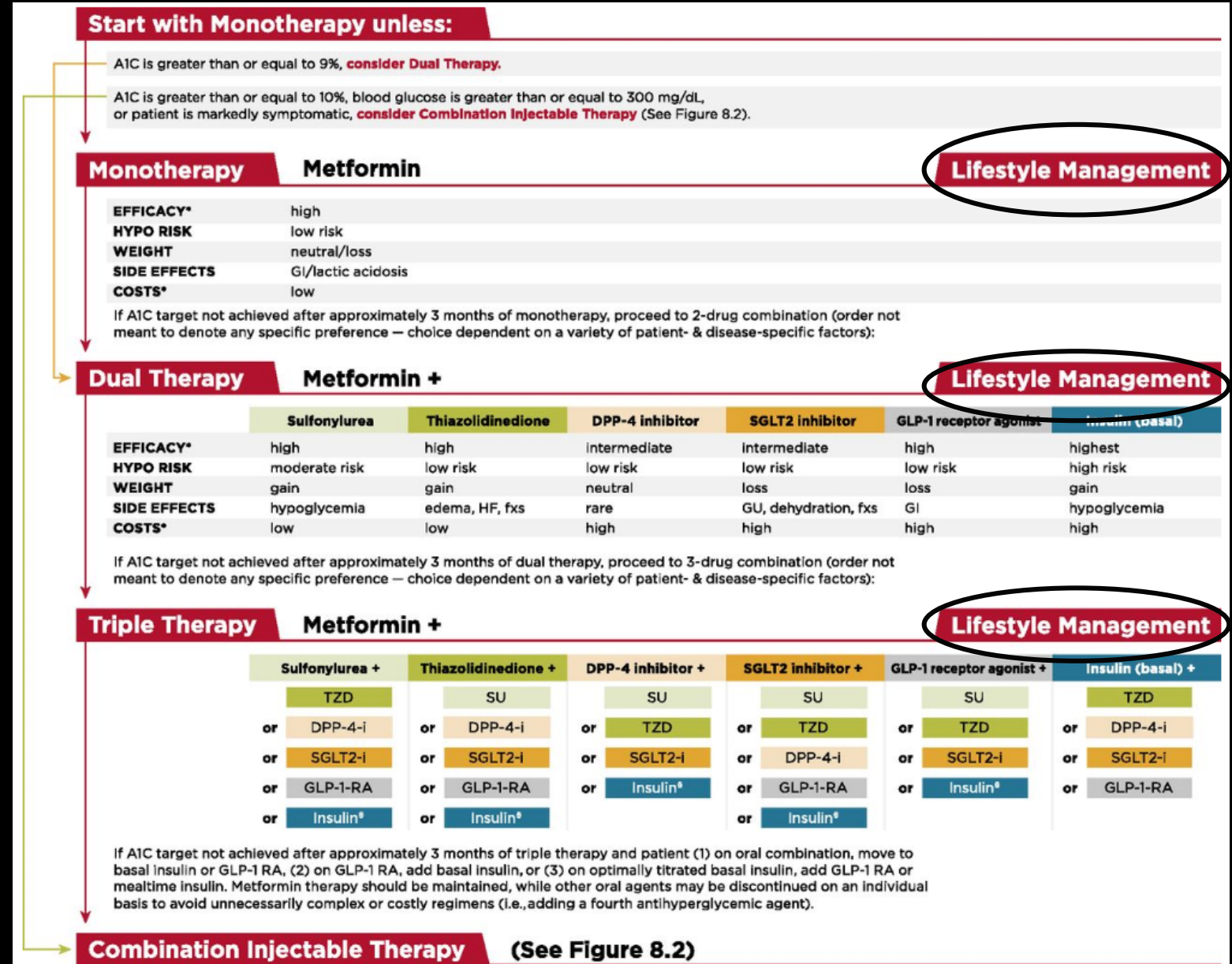
- a. Yes
- b. No
- c. May be so.....
- d. No meds, lifestyle modifications

Approach to management of hyperglycemia:



What medication should you start?

- a. Glargine
- b. Sulfonylurea – Glyburide
- c. GLP-1 agonist – Liraglutide
- d. SGLT-2 inhibitor – Empagliflozin



Three month later the patient returns to the clinic for a sick visit appointment.

- She reports that for the past 2 days she has had extremely fatigue and lightheadedness.
- Last night she had an episode of urinary incontinence while she was asleep.
- She has lost 8 kg in the last 3 months and affirms increased thirst and urinary frequency/urgency.
- Denies burning during urination, but does having burning after she has voided.
- The skin around her vagina is dry and cracked.
- She has a thick white vaginal discharge for the past 1 week.

Urine Analysis:

- WBC: 1-5
- Nitrite: negative
- Leukocyte esterase: negative
- Glucose: 1000
- Ketones: Moderate

What is the diagnosis for her urinary symptoms?

- a. Urinary track infection
- b. Genital yeast infection
- c. Hyperglycemia
- d. Overactive bladder

Vital signs: Temp- 37.5 C / BP – 140/90 mmHg / HR – 120 beat/min / RR – 24 breaths/min / 96% on RA
Weight – 80 kg / BMI – 25.0

Labs:

11.7
10.2 270
39.0

140	102	30
3.4	18	1.2

470

GFR – 62
Anion Gap – 20.0

HgBa1c: 11.7%

Is this patient in diabetic ketoacidosis (DKA)?

- a. Yes
- b. No
- c. May be so.....

- 2 L of NaCl 0.9% saline and 10 units of regular insulin was administered.
- She was started on Glargine (Lantus) 20 units QHS with a titration up.
- Her astute PCP questioned the diagnosis of Type 2 Diabetes.
 - called a friend - Kena K. Desai MD (907-729-1500)
- Autoimmunity testing Type I Diabetes:
 - GAD-65: 80 (normal : 0-5)
 - C-peptide – 0.20 (normal : 0.8-3.1)

What is the diagnosis:

- a. Hyperglycemia
- b. Anabolic steroid induced diabetes
- c. Type 2 Diabetes
- d. Type I Diabetes
- e. Diabetes etiology unknown

What medication needs to be added?

- a. Sulfonylurea - Glyburide
- b. Rapid acting insulin – aspart (Novolog)
- c. GLP-1 agonist - Liraglutide
- a. SGLT-2 inhibitor – Empagliflozin

What is her glycemic goal?

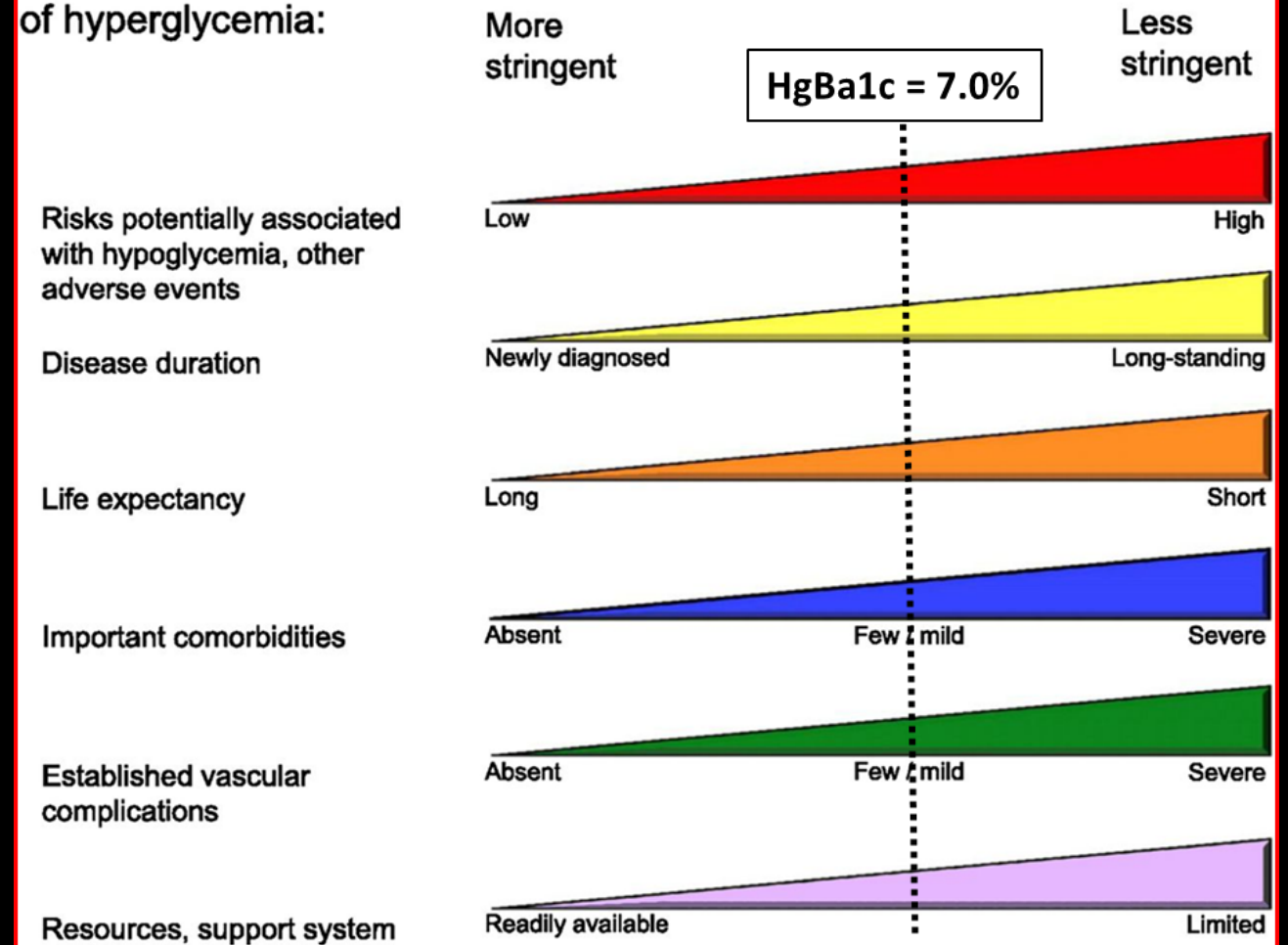
- a. HgBa1c < 7.0%
- b. HgBa1c – 7.0 to 8.0%
- c. HgBa1c – 8.0 to 9.0%
- d. HgBa1c < 9.5%

Specifically:

- HgBa1c < 7.0%
- AM fasting and pre-prandial finger-stick glucose levels: 80-130 mg/dl range
- 2 hour post-prandial: < 180 mg/dl

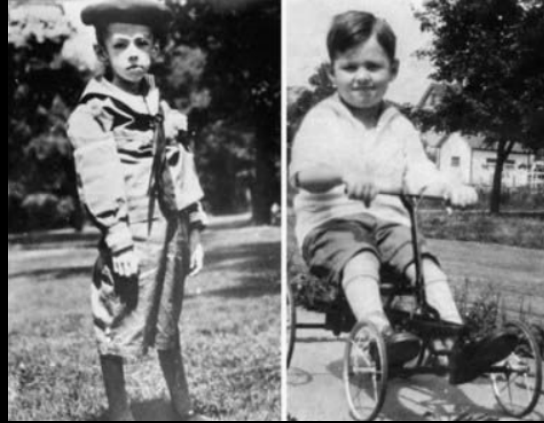
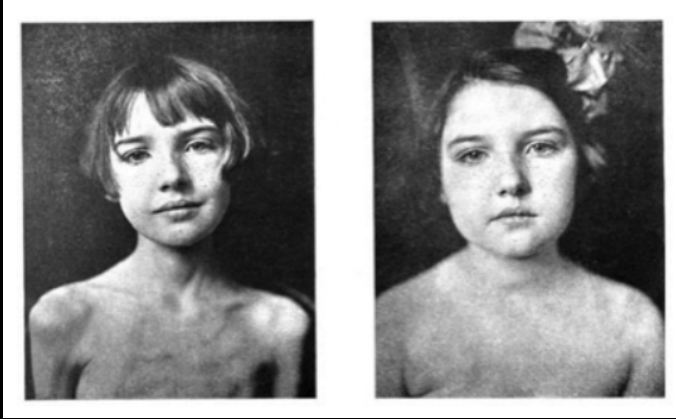
What is a key exception?

Approach to management of hyperglycemia:



Without Hypoglycemia

Faces of Diabetes then.....



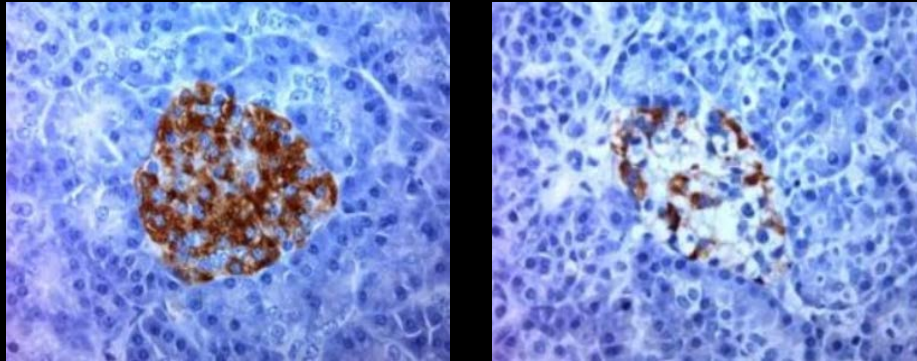
Faces of Diabetes Now.....



Type I and Type 2 Diabetes: Two Very Different Pathologies

Type I Diabetes:

- Autoimmune destruction of Beta cells
- Absolute insulin deficiency

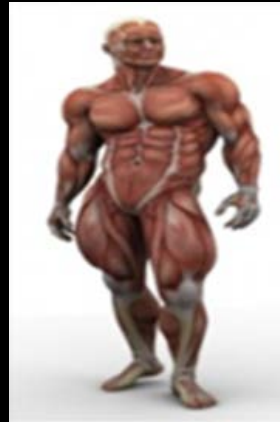


Latent Autoimmune Disease of Adulthood (LADA):

- Autoimmune destruction of Beta cells
- Gradual progress to total insulin deficiency

Type 2 Diabetes:

Increased Sensitivity
of Insulin Receptors



Decreased Sensitivity
of Insulin Receptors



= Insulin
Resistance



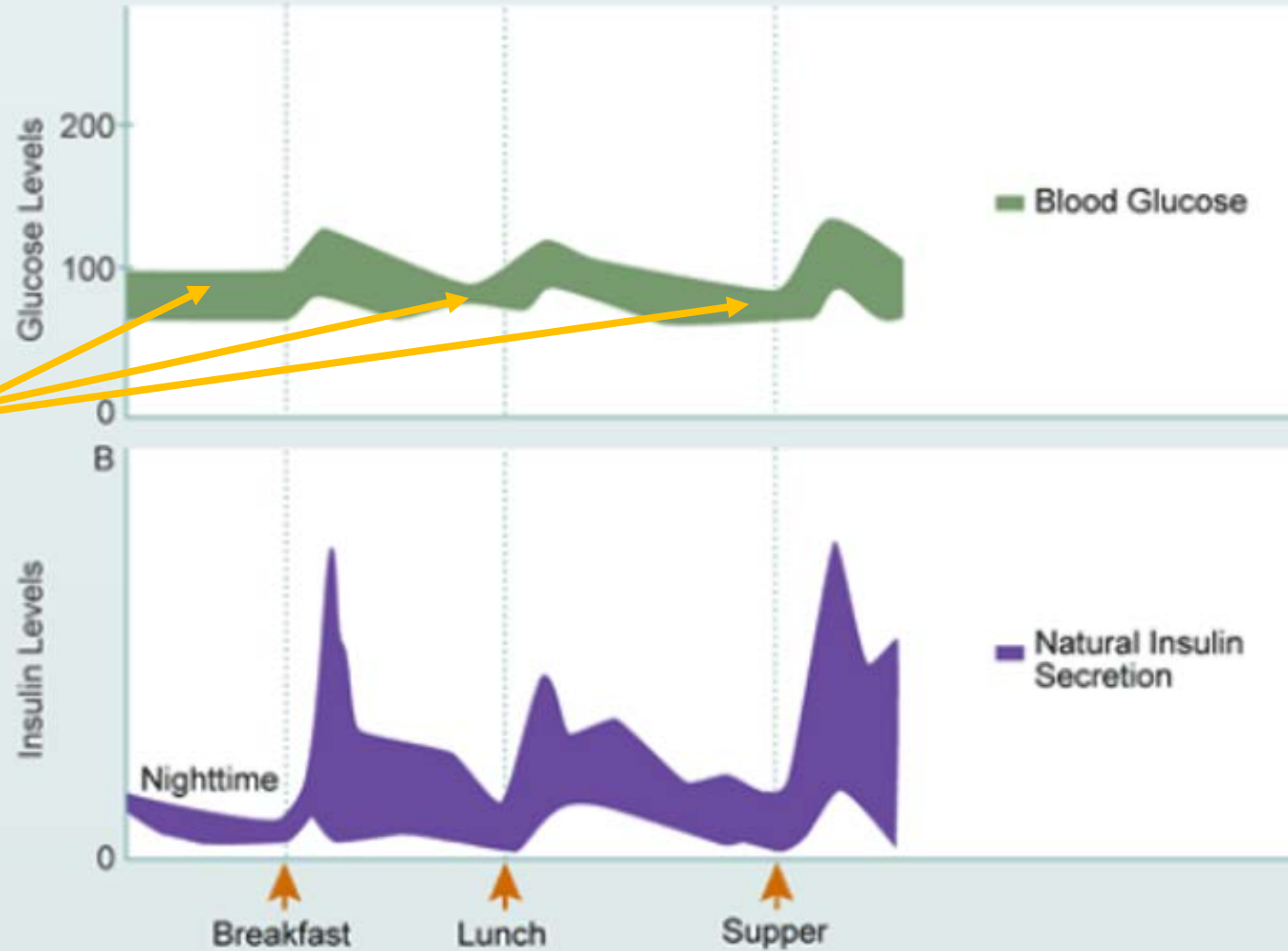
Relative insulin
deficiency

Increase insulin
production

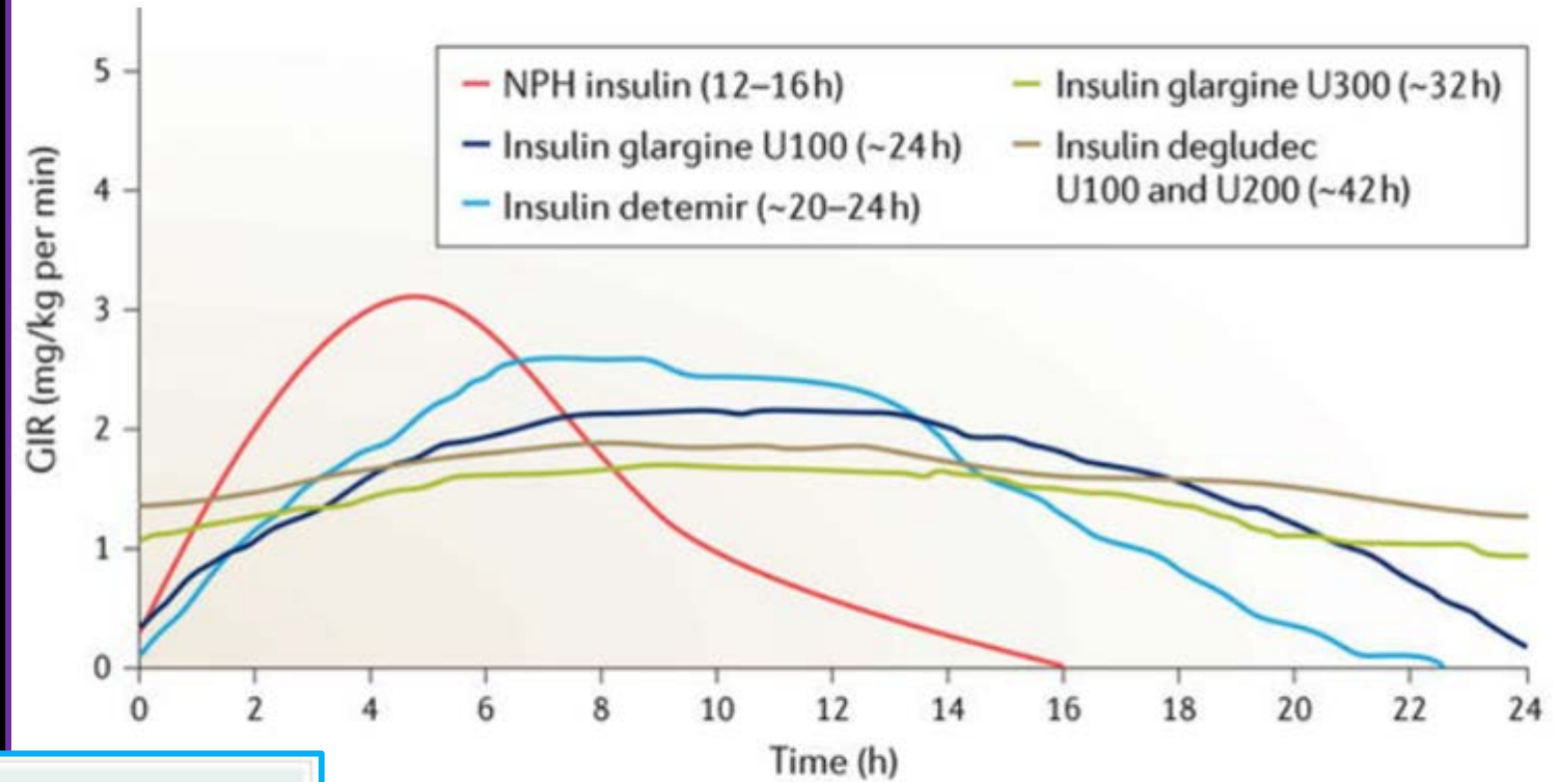




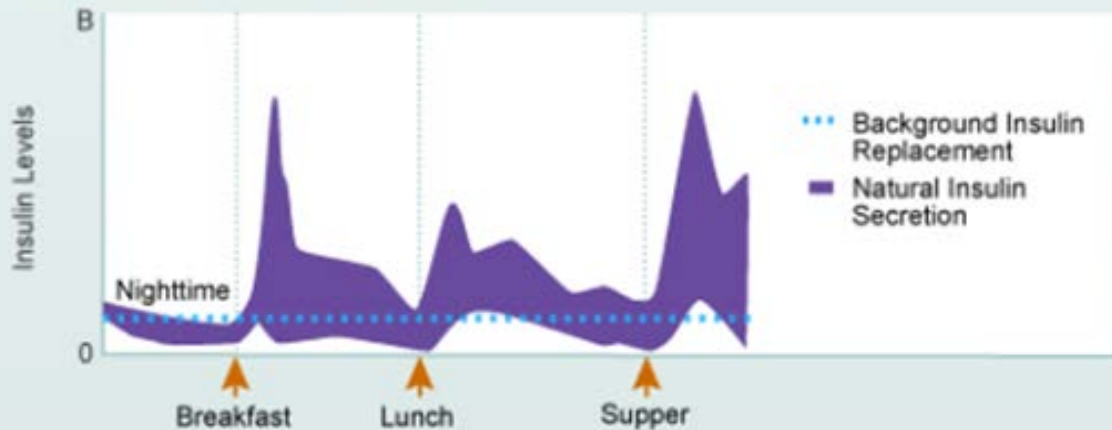
Normal (Non-diabetic) Blood Glucose and Insulin Levels over 24 Hours



Basal Insulins:

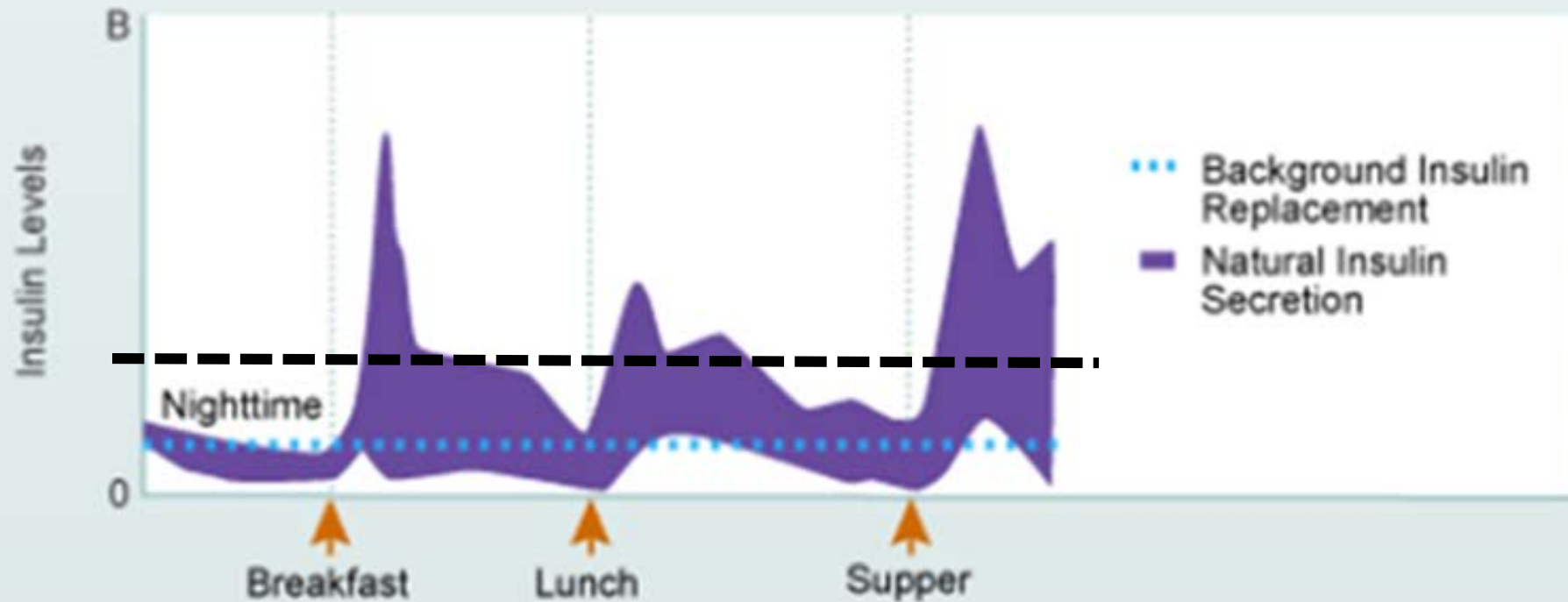


Background or Basal Insulin Replacement Compared with Natural, Non-diabetic Insulin Secretion



Jacobs DM Care 20:1279, 1997

Background or Basal Insulin Replacement Compared with Natural, Non-diabetic Insulin Secretion



Jacobs DM Care 20:1270, 1997

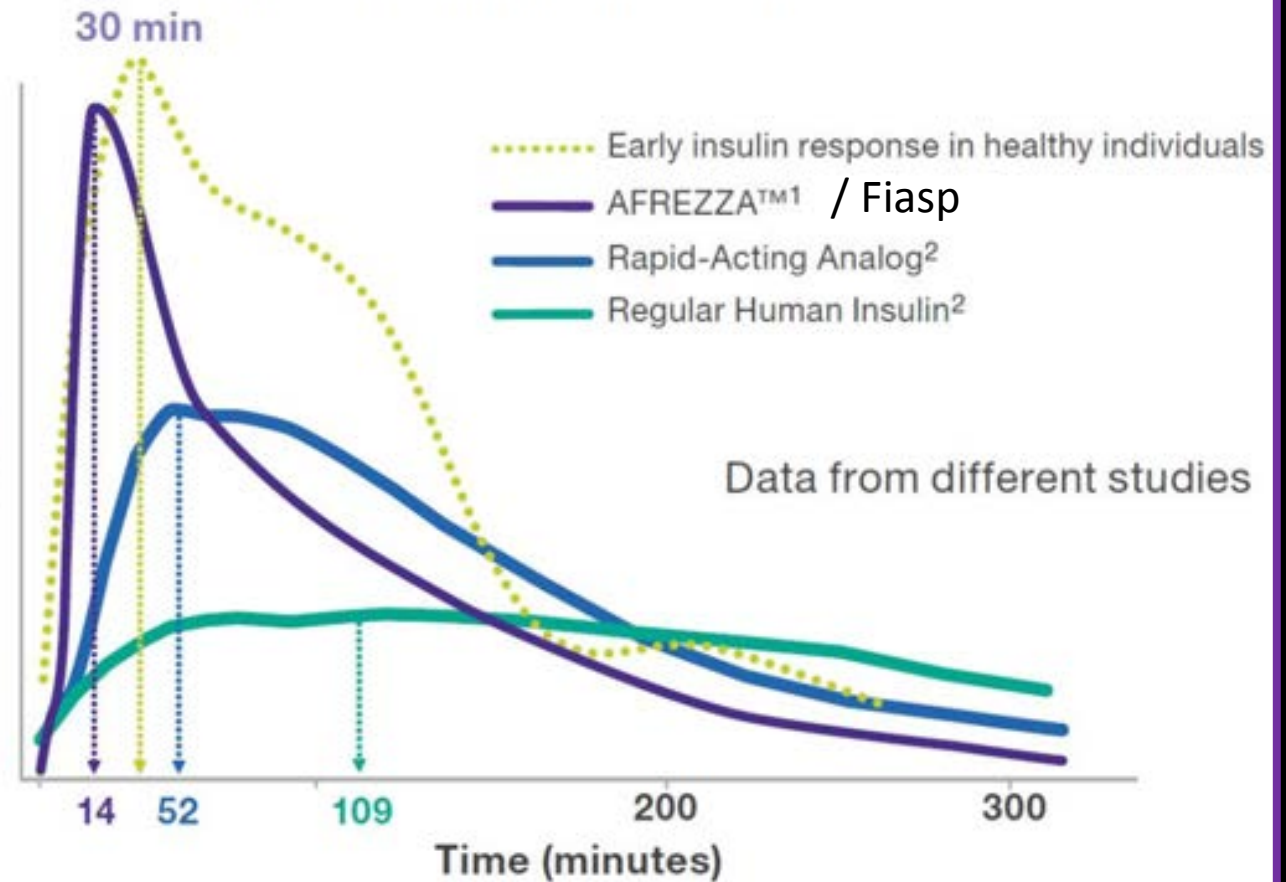
What happens if you over dose the basal insulin?

Hypoglycemia and weight gain

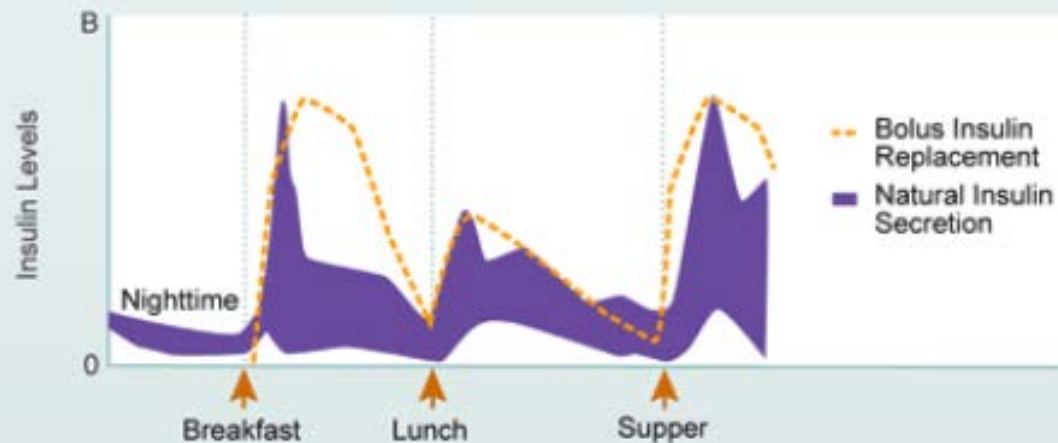
Prandial / Meal Associated / Bolus Insulins:

Plasma
Insulin
($\mu\text{U/mL}$)

Time to Peak Insulin Level



Mealtime or Bolus Insulin Replacement Compared with Natural, Non-diabetic Insulin Secretion



Mudaliar SR et al. Diabetes Care. 1999; 22: 1501-1506

Basal : Bolus Ratio – 50 % : 50 %

When I met the patient:

- Glargine 28 units QHS and metformin ER 1000 mg PO BID.
- HgBa1c was 10.2% and her finger-stick glucose levels were in the 100-300 mg/dl.
- She denied having any episodes or symptoms of hypoglycemia.

Her Total Daily of Insulin (TDI) = 28 units, however she was poorly controlled.

1. Increase (or decrease) total daily insulin in 10, 15 or 20% increments based on baseline glycemic control.

- $TDI = 28 \text{ units} \times 20\% = 5.6 \text{ units} + 28 \text{ units} = 33.6 \rightarrow 34 \text{ units}$

2. Readjust dosing so that it is 50% basal and 50% bolus.

- $TDI = 34 \text{ units} / 2 = 17 \text{ units}$
- Basal – Glargine 17 units QHS
- Bolus – Insulin to carbohydrate ratio – around 17 units

Calculate Insulin to Carbohydrate Ratio and Insulin Sensitivity Factor (correction factor).

Insulin: Carbohydrate Ratio: FOOD

$$500 / \text{TDI} = 500 / 34 \text{ units} = 15$$

1 units : 15 grams of carbohydrate

Insulin Sensitivity Factor: GLUCOSE MONITOR

$$1800 / \text{TDI} = 1800 / 34 \text{ units} = 53$$

1 units : 50 mg/dl glucose levels are greater
then 125 mg/dl (goal)

Nutrition Facts	
Serving Size 1 Package (241 g)	
Servings Per Container 1	
Amount Per Serving	
Calories 250	Calories from Fat 50
	% Daily Value*
Total Fat 6g	9%
Saturated Fat 3g	15%
Trans Fat 0g	
Polyunsaturated Fat 1g	
Monounsaturated Fat 1g	
Cholesterol 30mg	10%
Sodium 620mg	26%
Potassium 60mg	15%
Total Carbohydrate 40g	13%
Dietary Fiber 3g	12%
Sugars 10g	
Protein 10g	13%

Total Carbohydrates:
40 grams / 15 = 3 units



$$275 \text{ mg/dl} - 125 \text{ mg/dl} = 150 / 50 = 3 \text{ units}$$

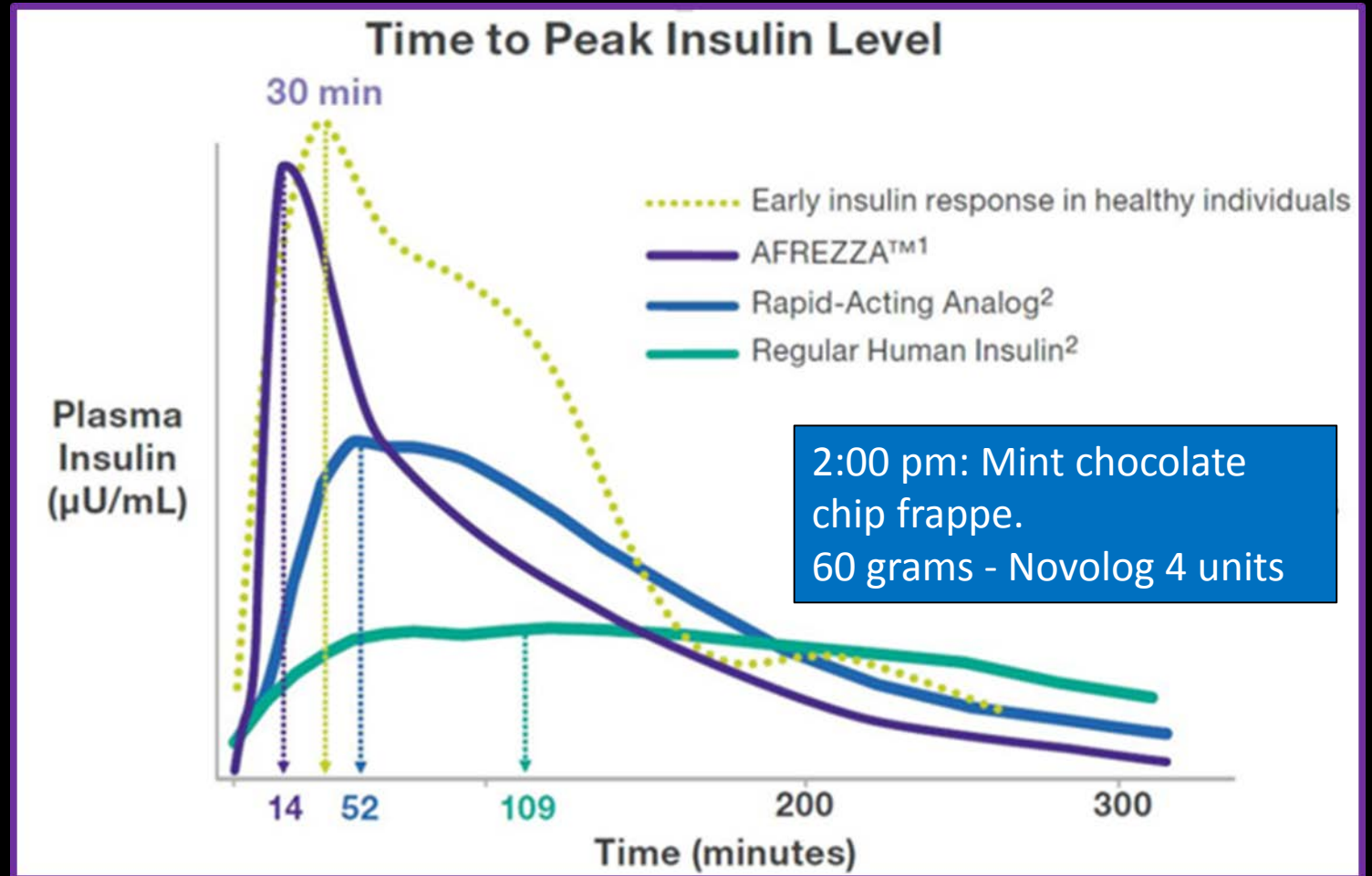
3 units + 3 units = 6 units

Stacking:

The patient asked if she should take rapid-acting insulin with meals, snacks and beverages that contain carbohydrates.

- a. Yes
- b. No
- c. May be so.....

Lunch: Novolog = 6 units



As the patient is leaving, she says “Hey Dr. Desai, do you think I can get an insulin pump?”

- a. Yes
- b. No
- c. May be so

Criteria for an insulin pump for patients with autoimmune diabetes (DM1/LADA):

1. Suboptimal glycemic control with a HgBa1c > 7.0%
2. Recurrent episodes of severe hypoglycemia (hypoglycemia unawareness)
3. History of severe glycemic excursions

Taken from Medtronic – Certificate of Medical Necessity

Had an insulin pump...



Before it was cool.

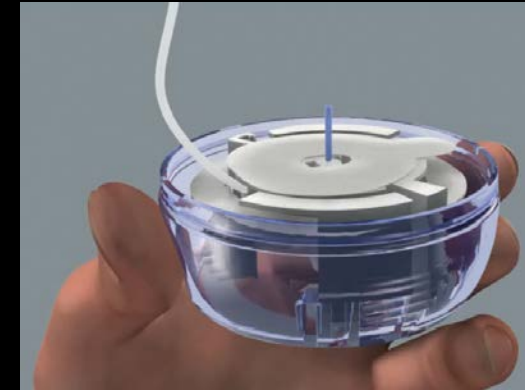
What type of insulin is used in insulin pumps?

- A. Basal Insulin (ex. Glargine)
- B. Rapid Acting Insulin (ex. Aspart)
- C. Basal Insulin and Rapid Acting Insulin
- D. Basal Insulin, Rapid Acting Insulin and Glucagon

Insulin Pump Anatomy



www.medtronicdiabetes.com



ipag.co.uk



1. Basal Setting

Standard (active)		Pattern A		Pattern B	
24-Hour Total	24.000 U	24-Hour Total	30.200 U	24-Hour Total	28.800 U
TIME	U/hr	TIME	U/hr	TIME	U/hr
0:00	1.00	0:00	1.05	0:00	1.20
12:00	1.00	10:00	1.55		
		13:00	1.55		
		20:00	1.05		

2. Bolus Settings (“Wizard”)

- Insulin : Carbohydrate ratio -> $500 / \text{TDI} =$
- Insulin Sensitivity Factor -> $1800 / \text{TDI} =$

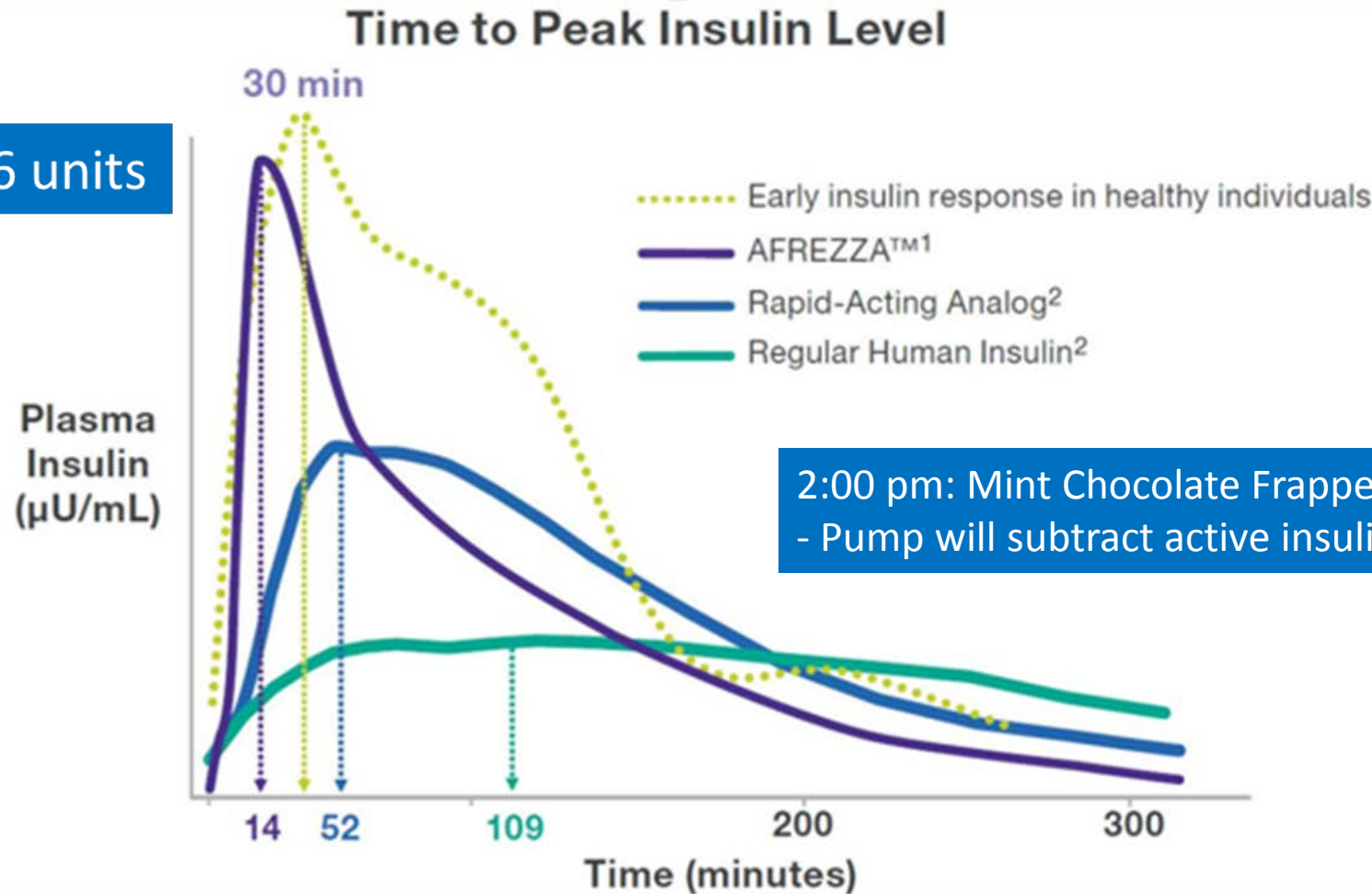
Carbohydrate Ratio (g/U)		Insulin Sensitivity (mg/dL per U)		Blood Glucose Target (mg/dL)		
TIME	Ratio	TIME	Sensitivity	TIME	Low	High
0:00	10.0	0:00	60	0:00	90	120

3. Active Insulin Time

Active Insulin Time (h:mm)	3:00
----------------------------	------

Stacking Insulin Prevention: Active Insulin Time

Lunch: Novolog = 6 units



2:00 pm: Mint Chocolate Frappe = 4 units
- Pump will subtract active insulin – 1.8 units

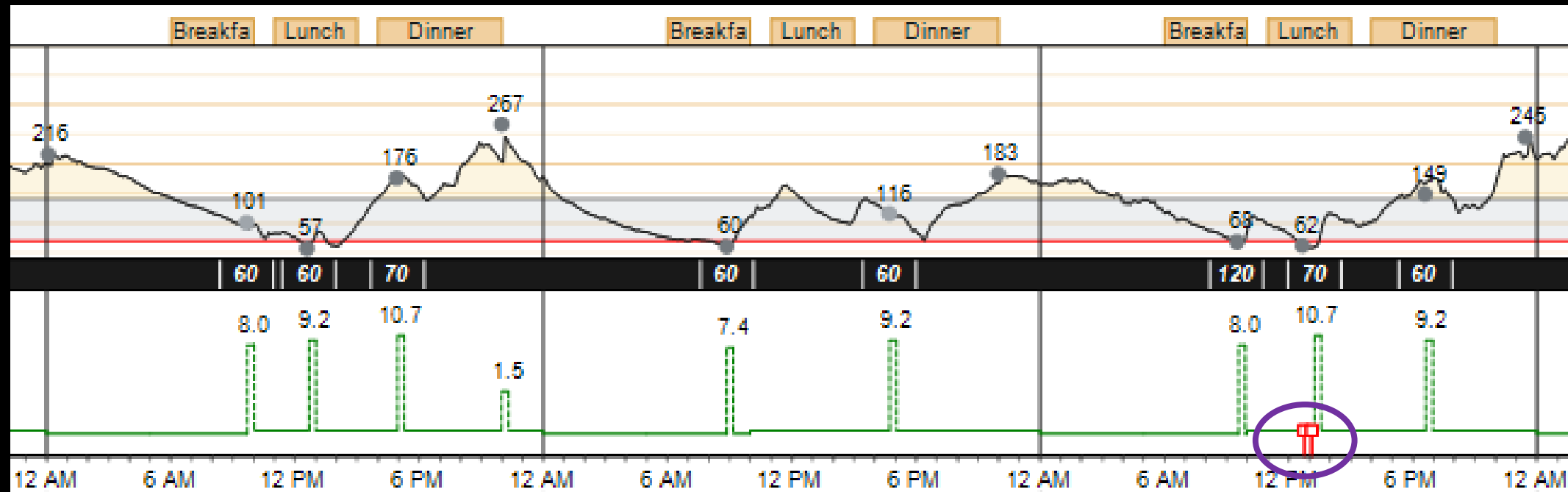
The most current insulin pumps with continuous glucose sensors can do which of the following?

- A. They can do everything a pancreas can... that is why they are call the Artificial Pancreas.
- B. Auto-regulate basal insulin administration.
- C. Auto-regulate basal and bolus insulin administration.
- D. There is no auto-regulating insulin pump and the Artificial Pancreas is an urban legend.

Continuous Glucose Monitor that interacts with the insulin pump



Sensor Augmented Insulin Pump



Suspend on low

Six month follow-up:

- Feeling the best she has in over 1 year
- Waking up in the early morning 2-3 times weekly with palpitations and sweats -> symptoms relieved with juice
- She has not been checking her finger-stick glucose levels when this occurs, but she “knows that she is low”

Labs: HgBa1c – 6.7 <- 9.2 %, fasting serum glucose – 72 mg/dl

- Definition of hypoglycemia : a blood glucose level of 70 mg/dl or less
- Symptoms: surprising similar to hyperglycemia -> if you don't check you don't know.
- Treatment : Medical condition....so medical treatment.
 - not time to eat whatever you want!!!
 - Glucose Tablets (4 grams of carbohydrates)
 - Glucose Gels (15 grams of carbohydrates)
 - Glucagon Kit



Medical Alert for First Responders



Medical Alert for First Responders



When a person with Type 1 Diabetes is found down, what is the first course of treatment?

- a. Panic
- b. CPR
- c. Check glucose levels
- d. Glucose gel per rectum
- e. Glucagon
- f. D25 –D50 infusion

Thank you

Bolus Insulin:

Insulin: Carbohydrate Ratio

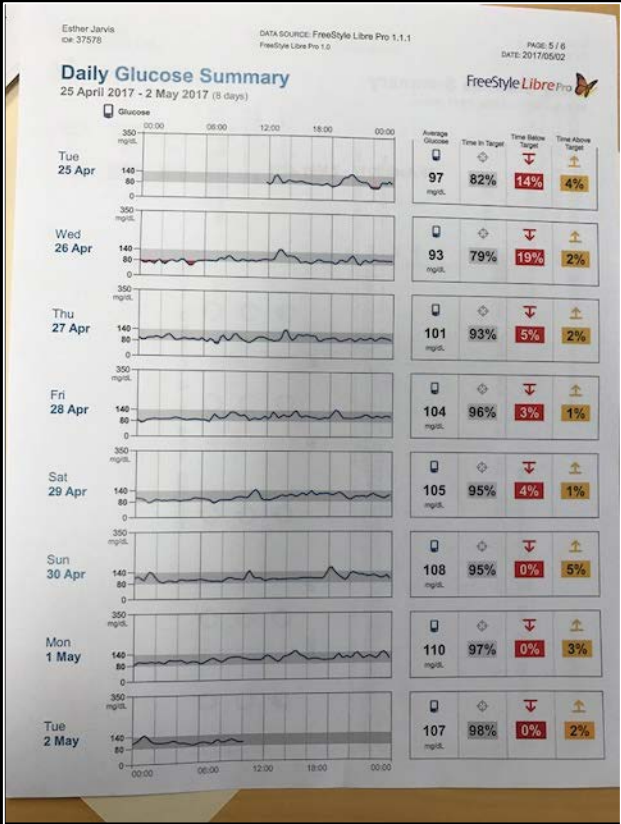
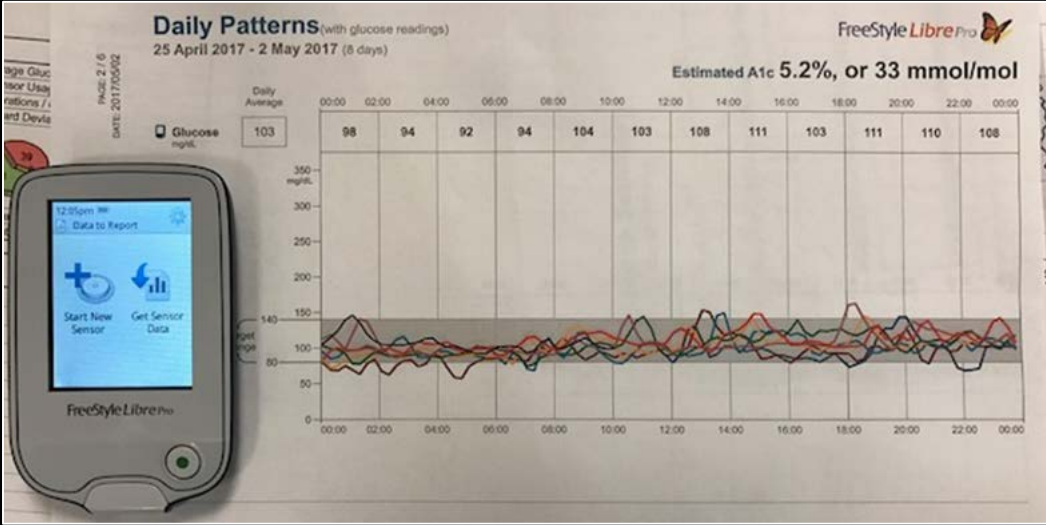
Insulin Sensitivity Factor

Active Insulin Time – Prevention of Stacking Doses

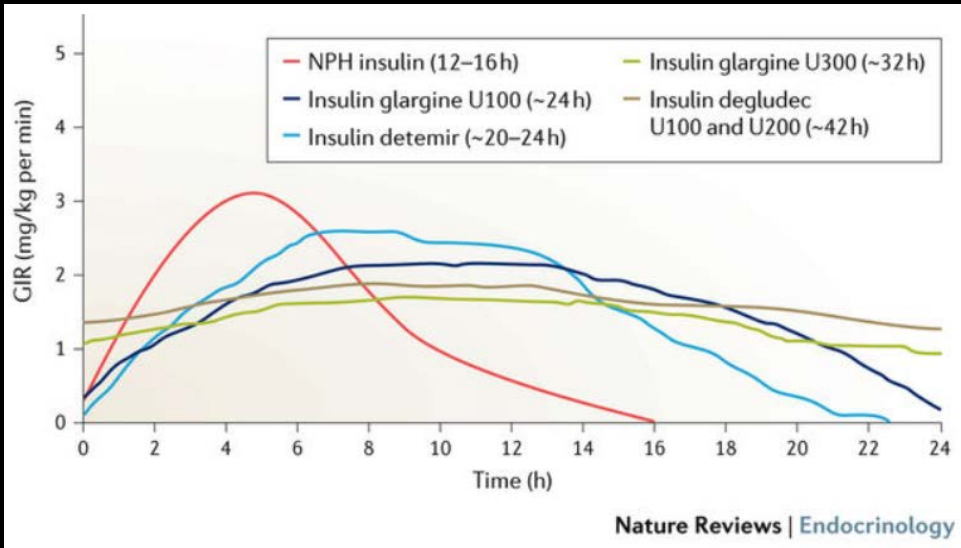




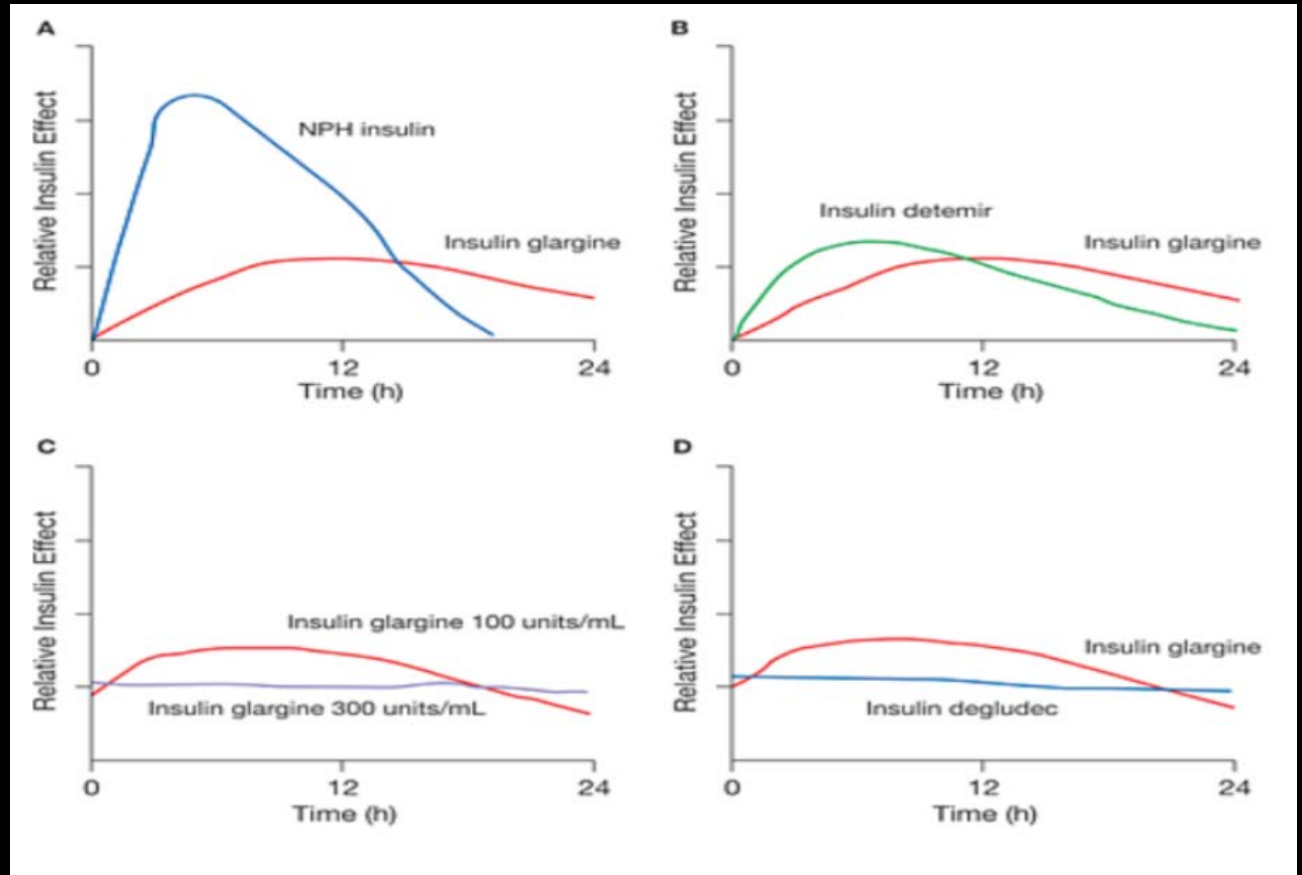
Continuous Glucose Monitor



Basal Insulins



Nature.com



Management of Type 1 Diabetes. Savitha Subramanian, MD, David Baidal, Jay S Skyler, M.D., and Irl B Hirsch, M.D. Endotext. Nov. 16 2016

Insulin Resistance in Diabetes Type II

