

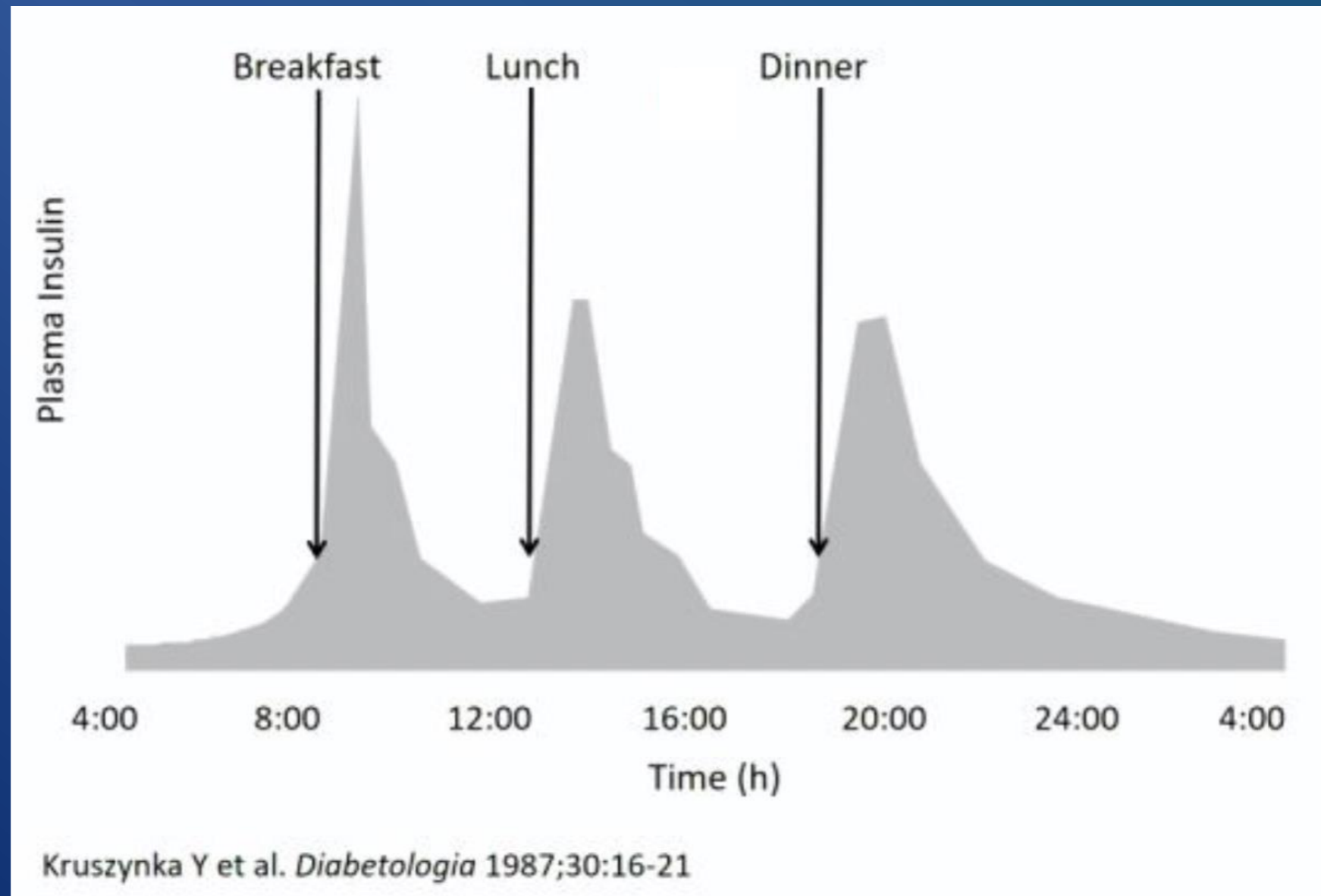
# **Insulin and Principles of Insulin Dose Adjustment**

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# Objectives

- Review physiology of insulin secretion
- Review types of insulin
- Learn individual insulin action
- Review different types of insulin therapy
- Learn how to recognize patterns in blood glucose readings
- Learn how to manage patterns in blood glucose readings

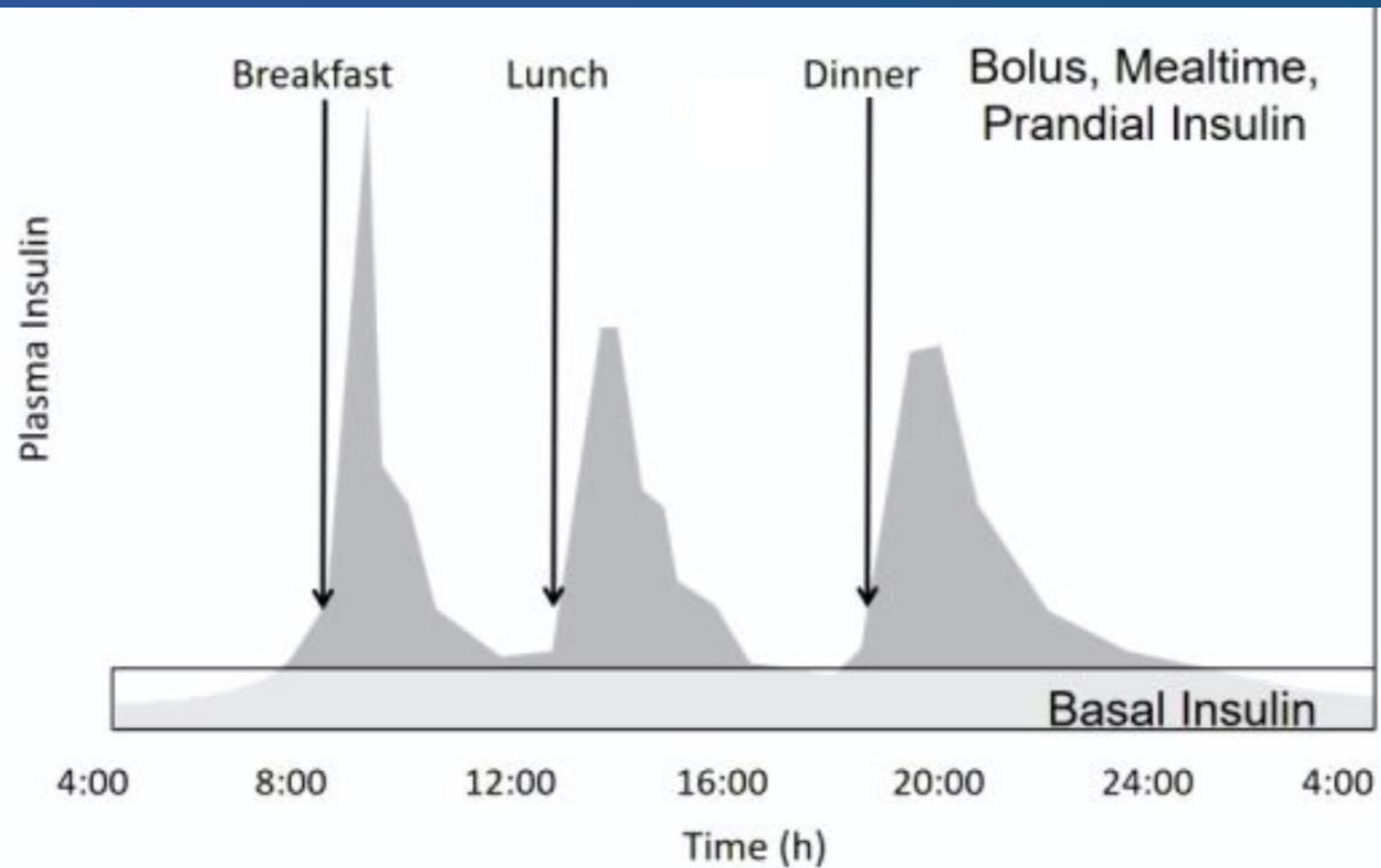
# Physiology of Insulin Secretion



# Goal of insulin therapy

- **exogenous insulin use to match the physiologic insulin output as closely as possible.**
- **Which translates to: best glycemic control possible with minimum hypoglycemic events.**

# Physiology of Insulin Secretion



Kruszynka Y et al. *Diabetologia* 1987;30:16-21

# Insulin Classification

- **Based on**
  - **Onset: time from injection to start of action**
  - **Peak: time insulin is working the hardest**
  - **Duration: length of time it works**
- **Rapid, short, intermediate, long, ultra long acting**
- **Often use more than one type of insulin to treat children with T1D on injections**

# Insulin Comparison

TYPE	GENERIC	BRAND	ONSET	PEAK	DURATION
Rapid-Acting	Aspart Glulisine Lispro	Novolog Apidra Humalog Admelog	10-15min	30-90min	3-5 hr
Short-Acting	Regular	Humulin R Novolin R	30-60 min	2-4 hr	5-8 hr
Intermediate-Acting	NPH	Humulin N Novolin N	1-3 hr	6-12 hr	18-26 hr
Long-Acting	Degludec Detemir Glargine Biosimilar Glargine	Tresiba Levemir Lantus Basaglar	1-2 hr	No real peak	>42 hr 20-26 hr

# Pre-Mixed Insulin

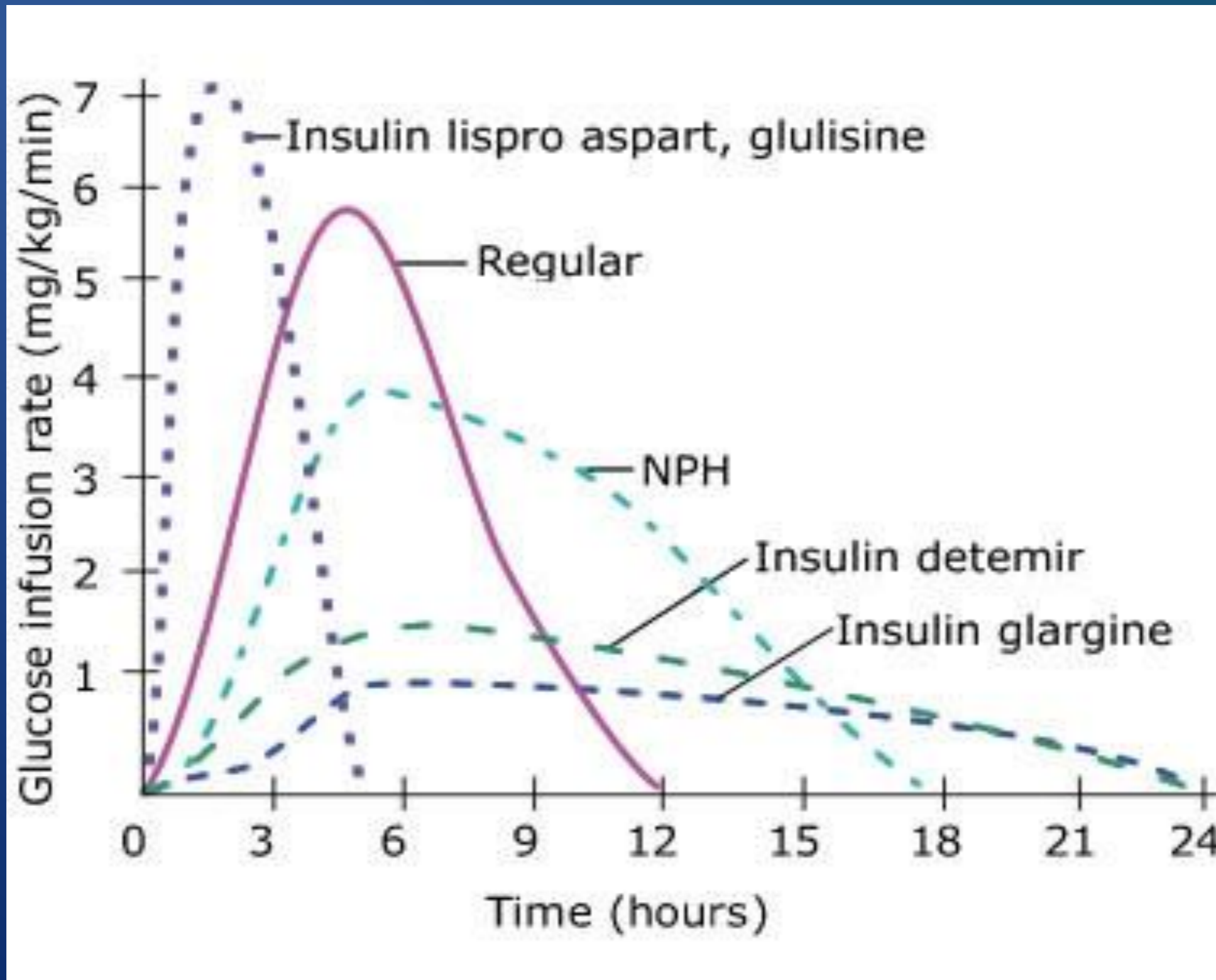
Type	Generic	Brand	Onset	Peak	Duration
Pre-Mix NPH	70%NPH/30%R  50%NPH/50% R	HumuLIN 70/30 NovoLIN 70/30 HumuLIN 50/50	30-60 min	Varies	10-16 hr
Pre-Mix Lispro	75% Lispro protamine/ 25% Lispro 50%lispro protamine/ 50% lispro	HumaLOG 75/25  HumaLOG 50/50	10-15 min.	Varies	10-16 hr
Pre-Mix Aspart	70% aspart protamine 30% aspart	NovoLOG 70/30	5-15 min.	Varies	10-16 hr



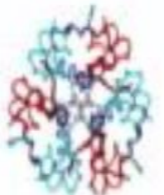
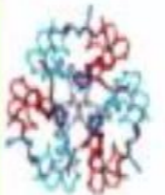


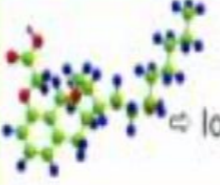
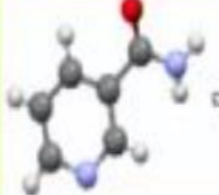


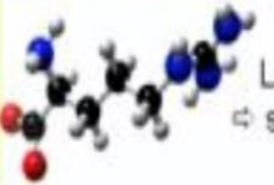
# Ultra Long Acting

GENERIC	BRAND	ONSET	PEAK	DURATION
U-100 Degludec	Tresiba	1-2 hr	No real peak	>42 hr
U-200 Degludec	Tresiba			
U-300 Glargine	Toujeo	6 hr		24-36 hr

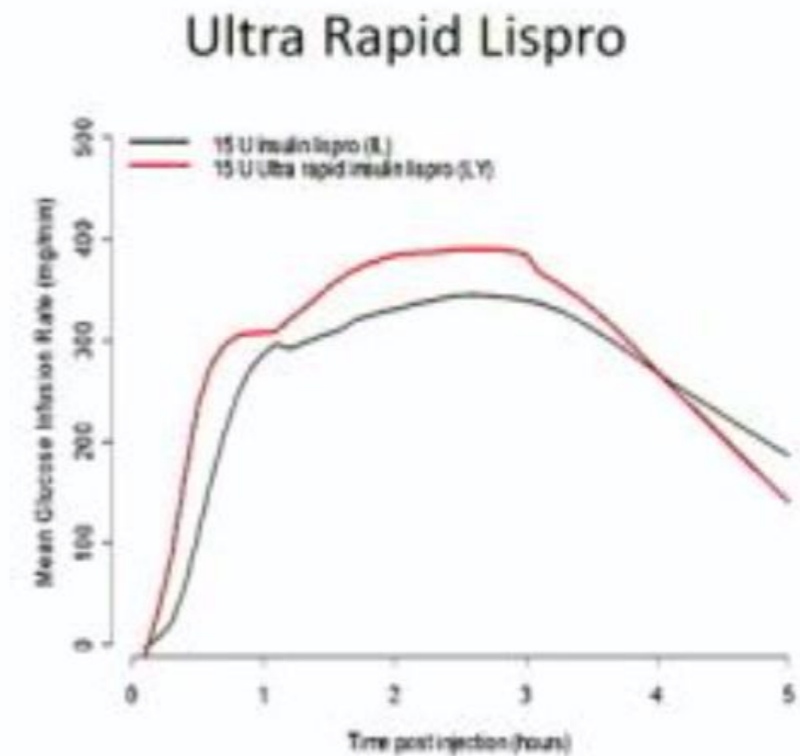
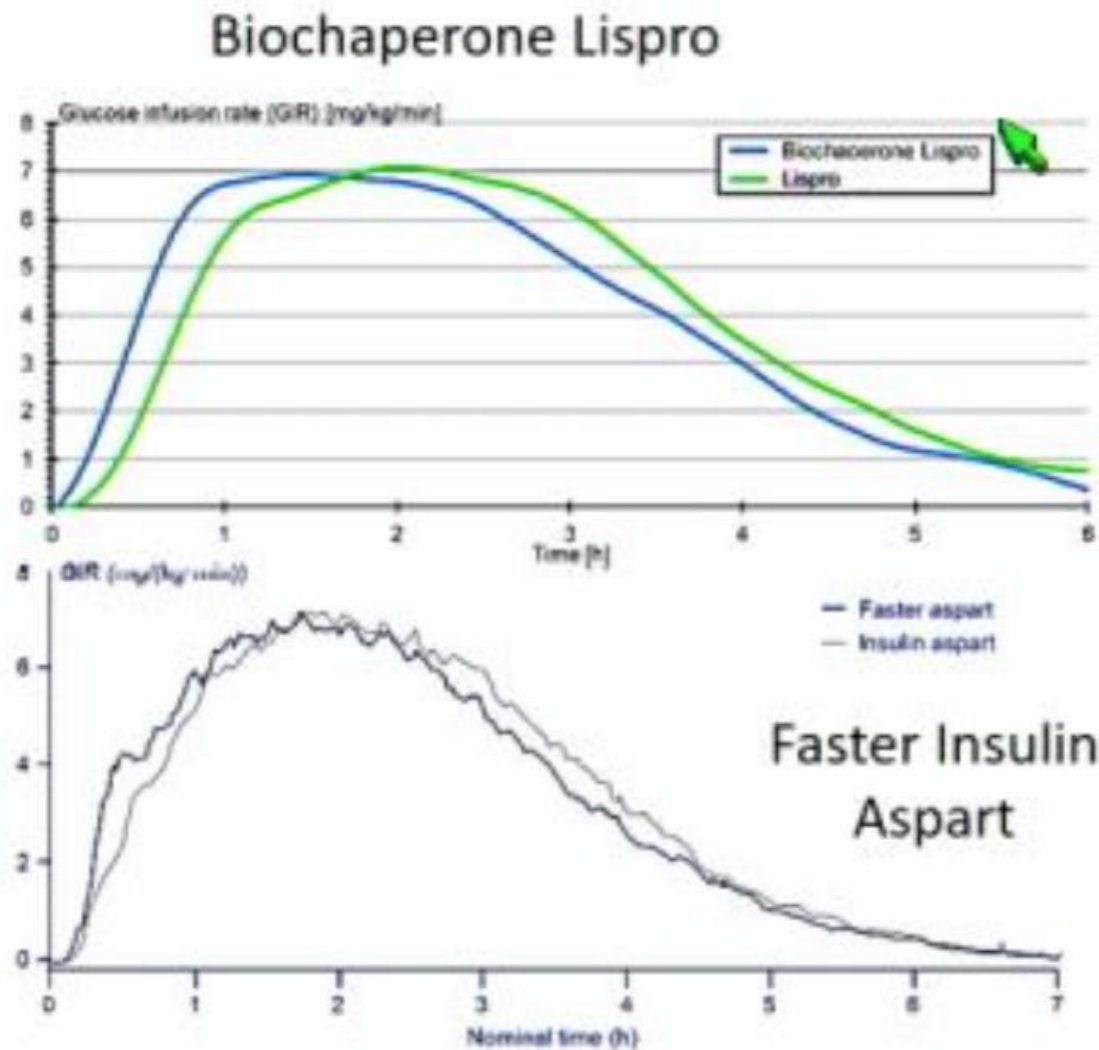
# Activity Profiles of Different Types of Insulin



# Faster Analogue Insulins

Biochaperone Lispro	Ultra-Rapid Lispro	Faster Acting Aspart
 <p>Insulin lispro</p>	 <p>Insulin lispro</p>	 <p>Insulin aspart</p>
 <p>Biochaperone 222 ⇨ faster hexamer dissociation</p>	 <p>Treprostinil ⇨ local vasodilation</p>	 <p>Niacinamid ⇨ faster hexamer dissociation</p>
 <p>Citrate ⇨ higher vascular permeability</p>	 <p>Citrate ⇨ higher vascular permeability</p>	 <p>L-arginine ⇨ stabilization</p>

# Faster Acting Analogue Insulins vs Rapid Acting Insulins



Anderson G et al. Diabetes Obes Metab 2018; 1-6. <https://doi.org/10.1111/dom.13442>

, Leohr J et al. Diabetes 2017;66 (suppl. 1):A253, Heise T et al. Clin Pharmacokinet 2017; 56:551-559

# Short Acting (Human) Insulin

- **Regular Insulins**
  - Humulin R
  - Novolin R
- **Onset: 30-60 min.**
- **Peak: 2-4hr.**
- **Duration: 5-8hr.**
- **Delivery: Vial/syringe**
- **Dose 30 min prior to meal ideally**

# Rapid Acting (Analog) Insulin

- **Brands:** Apidra, Humalog, Novolog, Admelog
- **Should NOT** dose 30min prior to meal due to onset
- **Onset:** 10-30 min.
- **Peak:** 30 min. to 3 hr.
- **Duration:** 3-5 hr
- **Delivery:** vial/syringe, pen, pump

# Intermediate-Acting Insulin

- **NPH**
  - Humulin N
  - Novolin N
- **Zinc reduces the solubility of insulin so insulin lasts longer in the body**
- **Onset: 1-3hr.**
- **Peak: 6-12 hr.**
- **Duration: 18-26 hr.**
- **Delivery: Vial/syringe, pen**
- **Taken daily or BID**
- **Variability dependent on how well mixed.**

# Long-Acting Insulin

- **Basaglar, Lantus, Levemir, Tresiba, Toujeo**
- **Onset: 1-2 hr.**
- **Peak: basically peakless**
- **Duration: 20-26 hr.**
- **Delivery**
  - **Lantus, Levemir available in vial or pen**
  - **Tresiba & Toujeo do not come in vial**



# Basaglar

- **Long-acting insulin (Glargine)**
- **Available as U100/ml**
- **FDA approval for 6 yo and older**
- **Available in pen only.**

# Tresiba

- **Greater flexibility of dosing is selling point**
- **Not approved for kids <1 yo**
- **Comes in 100units/ml and 200 units/ml pens**

# Toujeo

- **Concentrated glargine insulin 300 units/ml**
- **Once daily dosing, at approximately same time each day**
- **Not recommended for children**

# Pre-Mixed Insulin

## (Biphasic Insulins)

- **Brands**
  - **NPH with Regular**
    - **HumuLIN 70/30 (Pen)**
    - **NovoLIN 70/30 (Pen)**
  - **Lispro protamine with Lispro**
    - **Humalog Mix 75/25 (Pen)**
    - **Humalog Mix 50/50 (Pen)**
  - **Aspart protamine with Aspart**
    - **NovoLOG 70/30 (Pen)**

# Humalog U200

- **Rapid-Acting Insulin**
- **Do NOT draw from pen with a syringe**
- **Designed to use less pens/month**
- **Do NOT use in an insulin pump**

# Humulin R U-500

- **Not used in children**
- **Not used in insulin pump**
- **Extremely concentrated**
- **Use caution when drawing/dialing up dose; always verify dose with another licensed person.**

# Storage

- Store unopened insulin in fridge
- Do not freeze insulin
- Store away from direct sunlight and heat
- Once seal punctured, leave out at room temp



# Insulin Expiration

Insulin	Opened
Rapid Acting Insulins : Apidra, Humalog, Novolog	28 days
Short Acting Insulins: HumuLIN R	28 days
NovoLIN R	42 days
Intermediate-Acting Insulins: HumuLIN N	28 days (PEN 14 days)
NovoLIN N	42 days (PEN 14 days)
Pre-Mixed Insulins: HumuLIN 70/30, HumaLOG 75/25	28 days (Pen 10 days)
HumaLOG 50/50, NovoLOG 70/30	28 days (PEN 10 days) 28 days (PEN 14 days)
Long-Acting Insulins: Basaglar, Lantus	28 days
Levemir	42 days
Toujeo	28 days
Tresiba	56 days



# Insulin Regimens

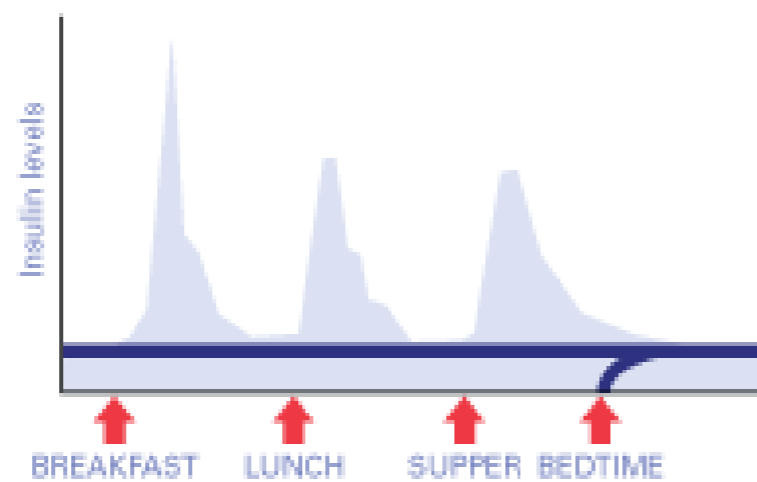
- **Basal-bolus / multiple daily injections insulin therapy**
  - **With Carb counting**
  - **Fixed dosing with exchange diet**
- **Split Mixed insulin therapy**
- **Pre-mixed**

# Basal/Bolus Regimen

- **Uses multiple daily injections of insulin**
- **Needs fingerstick glucose prior to meals**
- **Ideally uses carb counting, but can do a fixed dose at meals plus correction.**

# Basal/Bolus Regimen

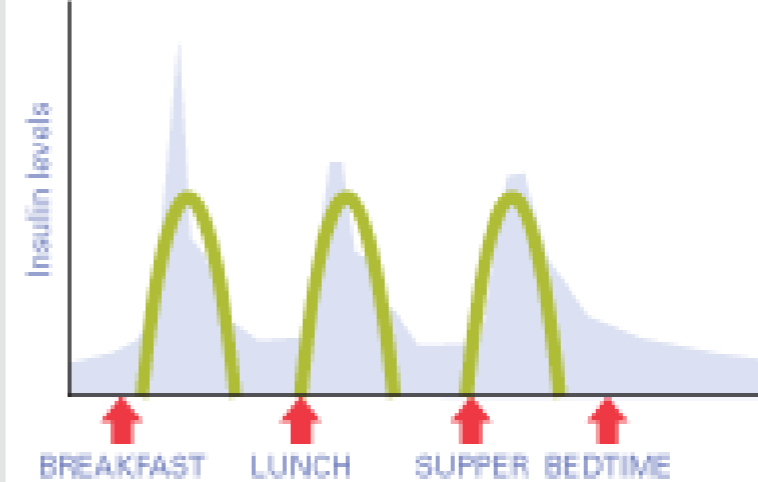
## **BASAL (Lantus®)** **LONG-ACTING INSULIN**



Onset  
**2-4 hours**

Duration  
**24 hours**

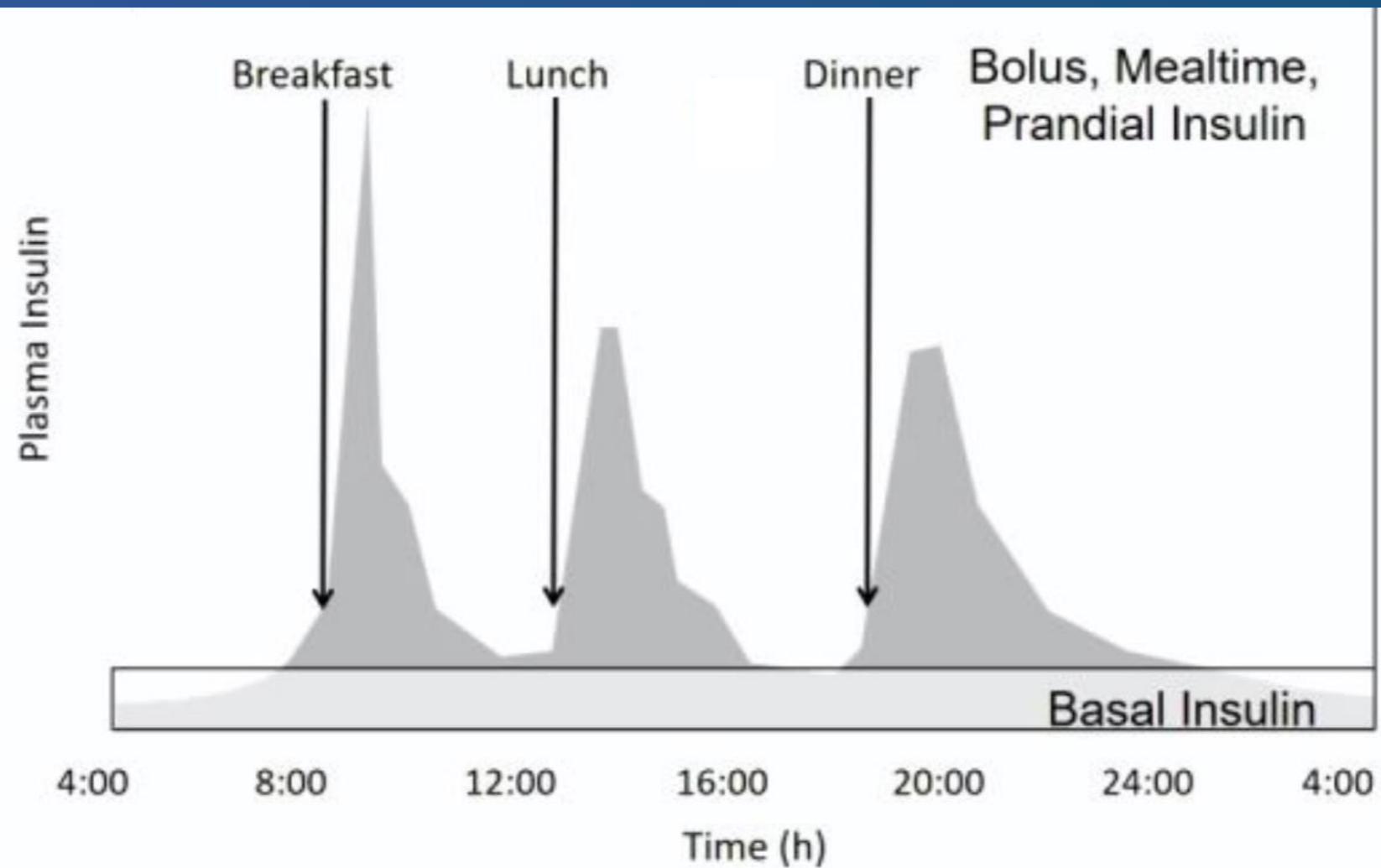
## **PRANDIAL** **RAPID-ACTING INSULIN**



Onset  
**~5 minutes**

Duration  
**4-5 hours**

# Physiology of Insulin Secretion

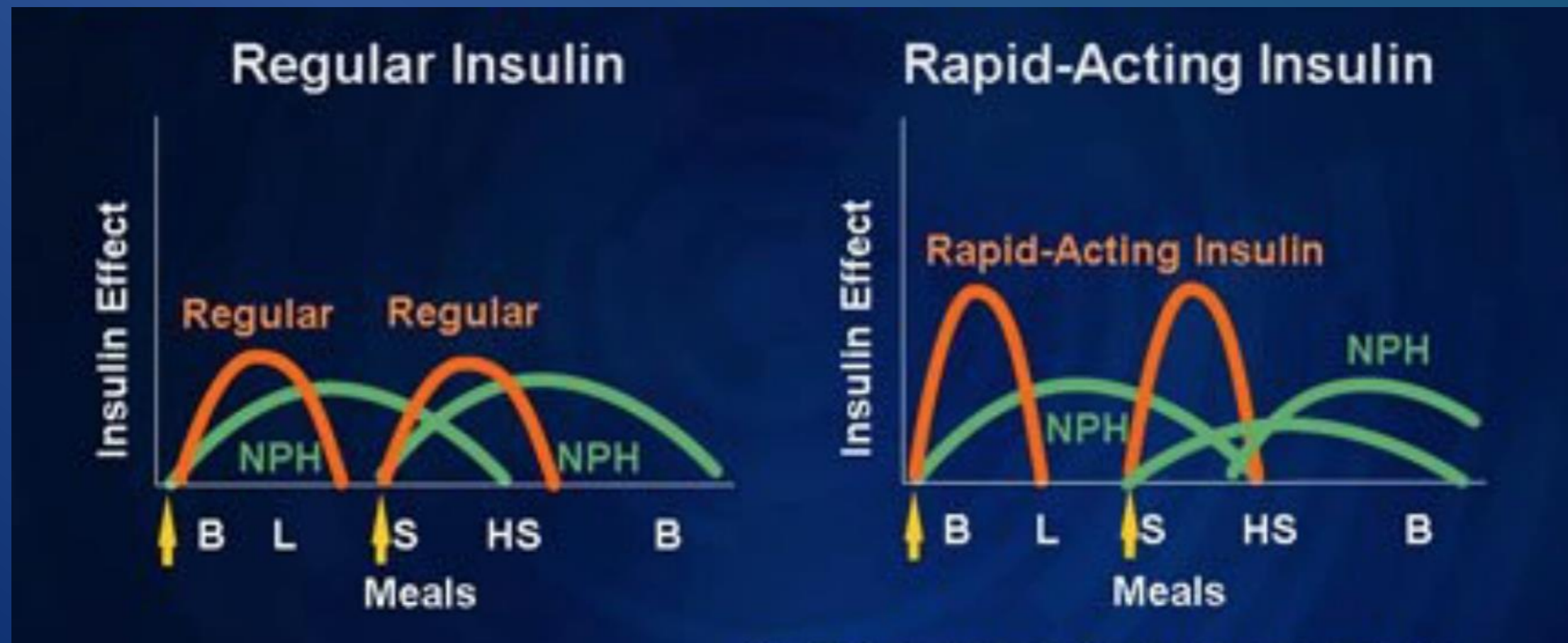


Kruszynka Y et al. *Diabetologia* 1987;30:16-21

# Split Mixed insulin Regimen

- **An older and now less commonly used regimen**
- **2-injection strategy: Intermediate + Regular/Rapid analog**
- **uses variable amount of intermediate insulin mixed by the patient with a variable amount of regular insulin or a rapid analog**

# Split Mixed insulin



# Split Mixed insulin

- **Pros:**

- **similar glycemic responses vs basal/bolus**
- **convenience in younger school aged patients who need adults to inject for them**

- **Cons:**

- **strict adherence to carb exchange diet**
- **lack of flexibility in eating/exercise patterns**
- **risk of nighttime hypoglycemia**

# Pre-Mixed Insulin

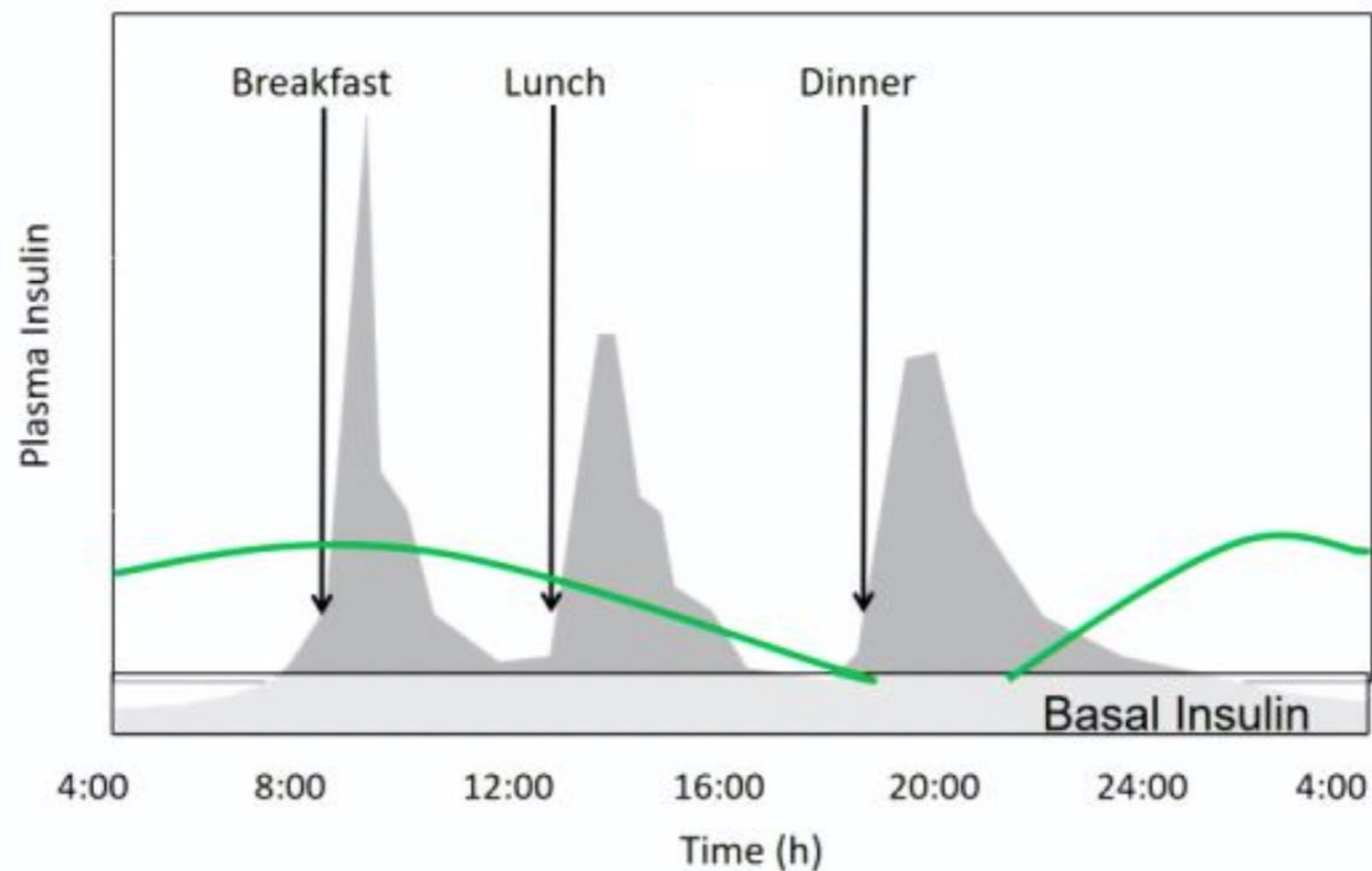
## (Biphasic Insulins)

- **Pros:**
  - developed to decrease number of injections/day
  - Alternative for those that cannot draw & mix insulin from vial in beginning
  - May be considered for noncompliant patients ?
- **Cons:**
  - must be re-suspended before injection...must be mixed
  - Absorption is affected by re-suspension; can cause great variability
  - Neither component can be adjusted separately.



# Physiology of Insulin Secretion

Hypoglycemia is a Consequence of Non-physiologic Basal Insulin Secretion: NPH



Kruszynka Y et al. *Diabetologia* 1987;30:16-21

# Glucose Patterns

- **Spot high or low patterns in your blood glucose results**
- **Try to find the likely cause**
- **Plan how to address the cause**
- **Monitor the effects of the changes made**
- **REPEAT**

# Spotting Patterns

- Go through results in diary
- Use a data management program that comes with your meter
- Go through the results log on your meter
- Use a meter with pattern identification

**Blood Glucose RECORD**

Name \_\_\_\_\_  
Phone Number \_\_\_\_\_

Week of \_\_\_\_\_

Instructions: Talk with your doctor

		Breakfast	Snack	Lunch
Monday	Time			
	Glucose			
	Carbs			
	Insulin			
	Other Medicine Carb:Insulin Ratio			
Tuesday	Time			
	Glucose			
	Carbs			
	Insulin			
	Other Medicine Carb:Insulin Ratio			

# Pattern identification

- **High or lows at similar times of day - e.g. regular high levels before lunch**
- **High or low levels through the day**
- **Highs or lows after particular events - e.g. lows following exercise**

# Causes of glucose variability

Causes of highs	Causes of lows
<b>Underestimating carbs</b>	<b>Overestimating carbs</b>
<b>Going through illness</b>	<b>Taking part in exercise earlier in the day</b>
<b>Overtreating lows</b>	<b>Overcorrecting highs</b>

# Making adjustments

- Adjustments depend on suspected cause.
- Changes could include taking more exercise, taking more or less carbohydrate or ensuring meals aren't skipped or delayed.
- In some cases, the action to take will be to increase or decrease insulin doses.
  - gradually to minimize the risk of hypoglycemia
- Seek help

# Evaluate

- **monitor the effect of the change**
- **if the change does not have the desired effect**
  - **re-evaluate the possible cause**
  - **choose an alternative or additional method to resolve the problem**

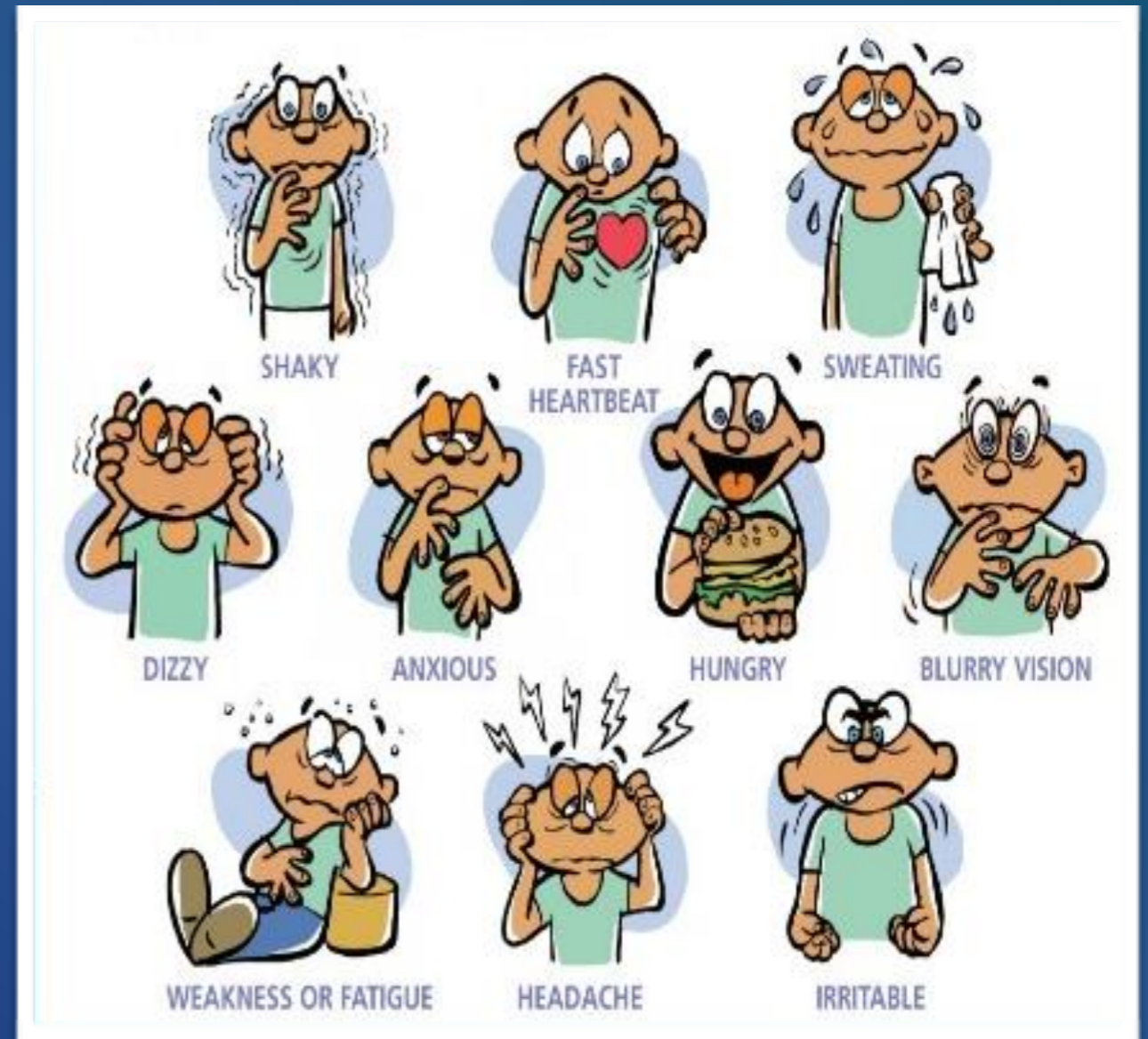
# Basics of Insulin Adjustment

- **Low blood sugar/Insulin Reaction**
  - **explained**
  - **unexplained**



# Insulin reaction/Hypoglycemia

- Types
  - Mild
  - Moderate
  - Severe
- Possible Causes:
  - Too much insulin
  - Not enough carbohydrates
  - Gave wrong insulin
  - Increased activity



# Basics of Insulin Adjustment

- **High in the morning**
  - **adjust long-acting insulin if it is taken at bedtime.**
  - **If taken in am, and high at bedtime, consider adjusting long-acting insulin.**

# Basics of Insulin Adjustment

- **High at a meal-time**
  - **adjust rapid-acting insulin at prior meal.**  
**(Change the insulin to carb ratio)**
- **If blood sugar never returns to target, consider adjusting sensitivity factor/sliding scale.**

# Example #1

Breakfast	Mid Morning	Lunch	Mid Afternoon	Supper	Bedtime
106		136		65	165
111		99		71	132
99		122		58	199
119		89		63	162
130		132		45	404
158		141		74	149
87		131		89	141
99		106		59	151
136		142		62	207

# Example #2

Breakfast	Mid Morning	Lunch	Mid Afternoon	Supper	Evening	Bedtime
249		97		112		300
288		104		122		278
197		121		119		269
301		133		128		199
189		116		99		243
232		140		103		305
267		151		64		452
199		124		108		189
313		104		119		234

# Example #3

Breakfast	Mid Morning	Lunch	Mid Afternoon	Supper	Evening	Bedtime
131		126	98	211		167
127		145	103	221		154
129		138	112	243		149
99		117	80	285		137
118		120	78	305		142
130		121	82	432		189
107		130	81	232		167
126		145	92	305		160

# Example #4

Breakfast	Mid Morning	Lunch	Mid Afternoon	Supper	Bedtime
107		189		225	107
121		209		197	121
98		211		267	98
116		232		289	116
99		178		234	99
123		199		241	123
89		240		276	89
119		185		233	119
133		230		199	133

# Example #5

Breakfast	Mid Morning	Lunch	Mid Afternoon	Supper	Bedtime
107		64		118	112
121		55		120	115
98		62		144	120
116		60		160	94
99		100		115	99
123		120		180	84
89		130		112	130
119		58		94	160
133		66		96	74



# Example #6

Breakfast	Mid Morning	Lunch	Mid Afternoon	Supper	Evening	Bedtime
249		97		112		118
288		104		122		120
197		121		119		144
301		133		128		160
189		116		99		115
232		140		103		180
267		151		64		112
199		124		108		94
313		104		119		96

# Objectives

- Review physiology of insulin secretion
- Review types of insulin
- Learn individual insulin action
- Review different types of insulin therapy
- Learn how to recognize patterns in blood glucose readings
- Learn how to manage patterns in blood glucose readings

# Questions?

