Back to Basics: Best Practices in Insulin Use

Jay Shubrook, DO

June 14, 2019

Technical Instructions

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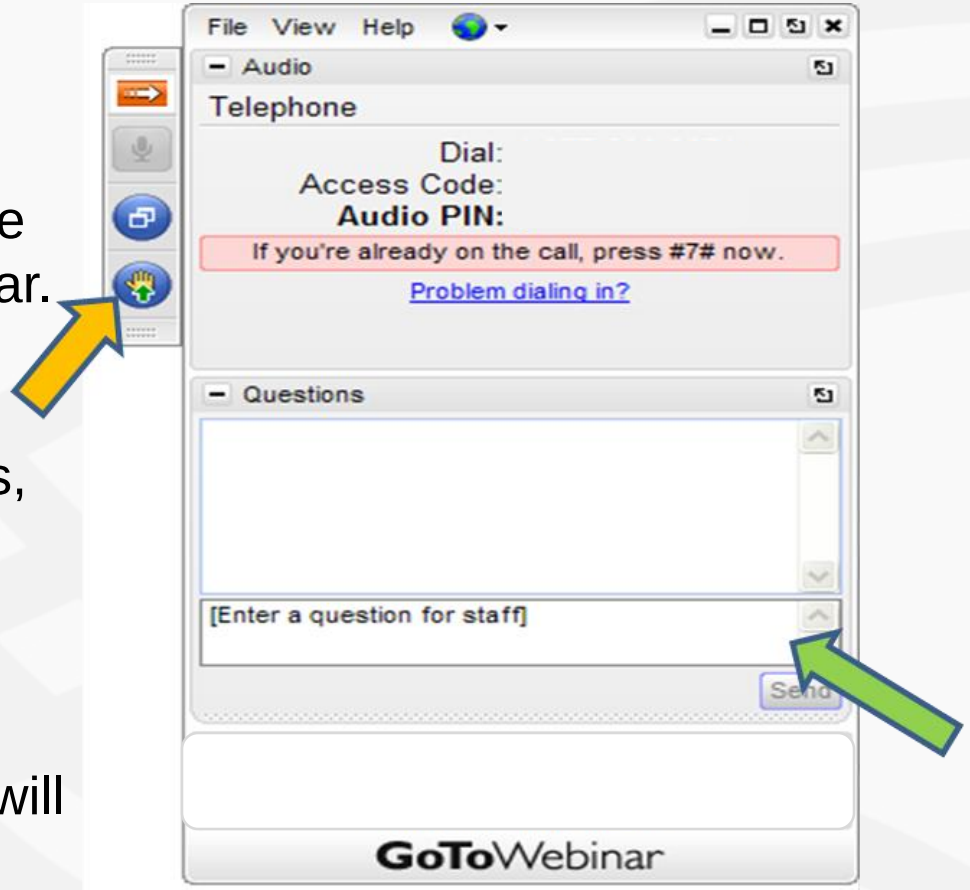

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About Me

- Jay Shubrook DO
- Professor and Diabetologist
- Director of Diabetes Services
- Touro University California
- Jay.shubrook@tu.edu

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Objectives

Review Physiologic Insulin Secretion

Use a Case-based Approach to Demonstrate Best Practices for Insulin Use in T2DM

Discuss Clinical Aspects of Pharmacologic Insulin Formulations

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History of Insulin Development

- Animal Insulin (1922)
- Human insulin (1980s)
- Analog insulin (1990s)
- Inhaled insulin (2006)
- Withdrawal inhaled insulin (2008)
- Inhaled insulin returns (2015)
- First ”follow on” insulin (2016)

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Insulin Biosynthesis

Produced by Pancreatic Beta cell

- Pro-insulin
  - C-peptide + insulin

Stored in pancreatic vesicles

Released in a pulsatile manner

- 6 minutes/40 minutes
- Release in day > night

Released in response to prandial hyperglycemia

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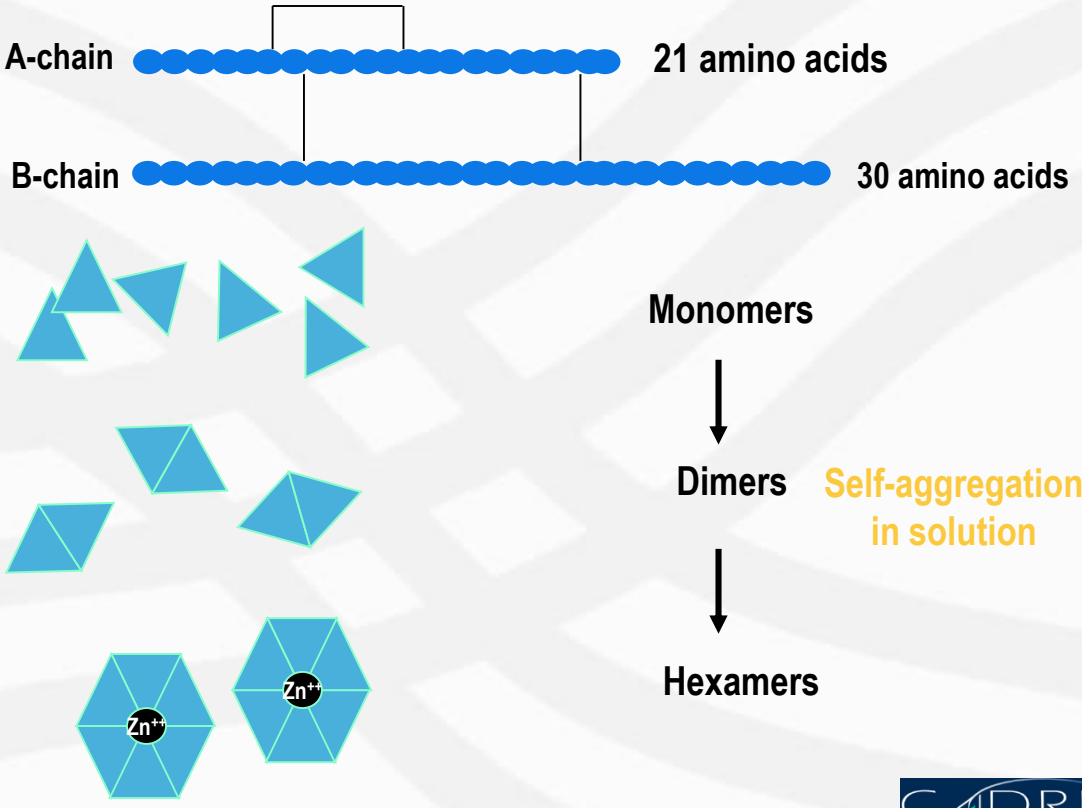
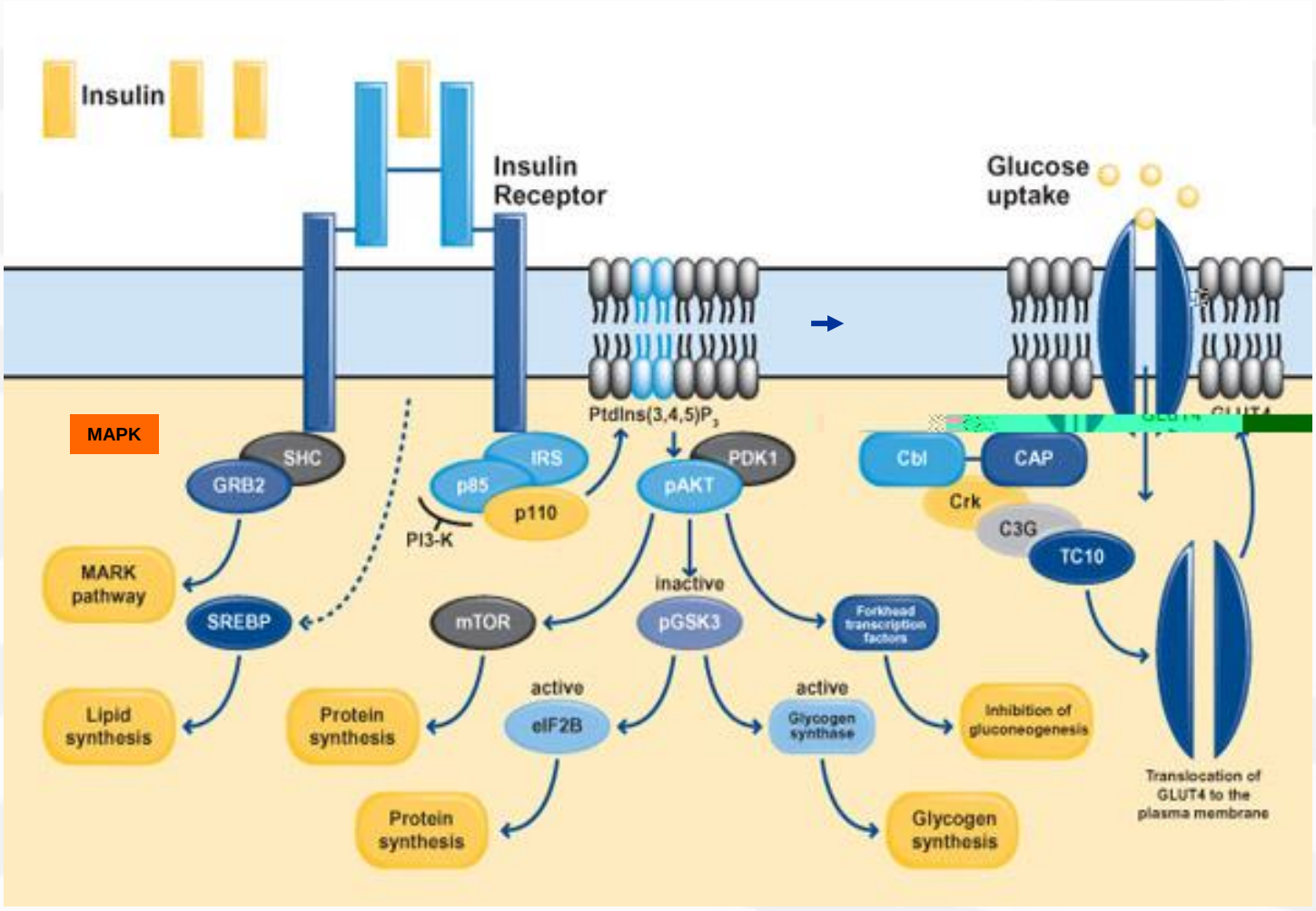
Human Insulin



Human Insulin



Insulin Signaling Pathways by C. Hooper http://www.abcam.com/index.html?pageconfig=resource&rid=10602&pid=7

Regulation of Fasting Glucose

Primary factor: Hepatic glucose production

Regulated by:

- Fasting plasma insulin
- Hepatic insulin sensitivity
- Fasting substrate availability

Fasting glucose is often the hardest glucose to change with lifestyle alone

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Glucose/Insulin Action

Basal insulin just enough to suppress hepatic glucose production to rate of uptake of glucose

- Insulin independent tissues
- Utilize glucose (brain, kidney)
- Insulin dependent tissue
- Utilize free fatty acids from TG

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Glucose/Insulin Action

Fed State-meals

- Glucose absorption –180 minutes
- Insulin will be released in response to hyperglycemia
  - 1st phase release rapid (approx. 10 minutes)
    - Hepatic glucose production suppressed
  - 2nd more sustained release
- 40 percent of glucose to liver
- Insulin sensitive tissues

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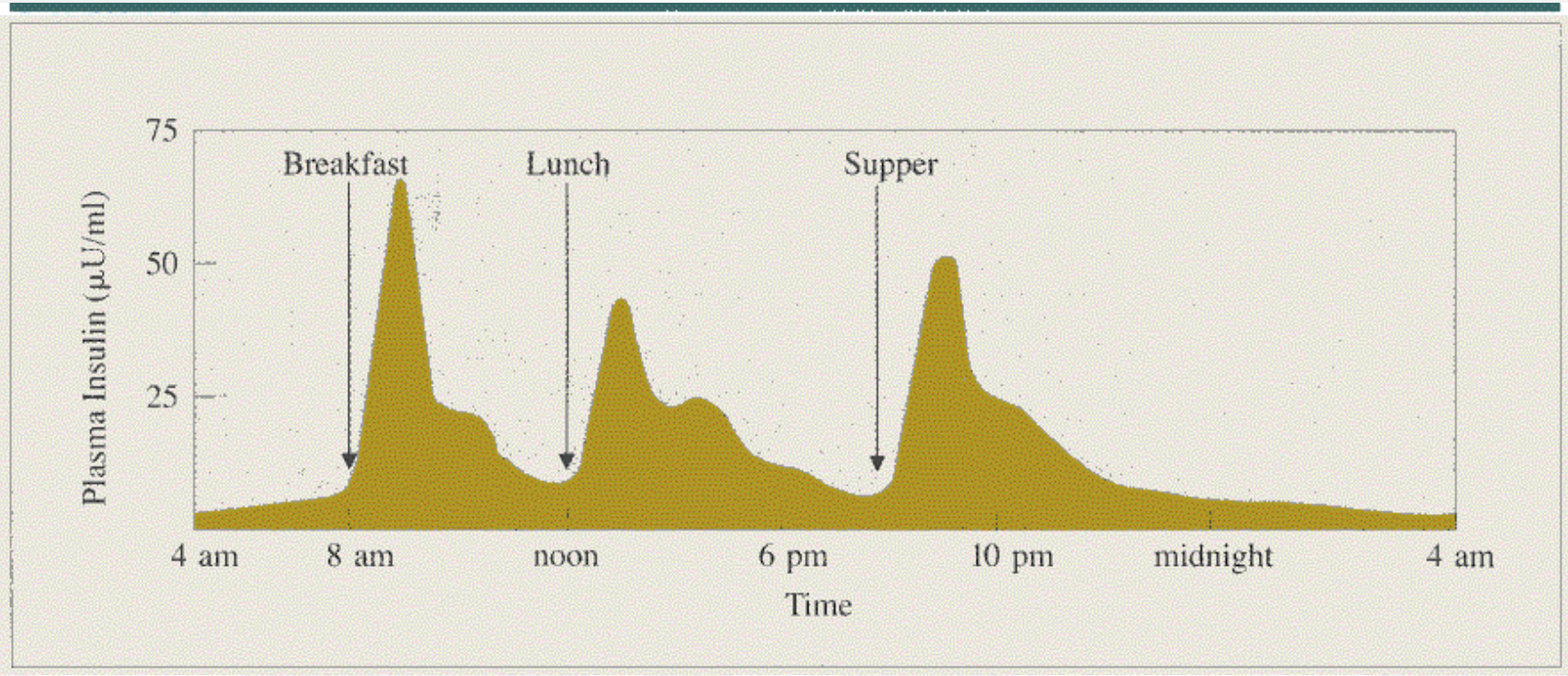
Physiologic Insulin Release



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Basal and Prandial Insulin

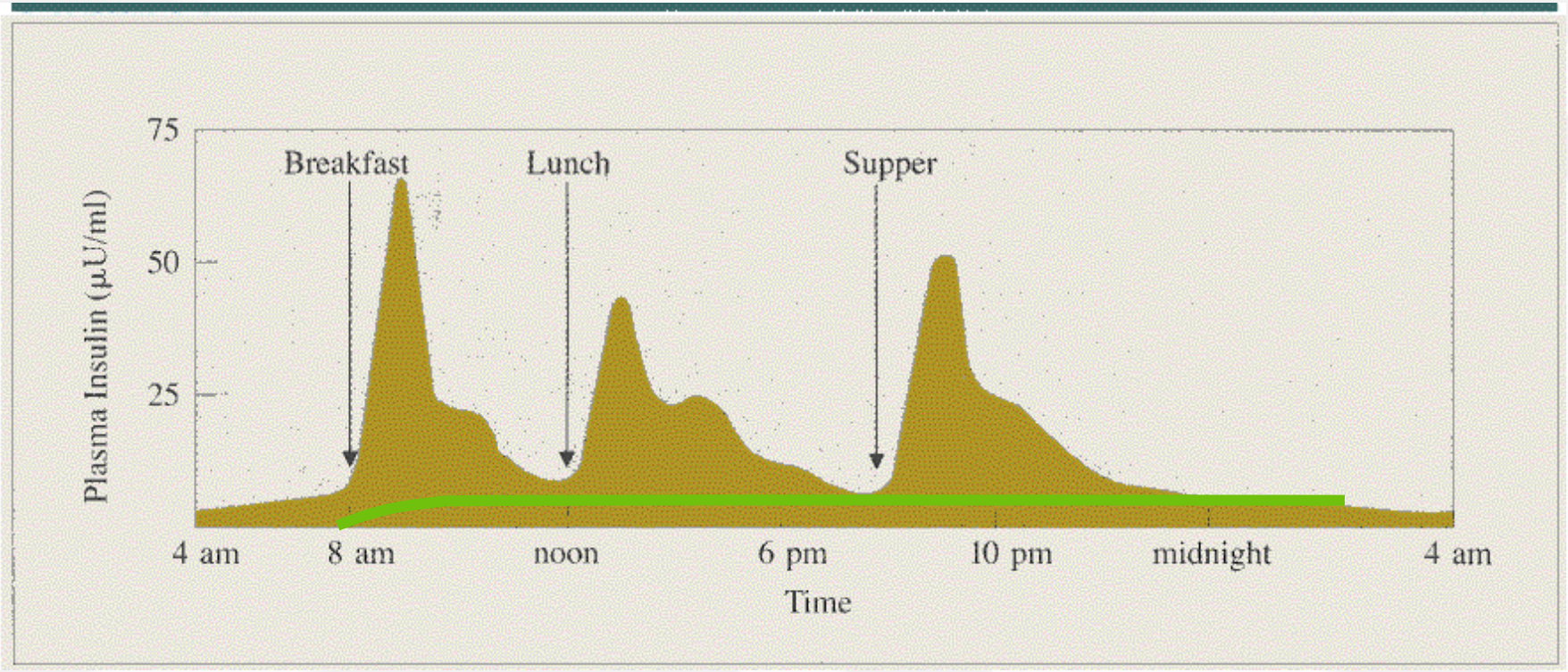
Basal insulin

- Required for resting metabolic needs
- Suppresses glucose production at night and between meals
- Stays relatively constant
- Usually is half of total daily insulin needs

Prandial insulin

- Limits/prevent post-prandial hyperglycemia
- Physiologic two phase release
  - First phase immediate and lasts 1-2 hours
  - Delayed slower to peak second phase
- Each meal about 10-20% of daily insulin needs

Physiologic Insulin Release



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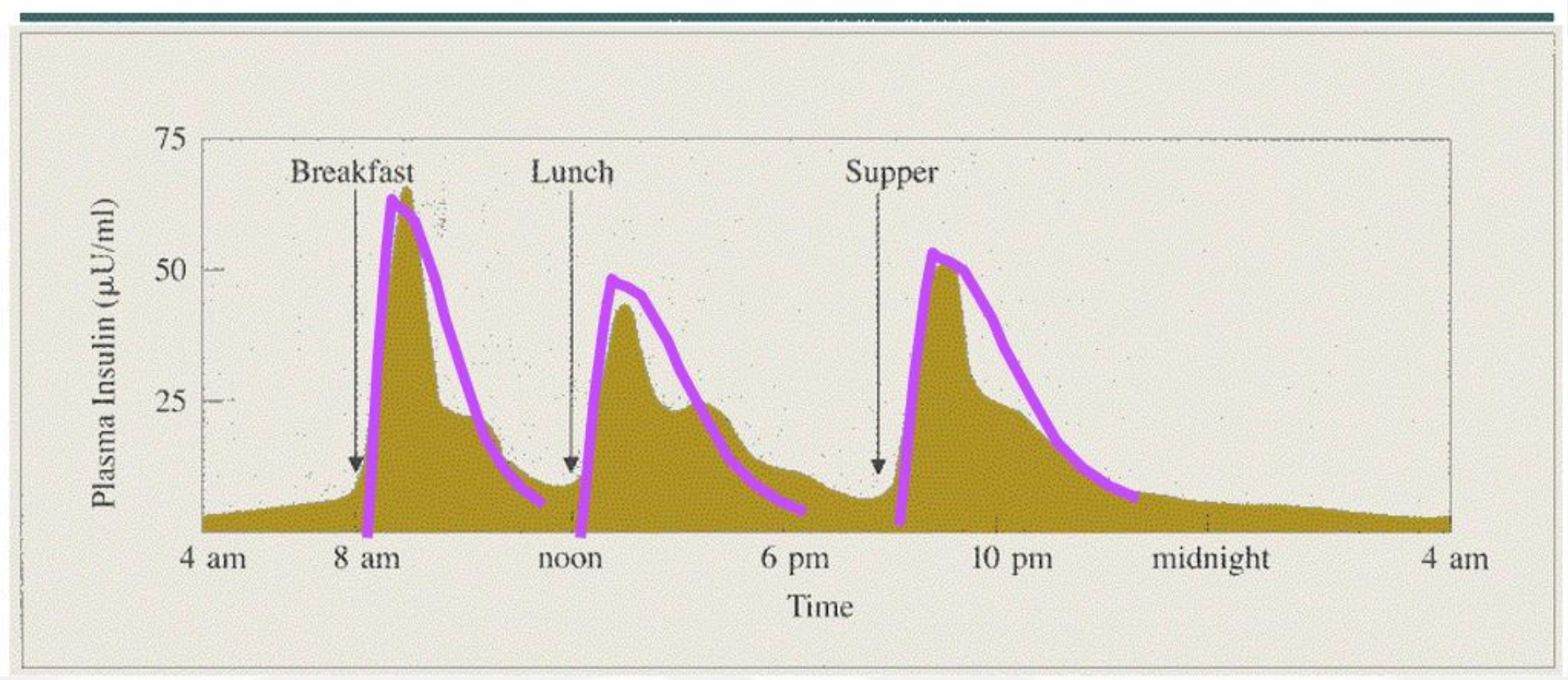
Physiologic Insulin Release



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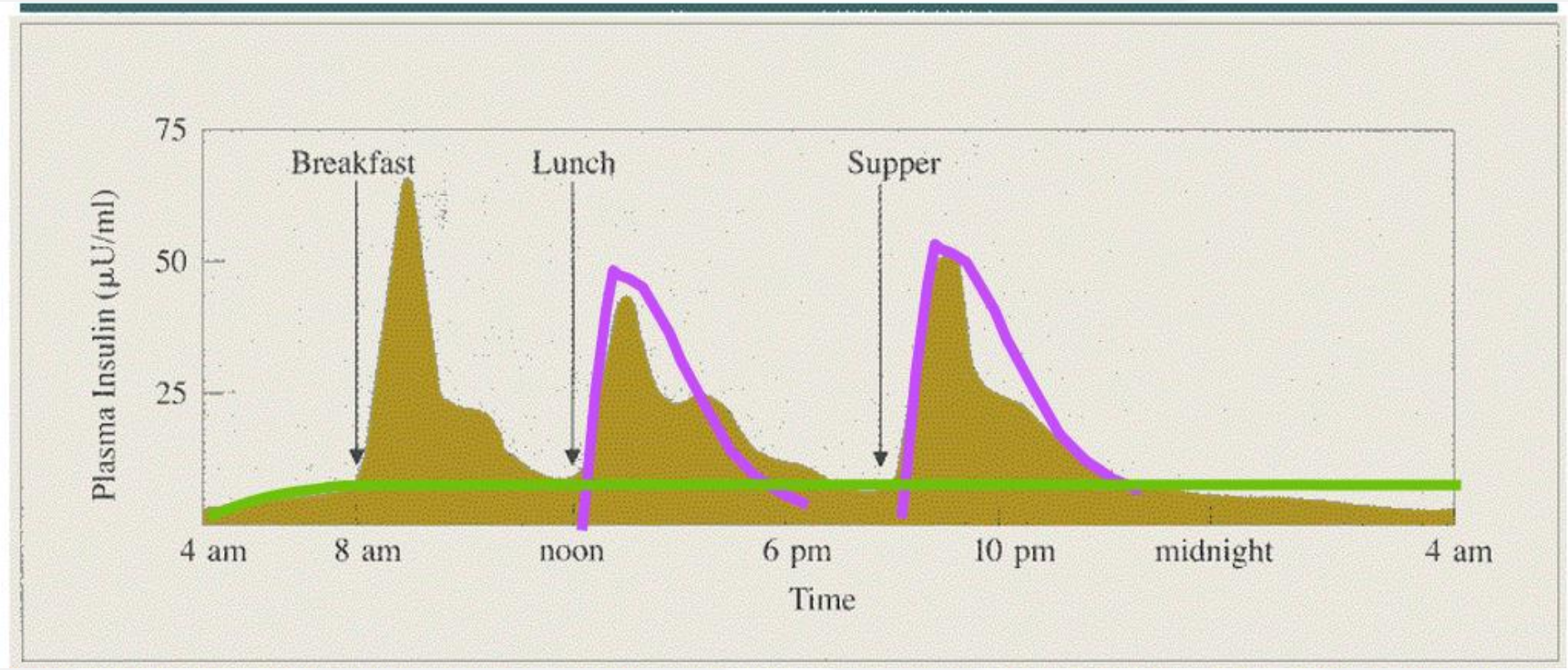
Physiologic Insulin Release



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Factors Affecting Absorption

- Injection site
- Depth of injection
- Exercise
- Body temperature
- Insulin type and dose
- Insulin mixture

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Case 1: Betty

Betty is a 48 year old female with 10 years of type 2 diabetes. She had GDM with each of her three pregnancies, and it never went away after the birth of her third child.

She has been to diabetes education (in pregnancy) and thinks she has a good idea of how to handle it, but it is hard as she is the main caregiver for her family.

She currently takes metformin 1000 mg bid, glipizide 10 mg bid. This has worked in the past, but she is having a hard time keeping up with managing her diabetes.

Case 1: Betty

Vitals: Bp 128/78, P 72 R 12 Wt 220 lbs (100 kg), BMI 34

Exam – truncal obesity, acanthosis

Otherwise normal exam

HbA1c 11.4%

Fasting glucose 248 mg/dl

Random SMBG mean 278 mg/dl

Total cholesterol 248, Trigs 220, LDL 168, HDL 36 (diabetic dyslipidemia)

Mild elevation of AST, ALT

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Case 1: Betty

What is the next treatment step?

A. send to diabetes education- restart lifestyle efforts

B. start basal insulin

C. start a GLP-1 Receptor Agonist

D. start a SGLT-2 Inhibitor

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Case 1: Betty

Key times to recommend diabetes self management education and support

- At diagnosis
- When new complicating factors arise
- When transitions of care occur
- Annually for health maintenance

Diabetes education 10 years ago and while pregnant may look different than now

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Case 1: Betty / Starting Insulin

Key times to start insulin

- New diagnosis and unsure what type of diabetes
- When patient is experiencing glucose toxicity
- Polys and /or weight loss
- Fasting above 200 mg/dl

How to start a basal insulin (weight based is best)

- Glargine/Detemir– 0.2 units/kg once daily
- NPH- 0.1 unit/kg twice daily at least 10 hours apart

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Case 1: Betty

Case 1: Insulin titration Question

Which of the following has been shown to be most effective?

A. Health care provider driven insulin titration

B. Insulin titration only at face to face appointments

C. Insulin titration completed by patient with scheduled plan

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Case 1: Betty

Best Practices for Basal insulin initiation and titration

- Weight based dosing
- First injection is supervised/office
- Lay out titration plan
- Encourage SMBG as a tool for titration
- Set a ceiling to stop titration
- Recheck at expected time at ceiling

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Case 2: Maria

Maria is a 58 year old female with 10 years of type 2 diabetes. She currently takes metformin 1000 mg bid, glipizide 10 mg bid and Glargine 80 units once daily evening.

She is frustrated. She checks her glucose every morning and it is usually pretty good– 60mg/dl- 140 mg/dl. She does get random high readings some mornings and she is not sure why.

If she misses lunch she gets real hungry and shaky.

Every time she comes to the doctor, her glucose is high and she cannot seem to get her A1c below 8.4 percent

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Case 2: Maria

Case 2: Question

What do you suggest as a next step?

A. Move glargine injection to the morning
B. Split the glargine injection to half morning and half evening
C. Change to NPH twice daily
D. Add meal time insulin
E. Add a different agent

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Case 2: Maria's Logs

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
	142	68	112	120	56	246
278 church event				248 2 pm office		

What do you notice on these logs?

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Case 2: Maria

Case 2: Problem List

- She is over-basalized (too much basal insulin)
  - She has first am glucose variability
  - She will drop low if she misses a meal
- She has inadequate coverage for her meals
- She is on 2 agents that could drop her low (SU and insulin)
- She is not using her SMBG as a tool to her direct therapy

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Case 2: Maria

Best Practices

Limit titration of basal insulin to:

- Glucose in am at goal (Regardless of HgA1c)
- Dose of 1 unit/kg/day (risks> benefits about 0.7 units/kg/day)
- If there is a big drop in the BE.AM. –bedtime to am glucose

Target glucose monitoring to provide you with needed info

- First am while titrating basal insulin
- Once at goal move glucose checks to other times in the day

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Case 3: Junior

Junior is a 64-year-old male who says his insulin is not working anymore. He has had diabetes for 15 years, and he has been on insulin for 5 years. He is taking glargine (U100) 60 units per day.

He said he really noticed a difference when he started this, but he thinks his body is rejecting it now. He also is between jobs, and he is worried about the cost of his insulin.

He also takes metformin 1000 mg bid, glipizide 10 mg bid, lisinopril HCT 20/25 daily and atorvastatin 40 mg daily.

He is recently divorced and has had to assume more self care.

His A1c is 10.2% and he is wanting to get back in control to have more time with his grandkids.

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Case 3: Junior

Question: Next Steps?

What would you do next to evaluate Junior?

A. Review timing of medication schedule
B. Send back to diabetes education
C. Review location and technique of insulin dosing
D. Remind him that diabetes is progressive

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Case 3: Junior

Technique

- He has been doing his own injections for the past year
- Has his favorite spots
- Has gotten really good at doing it quick
- Admits he hits hard spots
- Says he can sometimes smell the insulin

Case 3: Junior

Junior's Injection Sites: What Do You See?

Injection Sites

Case 3: Junior

Clinical Tip

- Ask patients if they have received education on injection technique
- Specifically have they taken an injection before
- Prescribers may suggest education
- Pharmacists can train or recommend supplies back to clinic for training

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Case 3: Junior

Question

- The cost of his medications are major concern for him. What can we do to reduce his medication expenses?
- Assuming you want to put him on a human insulin routine how would you do this?
- Regular insulin alone
- NPH alone
- NPH and R together
- Premixed- NPH and R

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Human Insulin

Converting to Human Insulin

- Typically unit per unit switch
- Must decide if only replacing basal or basal and meal time needs
- NPH and R
- Typically 2/3 NPH 1/3 R and typically 2/3 a.m. and 1/3 p.m.
- BUT many Americans eat more than 50% of their calories after 6 p.m.
  - So I do a 50/50 dosing schedule but will do 2/3 NPH and 1/3 R-this would need to be dose 30 minutes before breakfast and dinner

Insulin Landscape: Basal Insulin

	Branded names	Onset	Peak	Duration	Cost	Notes
NPH	**HumuLIN** **NovoLIN** **ReliON**	1-2 hours	4-8 hours	6-12 hours	$100 $100 $26	Pens,vials Pens.vials vials
Glargine (U100)	Lantus **Basaglar**	1-4 hours	No peak	24 hours	$180 $286 $150 ($390)	Vials Pens Pens only
Detemir	Levemir	1-4 hours	No peak	20-23 hours	$313 $465	Vials Pens
Glargine U300	Toujeo Toujeo Max	6 hours	No peak	24 hours	$466 $620	Pens only
Degludec U100, U200	Tresiba	1 hour	No peak	42 hours	$600	Pens only

Insulin Landscape: Meal-Time Insulin

	Branded names	Onset	Peak	Duration	Cost	Notes
Regular (R)	**HumuLIN** **NovoLIN** **ReliON**	30-45 minutes	2-5hours	4-8 hours	$100 $100 $26	Pens, vials Pens, vials Vials only
Aspart	NovoLOG	15 minutes	1-2 hours	2-4 hours	$300 $500	Vials pens
Glulisine	Apidra	15 minutes	1-2 hours	2-4 hours	$206 $445	vials
Lispro	Humalog **Admelog**	15 minutes	1-2 hours	2-4 hours	$180 $240 $239 $454	Vials Pens Vials Pens

Bold products are PHP preferred

Human Insulin

Converting to Human Insulin: Example

He was taking 60 units of glargine and glipizide 10 mg bid. (Stop both)

Start Relion brand 70/30

- 30 units before breakfast
- 30 units before dinner
- Ideally 10-12 hours from breakfast to dinner

Alternative

- 23 units of NPH before Breakfast
- 7 units of R before breakfast
- 20 units of NPH before dinner
- 10 units of R before dinner

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Questions

- What are the questions you have in relation to interfacing with your patients and other providers when it comes to insulin and type 2 diabetes management?
- What are you commonly seen problems?
- What are the biggest challenges your patients face?
- Any best practices you want to share with the group?

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Questions

Thanks so much

Jay.shubrook@tu.edu

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