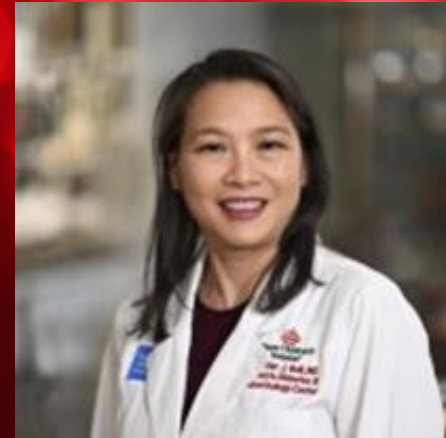


ALL ABOUT INSULIN – THE HORMONE AND THE MEDICINE

Jennifer Bell, MD
Pediatric Endocrinology



DIABETES & ENDOCRINE



2021 Virtual Diabetes Management Conference for School Nurses

Provided by Texas Children's Hospital

NURSING CONTINUING PROFESSIONAL DEVELOPMENT (NCPD)

Texas Children's Hospital is approved with distinction as a provider of nursing continuing professional development (NCPD) by the Texas Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

REQUIREMENTS FOR SUCCESSFUL COMPLETION

To receive contact hours for this nursing continuing professional development activity, the participant must:

- Register for the continuing professional development activity
- Attend at least one session
- Complete a pre and post survey
- Complete a participant evaluation online

Print and sign your contact hour "Certificate of Successful Completion" once you have completed the online evaluation.

LEARNING OUTCOME

As a result of this professional development activity, 90% attendees will intend to integrate what they have learned into their professional practice and be able to name one concept learned on the post activity evaluation.

CONFLICTS OF INTEREST

Explanation: A conflict of interest occurs when an individual has an opportunity to affect or impact educational content with which he or she may have a commercial interest or a potentially biasing relationship of a financial nature. All planners and presenters/authors/content reviewers must disclose the presence or absence of a conflict of interest relative to this activity. All potential conflicts are resolved prior to the planning, implementation, or evaluation of the continuing nursing education activity. All activity planning committee members and presenters/authors/content reviewers have had their Conflict of Interest assessed, identified and resolved by the nurse planner.

The activity's Nurse Planner has determined that the following planning committee member(s) and/or presenter(s)/author(s)/content reviewer(s) have a conflict of interest. Those conflicts of interest have been appropriately resolved.

- Planning Committee - Amber Smith – Ownership Interest in Tandem Diabetes Care

COMMERCIAL SUPPORT

This NCPD activity has received no commercial support.

OBJECTIVES

- Understand insulin mechanism of action
- Identify types and brands of insulin
- Calculate prandial insulin dosage



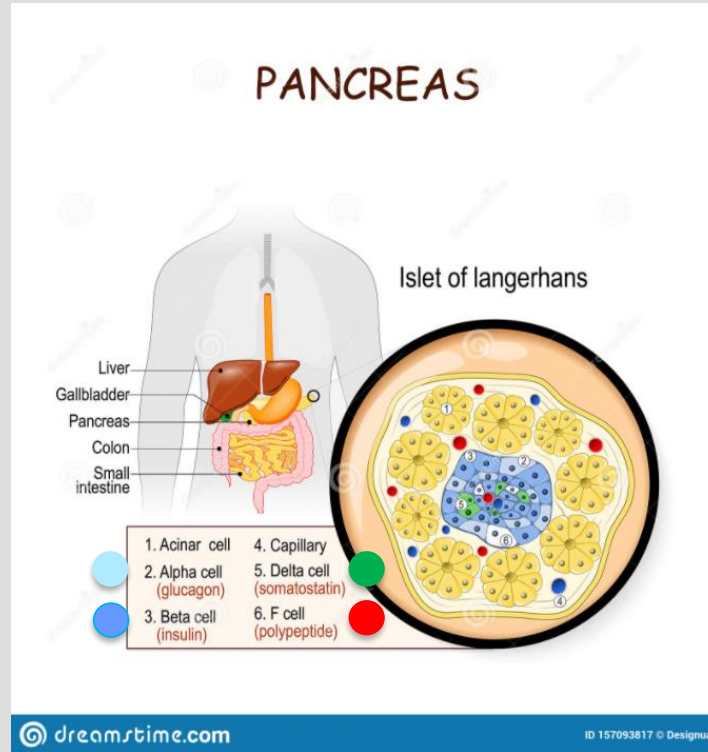
CELEBRATING

100 YEARS OF
INSULIN

DIABETES & ENDOCRINE

DISCOVERY OF ENDOCRINE ROLE OF THE PANCREAS

1869: Paul Langerhans, a medical student in Berlin discovers a distinct collection of cells within the pancreas. These cells would later be called the Islets of Langerhans.



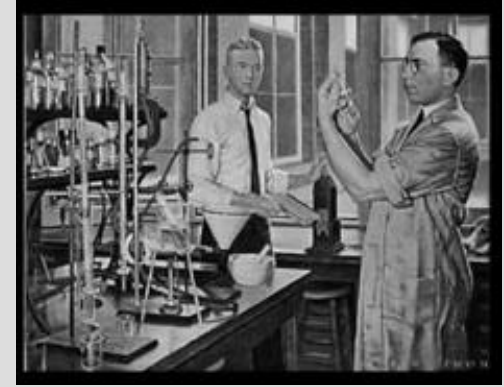
Paul Langerhans
Islets of Langerhans - Langerhans discovered these cells during his studies for his doctorate at the Berlin Pathological Institute in 1869.^[1]

DISCOVERY OF ENDOCRINE ROLE OF THE PANCREAS

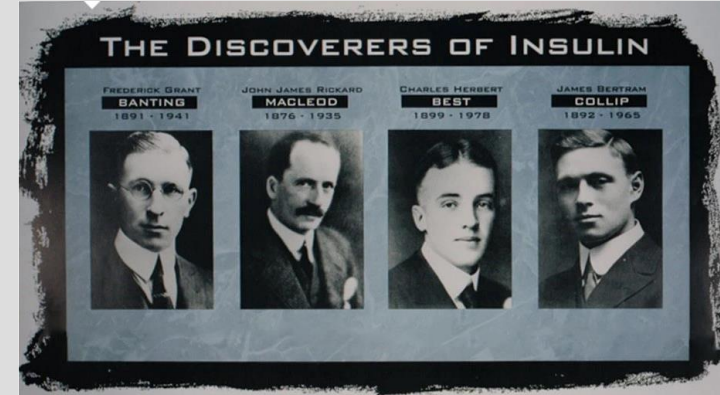
- 1889: Oscar Minkowski and Joseph von Mering remove the pancreas from a dog to study the effects on digestion.
 - Sugar is found in the dogs urine after flies were noticed to be feeding off the urine.
- 1901: Eugene Opie discovers that the Islets of Langerhans produce insulin and that the destruction of these cells resulted in diabetes

THE DISCOVERY OF INSULIN

- 1916: Romanian Professor, Nicolae Paulescu, develops an extract of the pancreas and shows that it lowers blood sugar in diabetic dogs.
 - World War 1 prevents the experiments from continuing & it is not until 1921 that Paulescu publishes evidence of the experiments. [81]
- 1921: In Toronto, Canada, Dr. Frederick Banting & medical student, Charles Best performed experiments on the pancreases of dogs.
 - Professor John Macleod provided Banting & Best with a laboratory and dogs to carry out experiments. The pancreas of a dog was removed, resulting in the dog showing signs of diabetes.
 - The pancreas was sliced & ground up into an injectable extract and injected a few times a day into the dog which helped the dog regain health.
 - Given early success, Macleod wanted to see more evidence that the procedure worked and provided pancreases from cows to make the extract which was named “insulin”.



Dr. Frederick Banting & medical student Charles Best



INSULIN 2021 – COMMEMORATING THE CENTENNIAL FOR THE DISCOVERY OF INSULIN

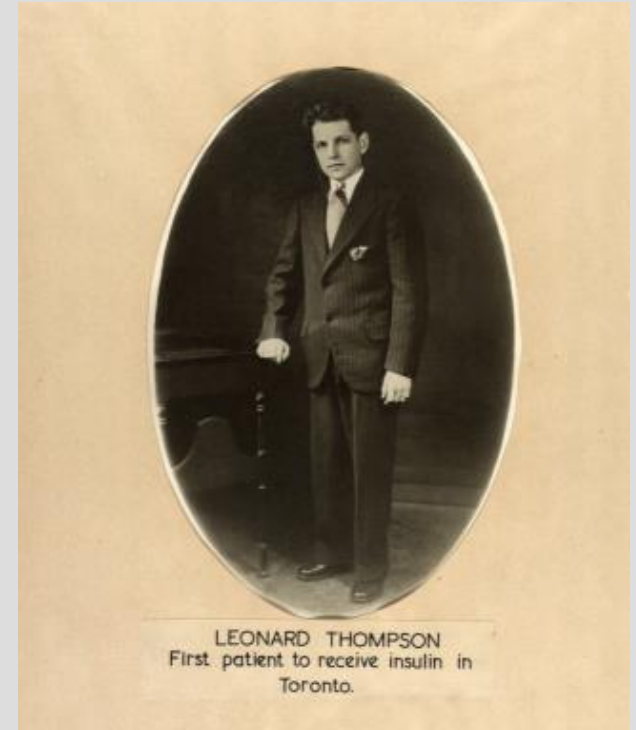


By Defining Moments Canada

DIABETES & ENDOCRINE

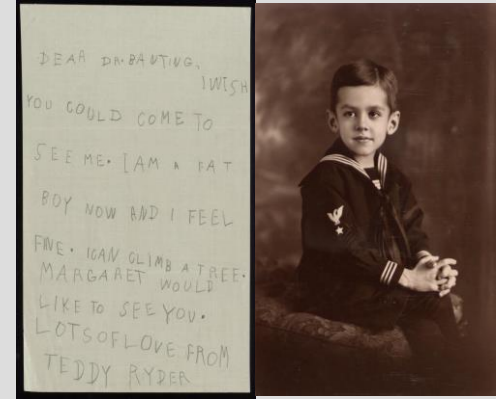
FIRST USAGE OF INSULIN AS A MEDICAL TREATMENT

- **1922:** The first patient, Leonard Thompson a 14 year old boy with type 1 diabetes is given the first medical administration of insulin.
- Leonard lived another 13 years before succumbing to pneumonia.

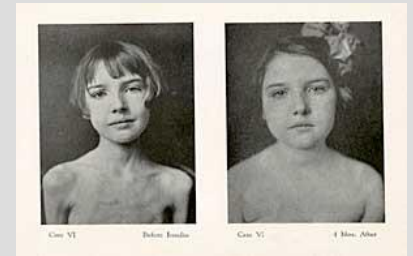


INSULIN THE MEDICINE

- **1922:** As news of insulin's success spread, Banting and Best begin receiving letters asking for help for others with type 1 diabetes.
 - Banting & Best improve their techniques for the production of insulin and Eli Lilly becomes the first insulin manufacturer.
- **1923:** Banting and Macleod are awarded the Nobel Prize in Physiology or Medicine.
 - Frederick Banting & John Macleod, however, felt Charles Best & James Collip were equally eligible and shared their prize money with the two colleagues. [82]



Teddy Ryder



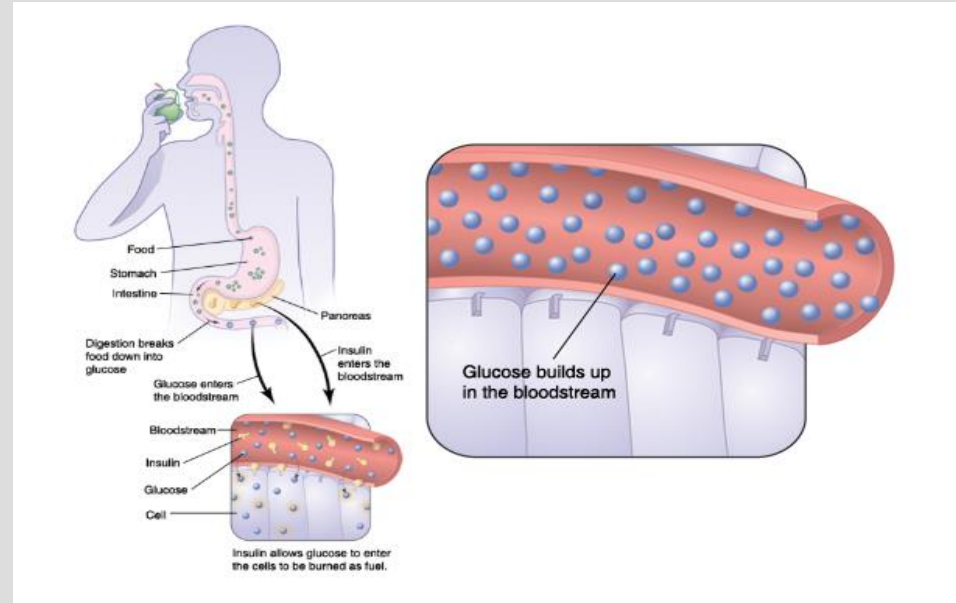
Q1 – HOW DOES INSULIN WORK?

- A) It breaks down carbohydrates to glucose
- B) It is released from the intestines into the blood stream
- C) It allows the glucose to enter cells to be burned as fuel
- D) Both B and C
- E) All of the above



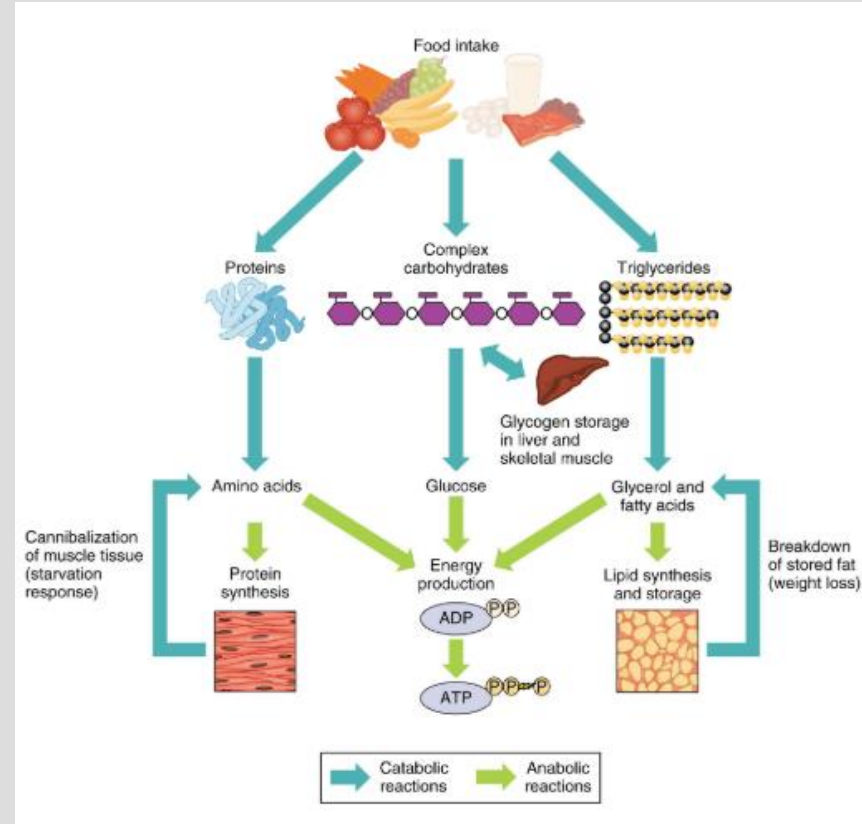
INSULIN THE HORMONE

- Digestion breaks down carbohydrates to glucose
- Insulin is released from beta cells from pancreas into blood stream upon eating
- Insulin allows the glucose to enter cells to be burned as fuel



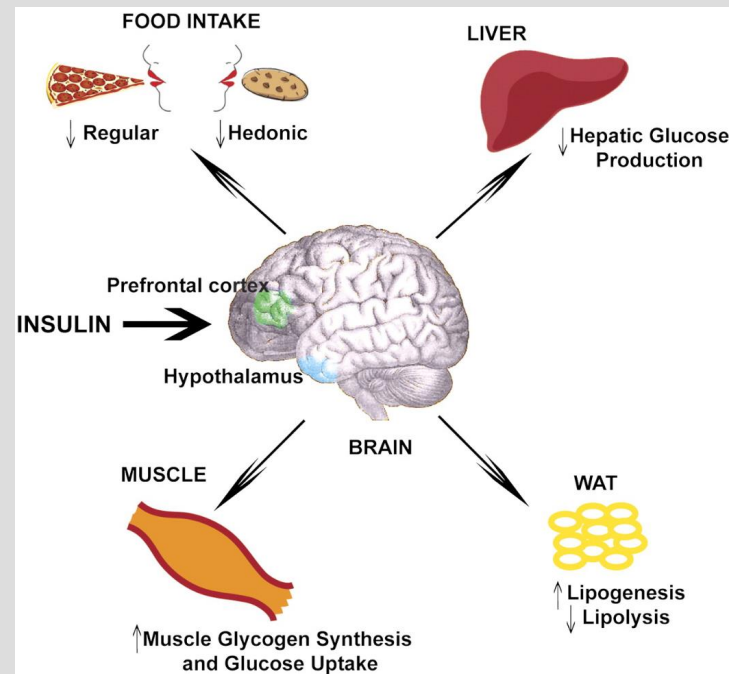
INSULIN THE HORMONE

- Digestion breaks down food (macronutrients) products to
 - Complex carbohydrates
 - Proteins
 - Fats - Triglycerides
- Insulin affects metabolism

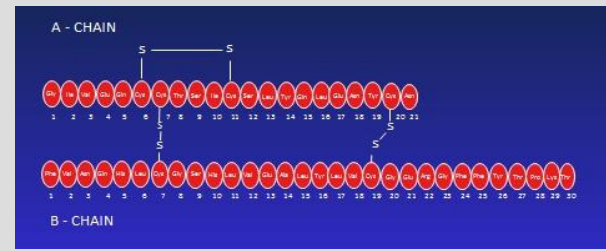


INSULIN THE HORMONE – STORAGE HORMONE

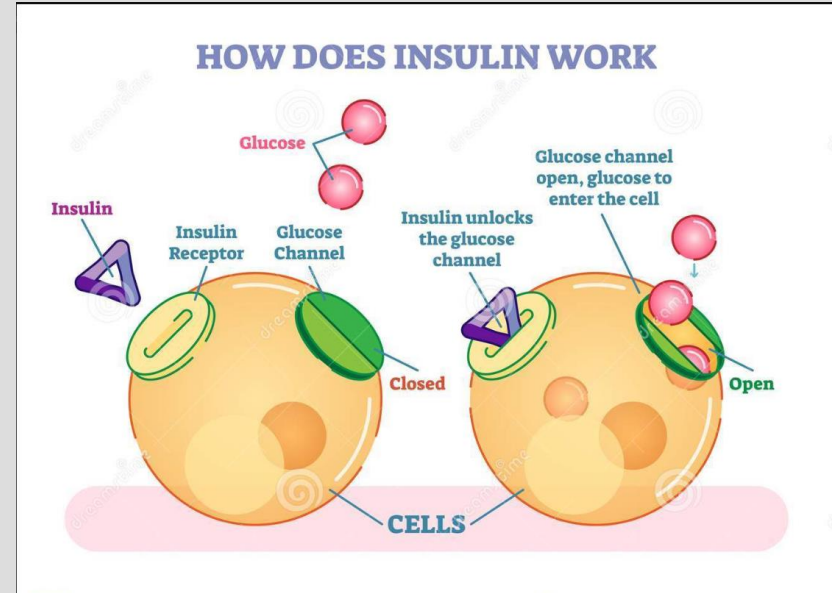
- Glucose metabolism
 - Stores glucose into liver
 - Increase glucose transport into fat and muscle
 - Stimulation of glycogen synthesis
- Lipid metabolism
 - Inhibits lipolysis
 - Stimulates fatty acid synthesis
- Protein metabolism
 - Increase transport of amino acids into muscles
 - Increase protein synthesis into muscle



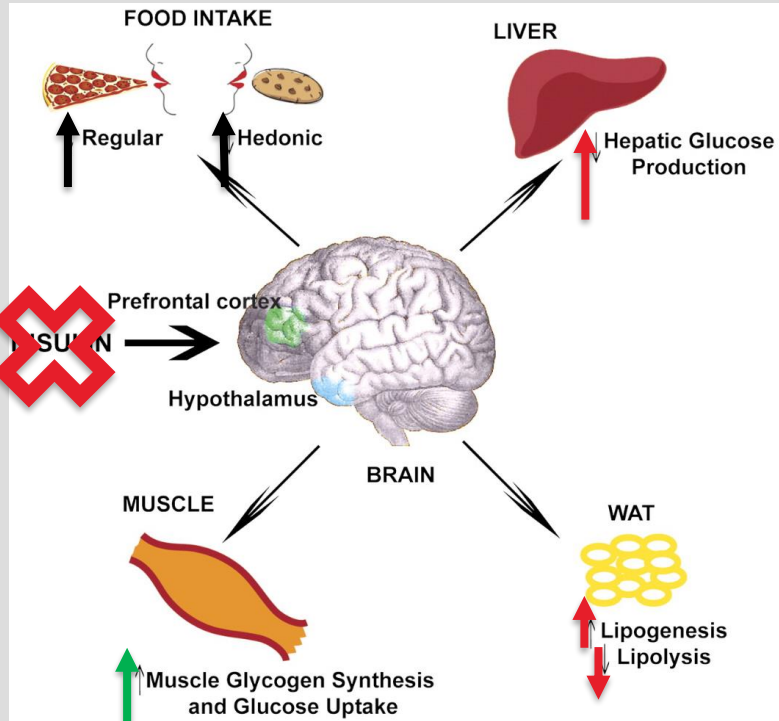
INSULIN THE HORMONE



- Insulin is a protein -
 - Alpha chain
 - Beta chain
- Without insulin, glucose is not able to enter cells nor to be used as fuel
- Type 1 diabetes is a result of insulin deficiency following destruction of pancreatic beta cells



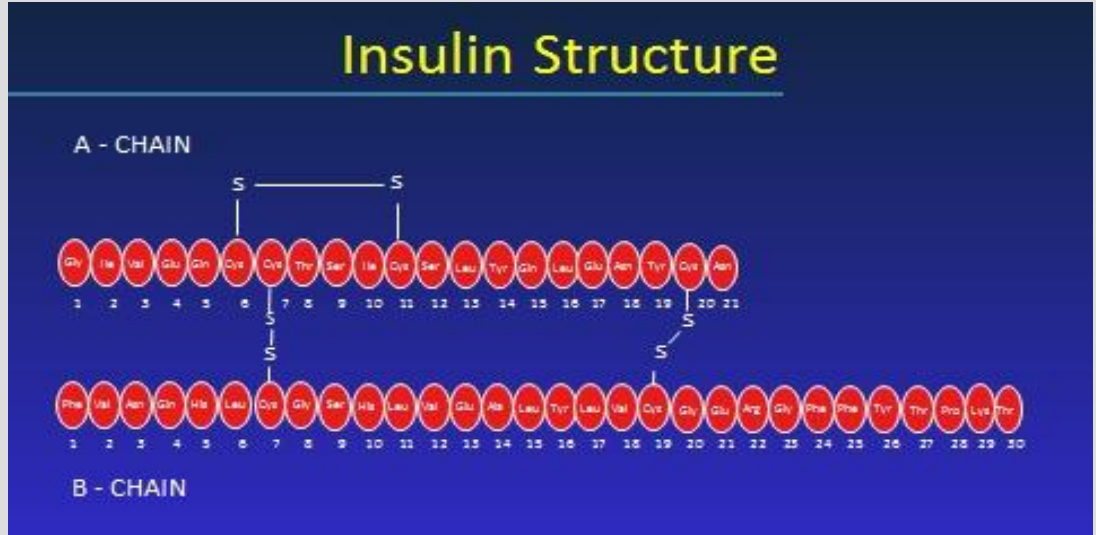
DIABETES MELLITUS IS A LACK OF INSULIN



- Food intake dysregulation
- Glucose metabolism – **Glucose is unable to enter cells**
 - Unable to store glucose into liver
 - Decrease glucose transport into fat and muscle
 - Inhibit of glycogen synthesis
- Lipid metabolism – **Body starts to burn fat → ketones**
 - Stimulates lipolysis
 - Inhibits fatty acid synthesis
- Protein metabolism – **Body is not able to make muscle**
 - Decrease transport of amino acids into muscles
 - Decrease protein synthesis into muscle

Q2 – HOW MANY TYPES OF INSULIN ARE AVAILABLE?

- A) 2
- B) 3
- C) 4
- D) 5 or more



TYPES OF INSULIN

- Rapid Acting - 4
- Short Acting - 1
- Intermediate Acting - 1
- Long Acting - 3
- Insulin Mixtures – 4
- >13 types of insulin

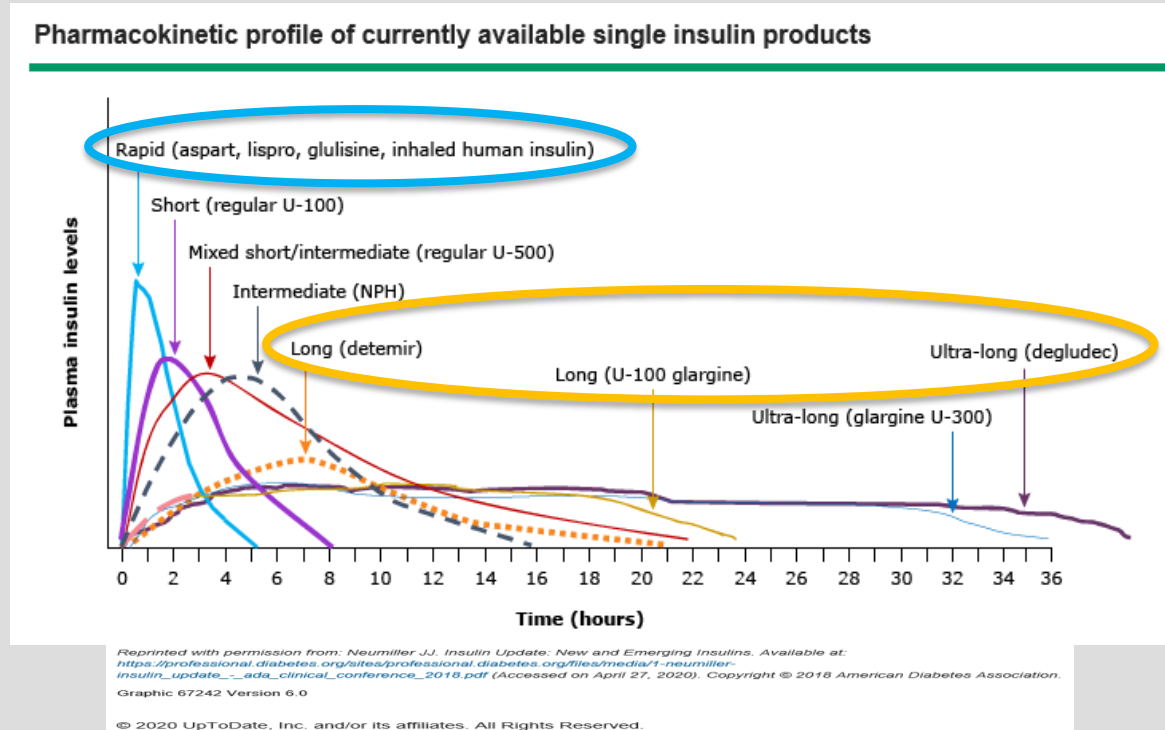
Table 2.

Insulins Commercially Available in the US (Recombinant DNA origin)

Category/Name of Insulin	Brand Name (manufacturer)	Preparation(s)
Rapid-Acting		
Insulin Lispro	Humalog (Lilly)	Vial, cartridge, disposable pen
Insulin Aspart	Novolog (Novo Nordisk)	Vial, cartridge, disposable pen
Insulin Glulisine	Apidra (Sanofi-Aventis)	Vial, disposable pen
Technosphere insulin	Afreeza	Inhaler
Short-Acting		
Regular Human	Humulin R (Lilly) Novolin R (Novo Nordisk)	Vial
Intermediate-Acting		
NPH Human	Humulin N (Lilly) Novolin N (Novo Nordisk)	Vial, disposable pen Vial
Long-Acting		
Insulin Detemir	Levemir (Novo Nordisk)	Vial, disposable pen
Insulin Glargine	Lantus (Sanofi-Aventis) Basaglar (Lilly) Toujeo (Sanofi-Aventis)	Vial, cartridge, disposable pen Basaglar is only available as a disposable pen Toujeo is only available as a disposable pen
Insulin Degludec	Tresiba (Novo Nordisk)	Disposable pen
Insulin Mixtures		
NPH/Regular (70%/30%)	Humulin 70/30 (Lilly) Novolin 70/30 (Novo Nordisk)	Vial, disposable pen Vial
Protamine/Lispro (50%/50%)	Humalog Mix 50/50(Lilly)	Vial, disposable pen
Protamine/Lispro (75%/25%)	Humalog Mix 75/25(Lilly)	Vial, disposable pen
Protamine/Aspart (70/30)	Novolog Mix 70/30 (Novo Nordisk)	Vial, disposable pen

PHARMACOKINETICS OF INSULIN MEDICATION

- Rapid Acting
 - Peaks at 1 hr
- Regular or Short Acting
 - Peaks at 2-4 hr
- Intermediate Acting
 - Peaks at 4-10 hr
- Long Acting
 - No peak
- Ultra Long acting
 - Peaks at 9 hr



RAPID ACTING INSULIN

- AKA mealtime/prandial insulin
- Begins to work about 15 minutes after injection
- Peaks in about one or two hours after injection
- Last between two to four hours.

- Insulin aspart ★
 - Fiasp – ultra fast
 - NovoLog
- Insulin glulisine ★
 - Apidra
- Insulin lispro ★
 - Admelog
 - Humalog

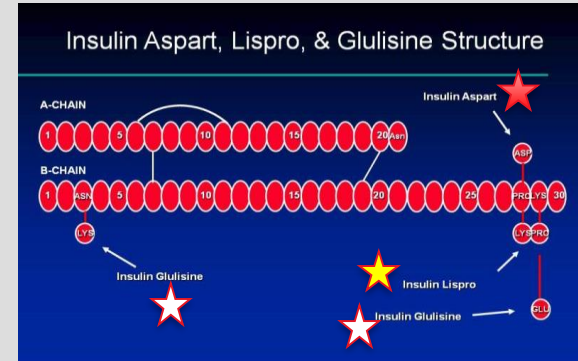


Table 3.

Insulin Pharmacodynamics (3-11,20,23-25,27)

Insulin	Onset (hr.)	Peak (hr.)	Duration (hr.)	Appearance
Fast-acting Insulin Aspart A	Within 5 min	~1	3-4	Clear
Insulin Lispro	within 15 min	~ 1	3-5	Clear
Insulin Aspart	within 15 min	1-3	3-5	Clear
Insulin Glulisine	0.25-0.5	0.5-1	4	Clear

TYPES OF LONG ACTING INSULIN

- Reaches the bloodstream several hours after injection
- Tends to lower glucose levels up to 24 hours

- Degludec (Tresiba) ★
- Detemir (Levemir) ☆
- Glargine (Basaglar, Lantus) ★

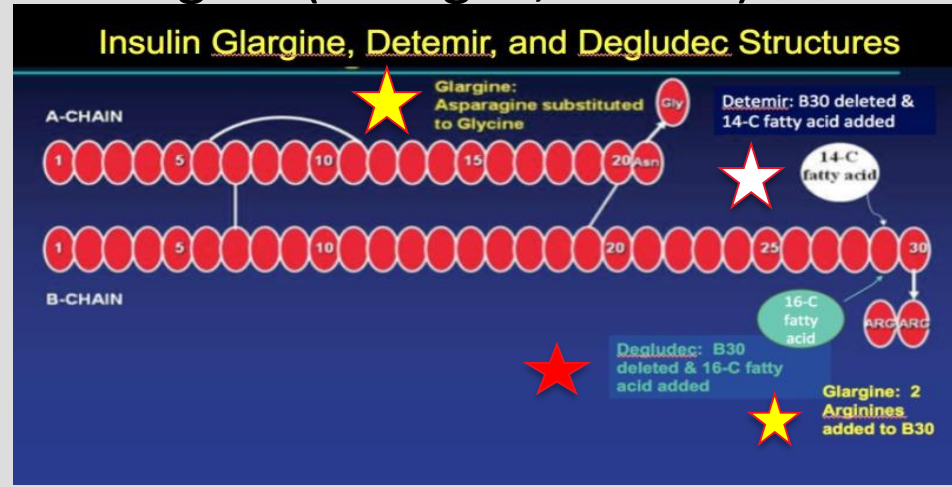


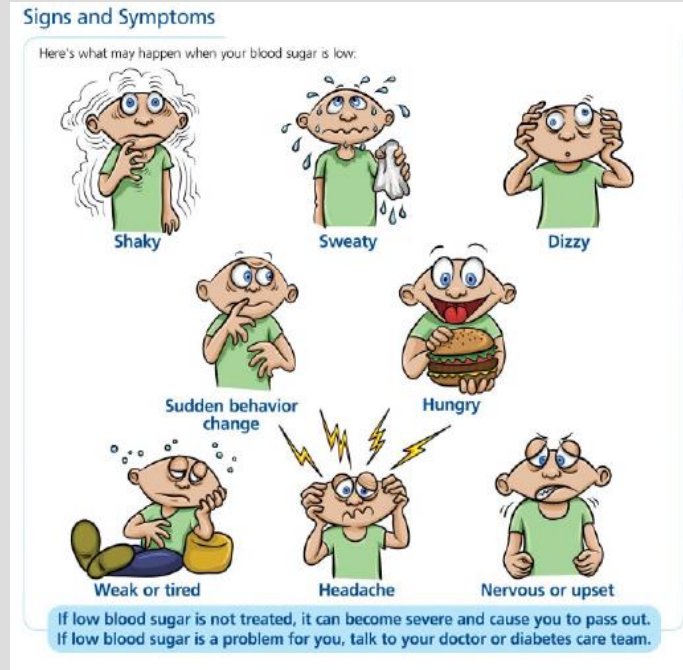
Table 3.

Insulin Pharmacodynamics (3-11,20,23-25,27)

Insulin	Onset (hr.)	Peak (hr.)	Duration (hr.)	Appearance
Insulin Detemir	3-4	6-8 (though relatively flat)	up to 20-24	Clear
Insulin Glargine	1.5	Flat	24	Clear
Insulin Degludec	1	9	42	Clear

ADVERSE EFFECTS OF INSULIN

- Hypoglycemia
- Weight gain
- Local reaction



Q3 – PICK FROM THE FOODS BELOW WHICH WOULD REQUIRE INSULIN THERAPY?

- A) Grilled chicken salad
- B) Pizza
- C) Peanut butter ball
- D) Ham and cheese roll-up
- E) Hamburger with bun



CARBOHYDRATES (CHO)

- Carbohydrates are the foods that are broken down into glucose (sugar) in our body.
 - Main foods that affect blood glucose.
 - Body's best source of energy
 - Necessary for optimal growth and development
- Carbohydrates have the most significant effect on blood glucose followed by protein and fat

Effect on Blood Glucose Level

Carbohydrates

Protein

Fat

Carbohydrate has the most significant effect on blood glucose, followed by protein and fat.



DIABETES & ENDOCRINE

Q4 – WHAT INFORMATION IS NEEDED TO CALCULATE MEALTIME INSULIN?

- A) Amount of carbohydrates eaten
- B) Blood sugar
- C) Amount of protein eaten
- D) Both A and B
- E) All of the above



INSULIN TO CHO RATIO (I:CHO)

- The amount of rapid acting insulin needed for a certain amount of carbohydrates eaten
- Carbohydrate ratio allows insulin dosage to be calculated for meals and snacks
- The CHO ratio will vary with each child and will change with time
- Types of rapid acting insulin are interchangeable

Table 3.

Insulin Pharmacodynamics ([3-11,20,23-25,27](#))

Insulin	Onset (hr.)	Peak (hr.)
Fast-acting Insulin Aspart A	Within 5 min	~1
Insulin Lispro	within 15 min	~ 1
Insulin Aspart	within 15 min	1-3
Insulin Glulisine	0.25-0.5	0.5-1

Rapid-Acting Insulin Pens

	Generic	Brand	Conc.
	Aspart	Novolog	U-100
		Fiasp	U-100
	Lispro	Humalog	U-100
		Admelog	U-100
	Glulisine	Apidra	U-100

CORRECTIONAL INSULIN OR INSULIN SENSITIVITY FACTOR (ISF)

- Amount of insulin given for high blood sugar
- This is the amount of insulin needed to bring blood sugar down to target
- The correctional insulin/ ISF will vary with each child and will also change with time
- Target blood sugar can vary with each child and change with time as well – target blood sugar is typically 100 mg/dL

HOW TO CALCULATE PRANDIAL INSULIN



Rapid-Acting Insulin Pens

	Generic	Brand	Conc.
Aspart		Novolog	U-100
		Fiasp	U-100
Lispro		Humalog	U-100
		Admelog	U-200
Glulisine	Apidra	U-100	

Using Insulin to Carbohydrate Ratio (ICR) & Correction Factor (CF)



Sample ICR: _____ CF: _____

Formula for Insulin to CHO Ratio (ICR). This means one unit of rapid insulin will cover this many CHO's

$$\boxed{} \div \boxed{} = \boxed{} = A$$

Number of CHO To be eaten at meal time Divided by ICR Insulin to CHO Ratio Units of rapid insulin to be given to cover that meal

Formula for CF. This means 1 unit of rapid insulin will bring the blood sugar down by this many points.

$$\boxed{} - \boxed{} = \boxed{} \div \boxed{} = \boxed{} = B$$

Blood Glucose before meal Minus Target Number of points above Target number Divided by CF Correction Factor Units of rapid insulin needed to CORRECT BG to bring it back to target number

Now add two doses together!

$$\bigcirc A + \bigcirc B = \boxed{} \text{ ————— Do not round up or down until the very end!}$$

Total units of rapid insulin your child will receive for this meal time only

If blood glucose is 70-100, there is no need to correct it! Simply give insulin calculated for the carbs to be eaten. Do not use CF. (For pregnancy, use range of 60-100 as reference to not use CF.)

If blood glucose (BG) is below 70, first treat with 15 grams of fast acting carbohydrates (such as 4 oz of juice), Then recheck BG 15 minutes later. After verifying that BG is > 70, give the rapid insulin calculated using ICR

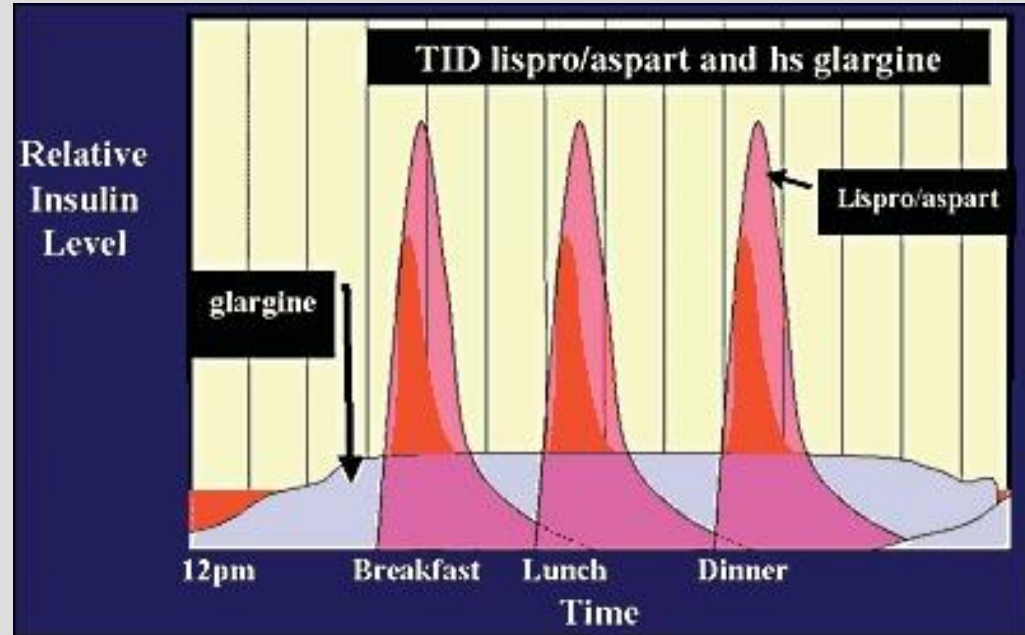
NEVER use correction factor (CF) with a high BG that is a result of a low BG treatment

NEVER include carbohydrates used to treat the low BG when calculating insulin for the food

Clinical Nutrition Services at Texas Children's Hospital©

MULTIPLE DAILY INSULIN INJECTIONS

- Insulin injections therapy is designed to mimic the pancreas
- Insulin is used to promote glucose utilization after eating
- Insulin should be given 10-15 minutes prior to meals



INSULIN MEDICATION STORAGE

- Once the vial or pen is opened, it may be kept at room temperature left unrefrigerated at a temperature between 59°F and 86°F (not above 90 degrees)
- Once the vial or pen is opened, it is good for 28 days, or the expiration date on the bottle, whichever comes first
- Insulin should be colorless, no cloudiness or yellowing
- Do not freeze insulin



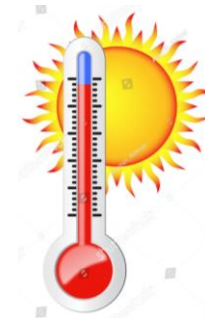
INSULIN MEDICATION SITE INJECTION

- Insulin can be injected into the fatty parts of the:
 - Upper back of arms
 - Abdomen
 - Upper Buttocks
 - Outer Thighs
- Do not inject 2-3 inches around or inside of the belly button
- Sites must be rotated to prevent scar tissue from forming!
- Unless otherwise instructed, insulin should be given **10-15** minutes **before** the meal.



FACTORS AFFECTING INSULIN ABSORPTION

Factor	Comment
Exercise of injected area	Strenuous exercise of a limb within 1 hour of injection will speed up insulin absorption. Clinically significant for regular insulin analogs.
Local Massage	Vigorously rubbing/massaging injection site will speed absorption.
Temperature	Heat can increase absorption rate, including use of a sauna, shower, or hot bath soon after injection. Cold has the opposite effect.
Site of Injection	Insulin is absorbed fast from the abdomen. Less clinically relevant with rapid-acting insulins, insulin glargine, and insulin detemir.
Lipohypertrophy	Injection into hypertrophied areas delays insulin absorption.
Jet injections	Increased absorption rate.
Insulin mixtures	Absorption rates are unpredictable when suspension insulins are not mixed adequately (i.e. they need to be resuspended).
Insulin dose	Larger doses delay insulin action and prolong duration.
Physical status (soluble vs suspension)	Suspension insulins must be sufficiently resuspended prior to injection to reduce variability



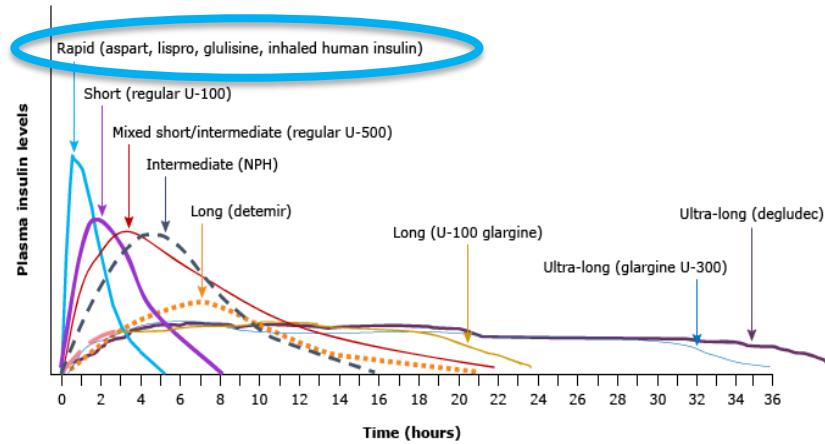
Q5 – WHAT TYPE OF INSULIN IS USED IN INSULIN PUMP?



Eric Hendershott

- A) Rapid Acting
- B) Short Acting
- C) Intermediate Acting
- D) Long Acting
- E) Insulin Mixtures

Pharmacokinetic profile of currently available single insulin products



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INSULIN PUMP

- Rapid acting insulin

- Aspart

- NovoLog

- Glulisine

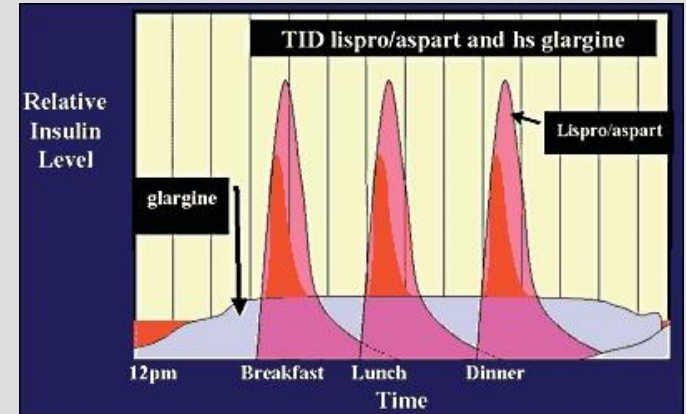
- Apidra

- Lispro

- Humalog

- Information needed for pump to give mealtime insulin

- Amount of CHO eaten
 - Blood sugar



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