Using Insulin

Designing safe and effective regimens

2014

Practical Management Skills

Jennifer Hone, MD, FACE

Jhone@AIHScorp.org

Outline

1. Diagnosis of Type 1 vs. 2:
2. What does control mean?
    1. A1c goals
3. How to do it?
    1. Phsyiologic insulin replacent
    2. Complications of Treatment
    3. Pattern Management
    4. Emerging tools

Diagnosis

When is diabetes Type 1 diabetes?

Case 1

- 55 yo F with 12 y h/o DM
- Always on insulin since Dx.
- 62 inches tall.
- 250#

Does she have Type 1 or 2?

What else do you want to know?

Case 1 continued

- Symptoms at time of diagnosis
- History of ketones or ketoacidosis
- Family history/ ethnicity
- Personal or FHx of autoimmunity
- History of how/ when weight gained
- History of GDM?
- Tests needed?

Type 1 vs Type 2

- ## Insulin Production
  - C-peptide WITH GLUCOSE

- ## Autoimmunity
  - GAD-65
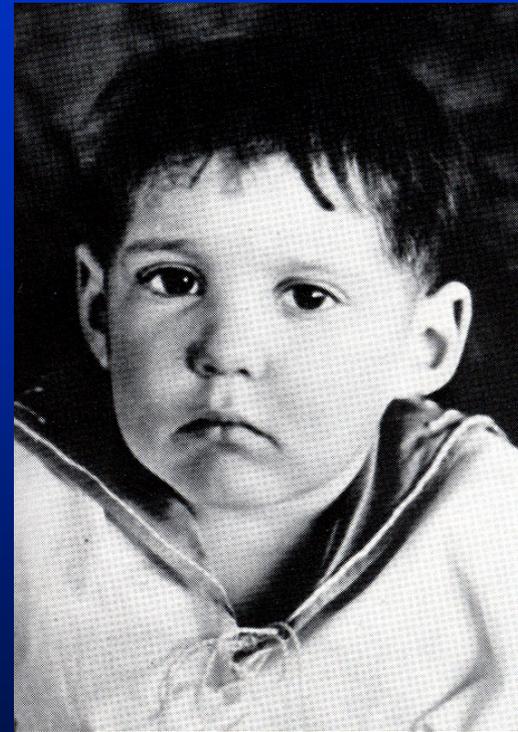 - Anti- IA-2
  - Anti-ICA antibodies

Treatment using insulin

GOALS,
AND
HOW TO GET THERE.

The Miracle of Insulin

Patient J.L., December 15, 1922

February 15, 1923

United Kingdom Prospective Diabetes Study (UKPDS)

Conventional Group

Intensive Group

A1C (%)

Years
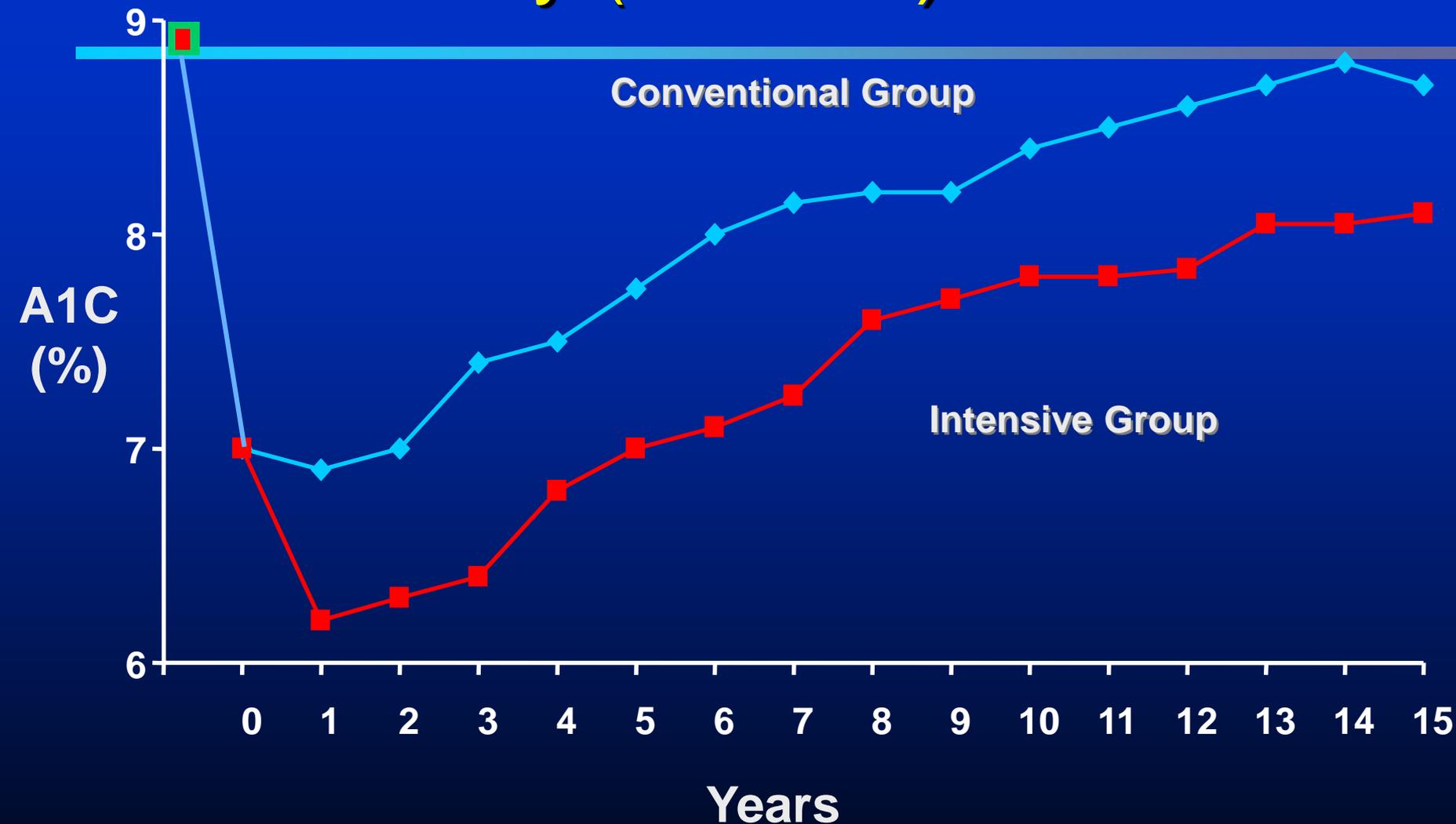
DCCT: the price of improved diabetic control – hypoglycaemia

severe hypoglycaemia

risk of retinopathy

Rate pf progression of retinopathy (per 100 patient years)

Rate of severe hypoglycaemia (per 100 patient years)

HbA$_{1c}$ (%)

Adapted from: N Engl J Med 1993;329:977–86
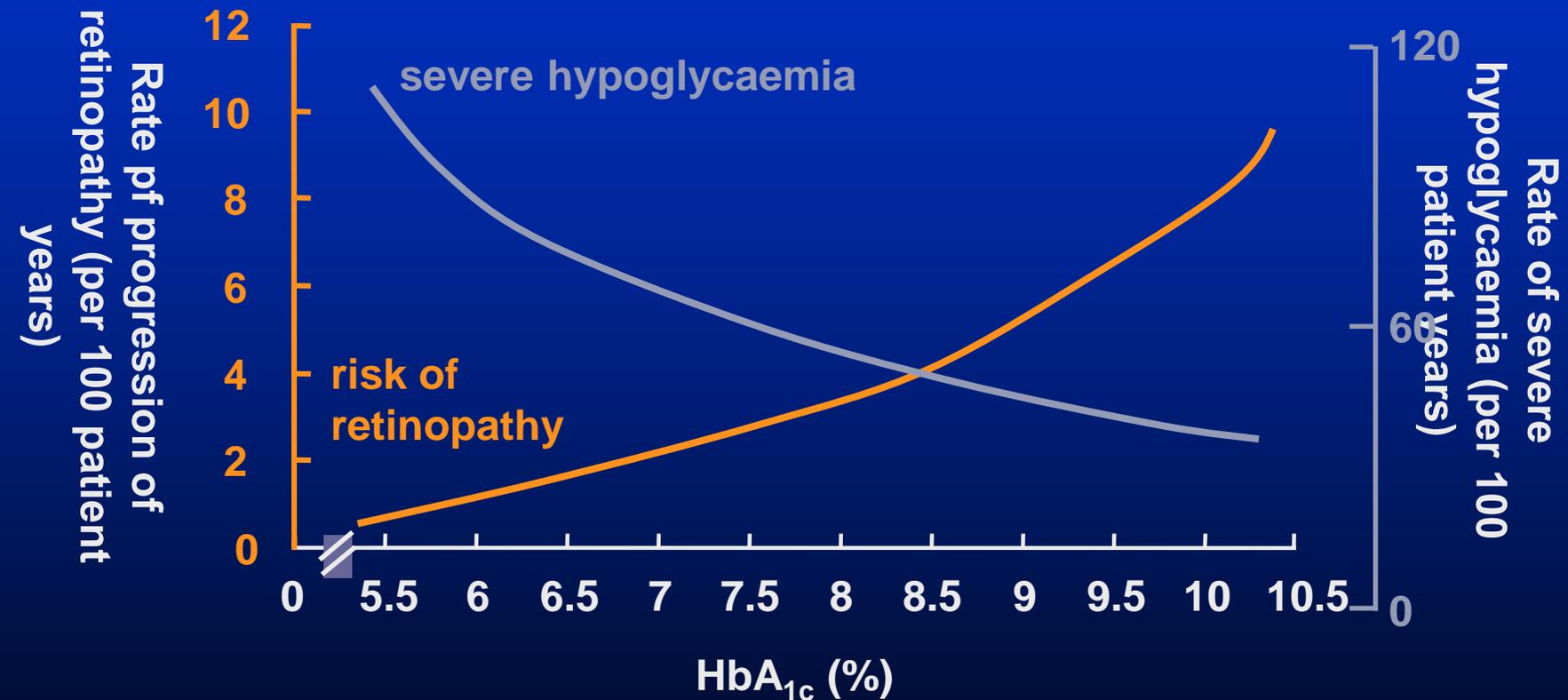
Consequences of Intensive Insulin Therapy

Intensive
Conventional

DCCT (Type 1)

Weight Gain
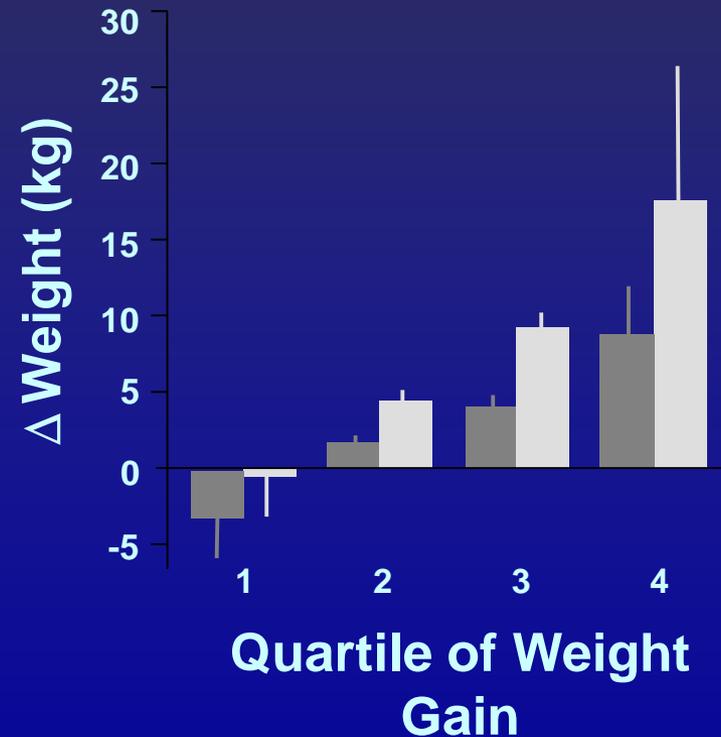
Does Variability matter separate from A1C?
i.e. Does HOW you get there matter?
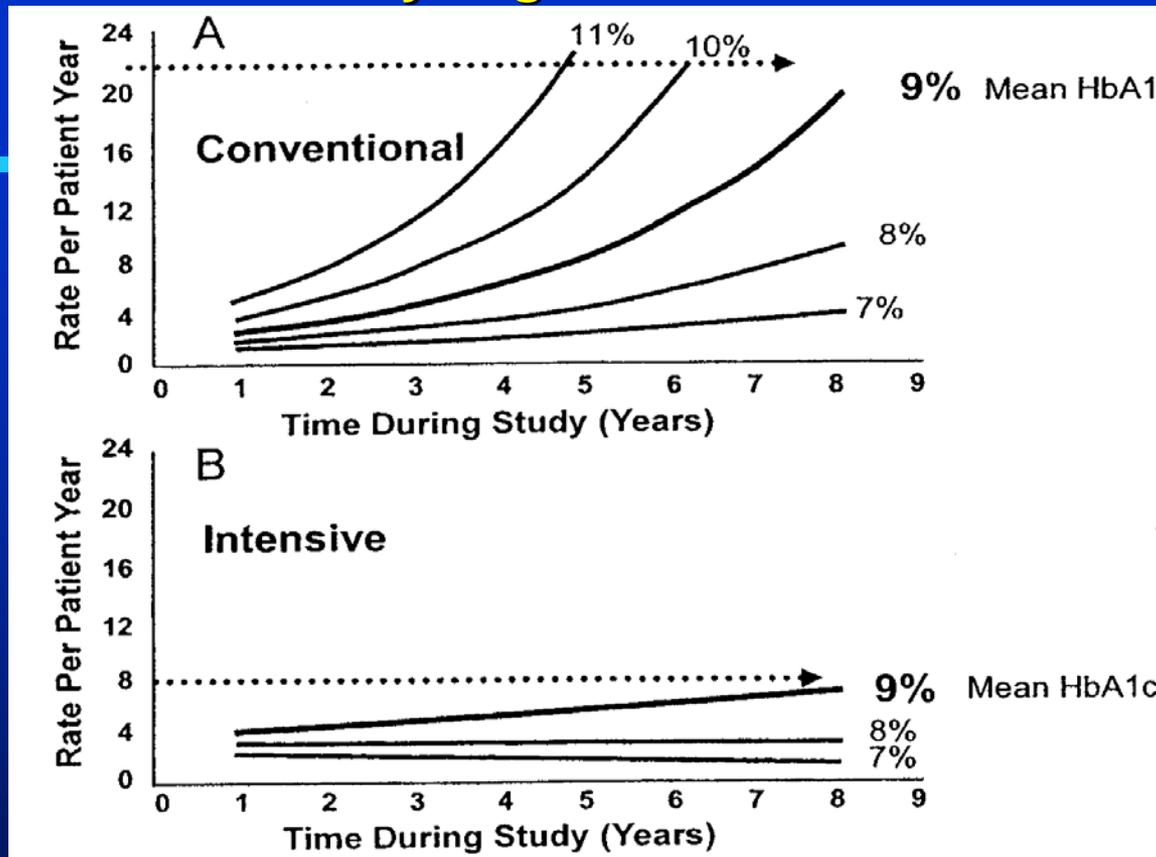
Fig. 1. Absolute risk of sustained retinopathy progression as a function of updated mean A1C (percentage) during the DCCTand the time of follow-up during the study (years), estimated from absolute (Poisson) regression models. (A) Conventional treatment group. (B) Intensive treatment group.

Reprinted with permission from DCCT Research Group (1995); n American Diabetes Association.

Goals must be individualized

- Glycemic target varies with:
  - Duration of DM
  - Age of person
  - Presence of CVD
- Assess readiness for change
- Tendency to hypoglycemia
- Co-morbid conditions
- Resources ($, and non-$!)

Approach to management of hyperglycemia:

	More stringent		Less stringent
Patient attitude and expected treatment efforts	Highly motivated, adherent, excellent self-care capacities		Less motivated, non-adherent, poor self-care capacities
Risks potentially associated with hypoglycemia, other adverse events	Low		High
Disease duration	Newly diagnosed		Long-standing
Life expectancy	Long		Short
Important comorbidities	Absent	Few / mild	Severe
Established vascular complications	Absent	Few / mild	Severe
Resources, support system	Readily available		Limited

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Treatment: Mimic Normal!

- What is normal??
  - Insulin
  - Glucose
  - Glucagon

Physiologic Insulin Secretion: 24-Hour Profile

Insulin (μU/mL)

50
25
0

Basal Insulin

Breakfast   Lunch   Dinner

Glucose (mg/dL)

150
100
50
0

Basal Glucose

7 8 9 10 11 12 1 2 3 4 5 6 7 8 9
A.M.   P.M.

Time of Day
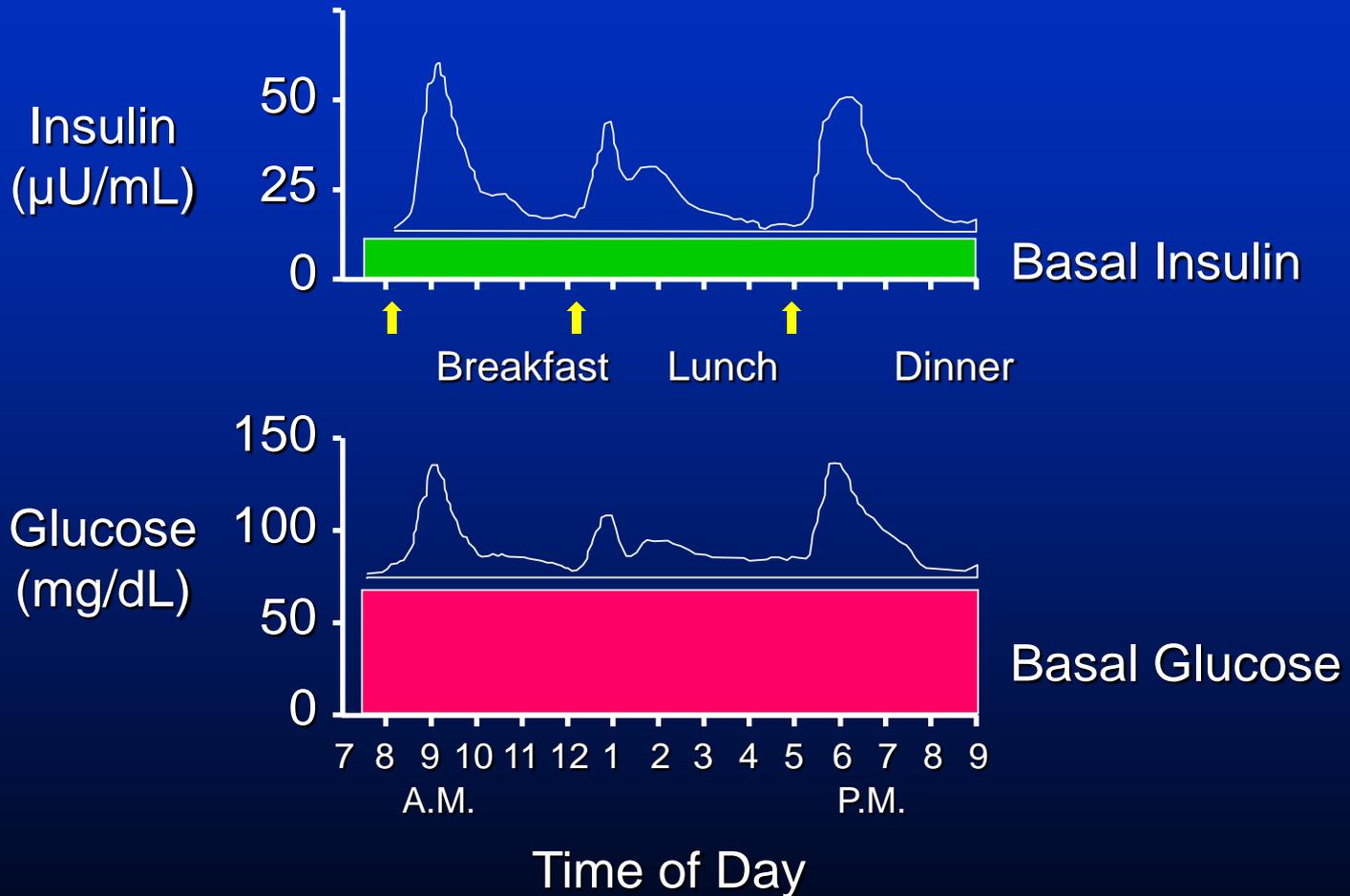
Glucagon is Reduced in Postprandial Period

Subjects Without Diabetes

CHO MEAL

Glucose — mg/dL
Insulin — μU/mL
Glucagon — pg/mL

Time (min): -60, 0, 60, 120, 180, 240

Data from Unger RH, et al. *N Engl J Med* 1971; 285:443-449
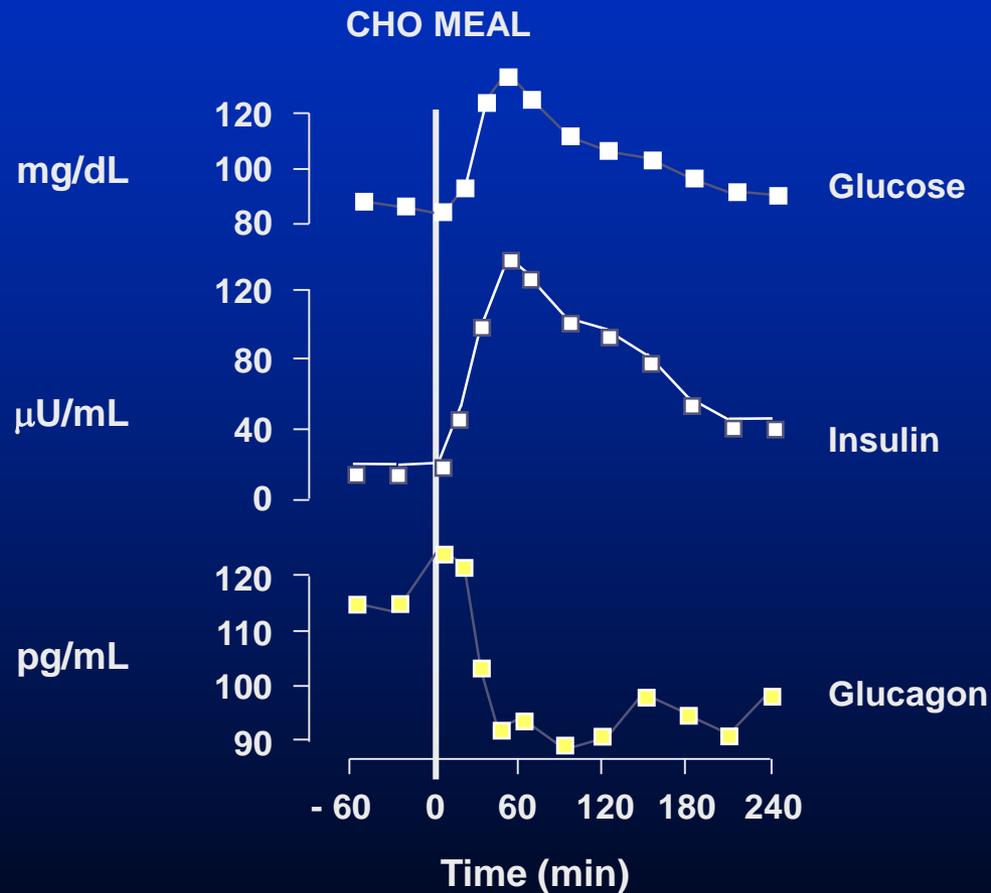
Insulin and Glucagon Responses Are Altered in Type 2 Diabetes

Carbohydrate Meal

Healthy Subjects
Type 2 Diabetes

Insulin (µU/mL)
120
60
0

Glucagon (pg/mL)
140
120
100

Meal

Glucose (mg/dL)
360
300
240
140
80

Time (min)
-60   0   60   120   180   240
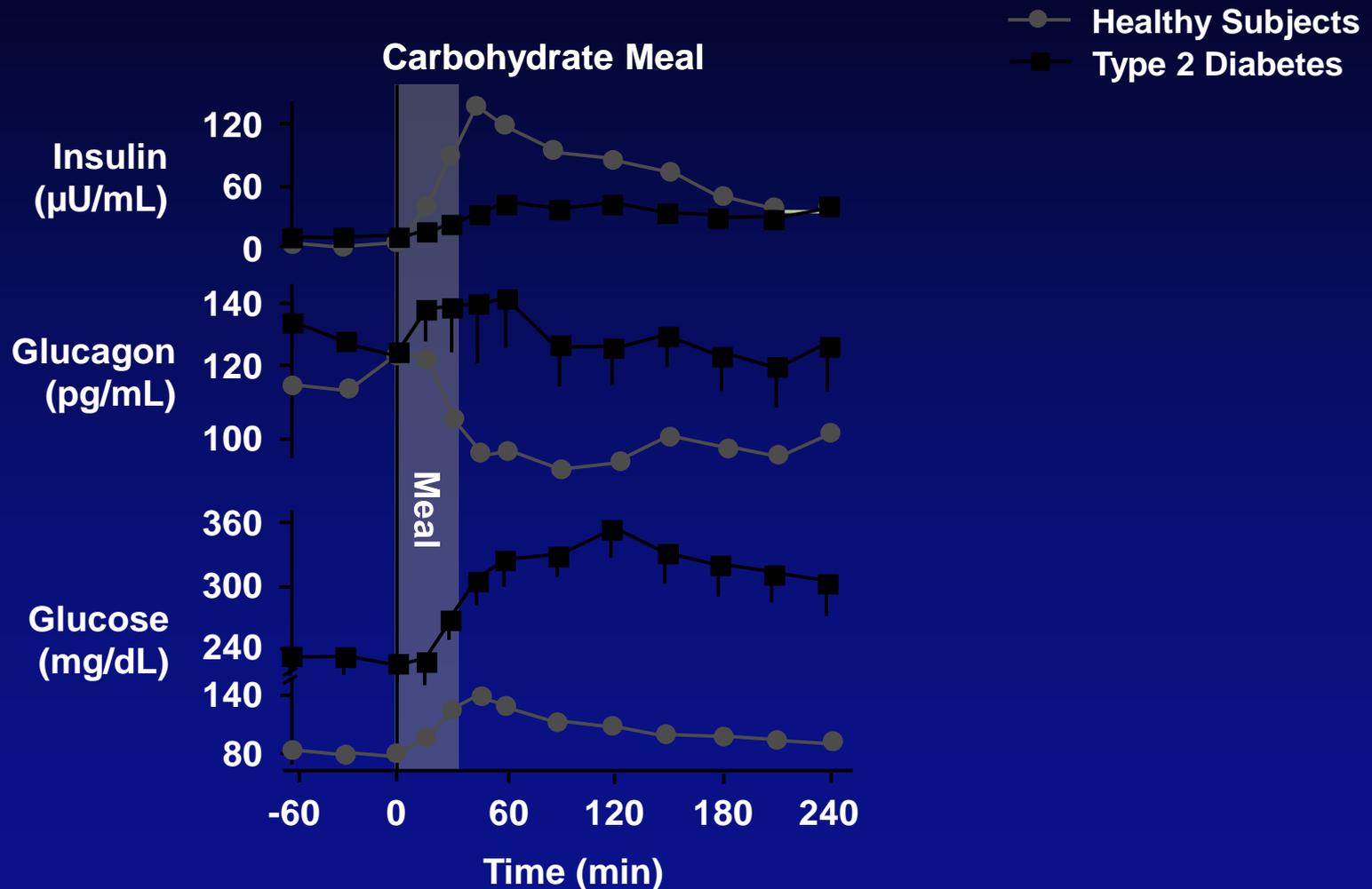
N = 26; Mean (SE)
Data from Müller WA, et al. *N Engl J Med.* 1970;283:109-115

INSULIN TACTICS
Comparison of Human Insulins and Analogues

Insulin Preparation	Onset of Action	Peak	Duration of Action
Lispro/ Aspart/ Apidra	15-30 minutes	0.5-1.5 hours	3-5 hours
Human Regular	30-60 minutes	2-4 hours	5-8 hours
Human NPH	1-3 hours	6-10 hours	12-20 hours
Detemir	1 hour	none	20-24 hours
Glargine	1 hour	none	~24 hours

The time course of action of any insulin may vary in different individuals, or at different times in the same individual. Because of this variation, time periods indicated here should be considered general guidelines only.

Biological Action of Insulin Rapid vs. Regular Insulin: Glucose Clamp Study in Healthy Subjects
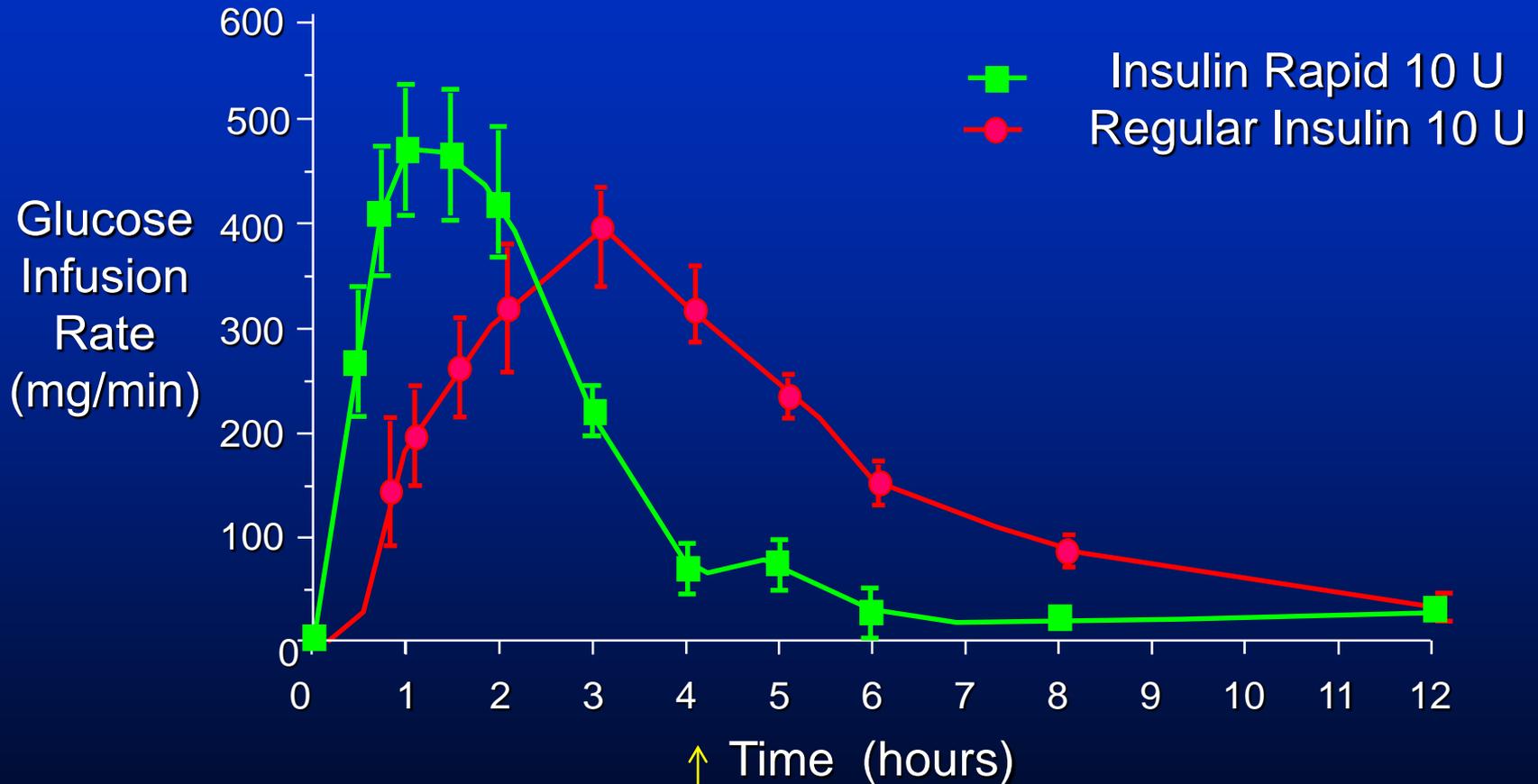
Data from Howey DC, et al. *Diabetes*. 1994;43:396-402.

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Glargine or Detemir Once Daily, Premeal Insulin Rapid
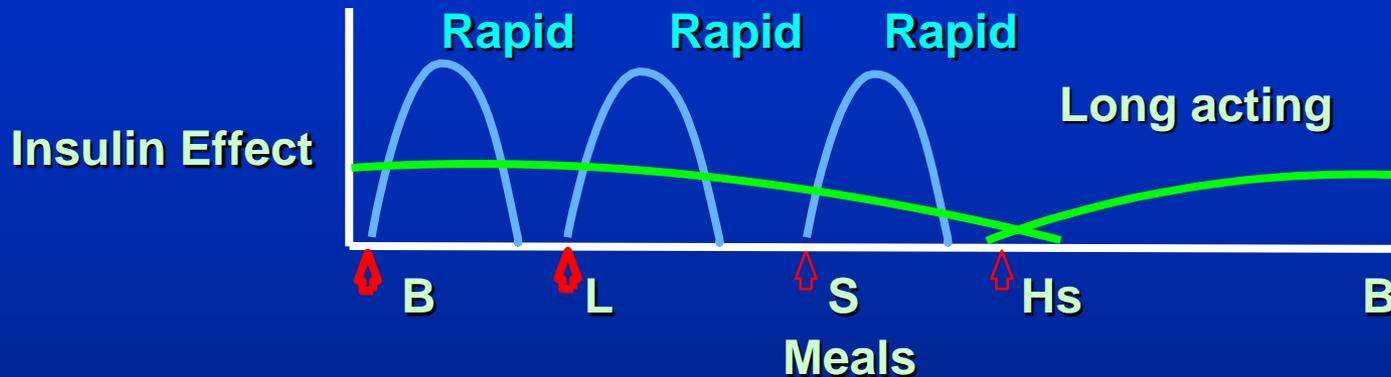
- Postprandial control at each meal

- Improve fasting glucose

- Provides basal coverage

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Mr. D, CASE 2:

- Mr D is a 46 year old male with a 4 year history of type 2 diabetes
- He's recently relocated to your community
- Chief complaint: Fluctuating glucoses
- Medical history:

  Negative except for the diabetes
- Accountant who is divorced and lives alone
- Activity - walks dog after supper 3-4 times a week
- Diet – avoid desserts
- Hgt 5'10", Wgt 226 (BMI 32.4 kg/m^2)

Initial Treatment

- Initially treated with:
  - 40 U NPH and 20 U Regular at 7:30 AM (total 0.60 U/kg)
  - Testing BID - FPG was $\leq$ 200 mg/dL, pre-supper 140s
- NPH dose was increased to 60 units (0.70 U/kg) then 80 units (0.9 U/kg) in an attempt to get FPG <140 mg/dL
  - However, he experienced frequent late afternoon hypos (symptoms of sweating and shaking) which he treated with a candy bar
  - HbA$_{1c}$ one year later was 7.8%

Mr. D One Year Ago

- Because of the afternoon hypoglycemia, he was switched to twice daily 75/25 insulin
  - 45 U pre-breakfast and 45 U at suppertime
  - The afternoon hypoglycemia resolved, and blood testing before breakfast and supper was usually in the 100 to 160 mg/dL range
  - However he developed nocturnal hypoglycemia
- The supper dose was decreased to 35 U 75/25
  - Middle of the night symptoms resolved but FPG rose well above 140 mg/dL

His Twice Daily 75/25 Regimen
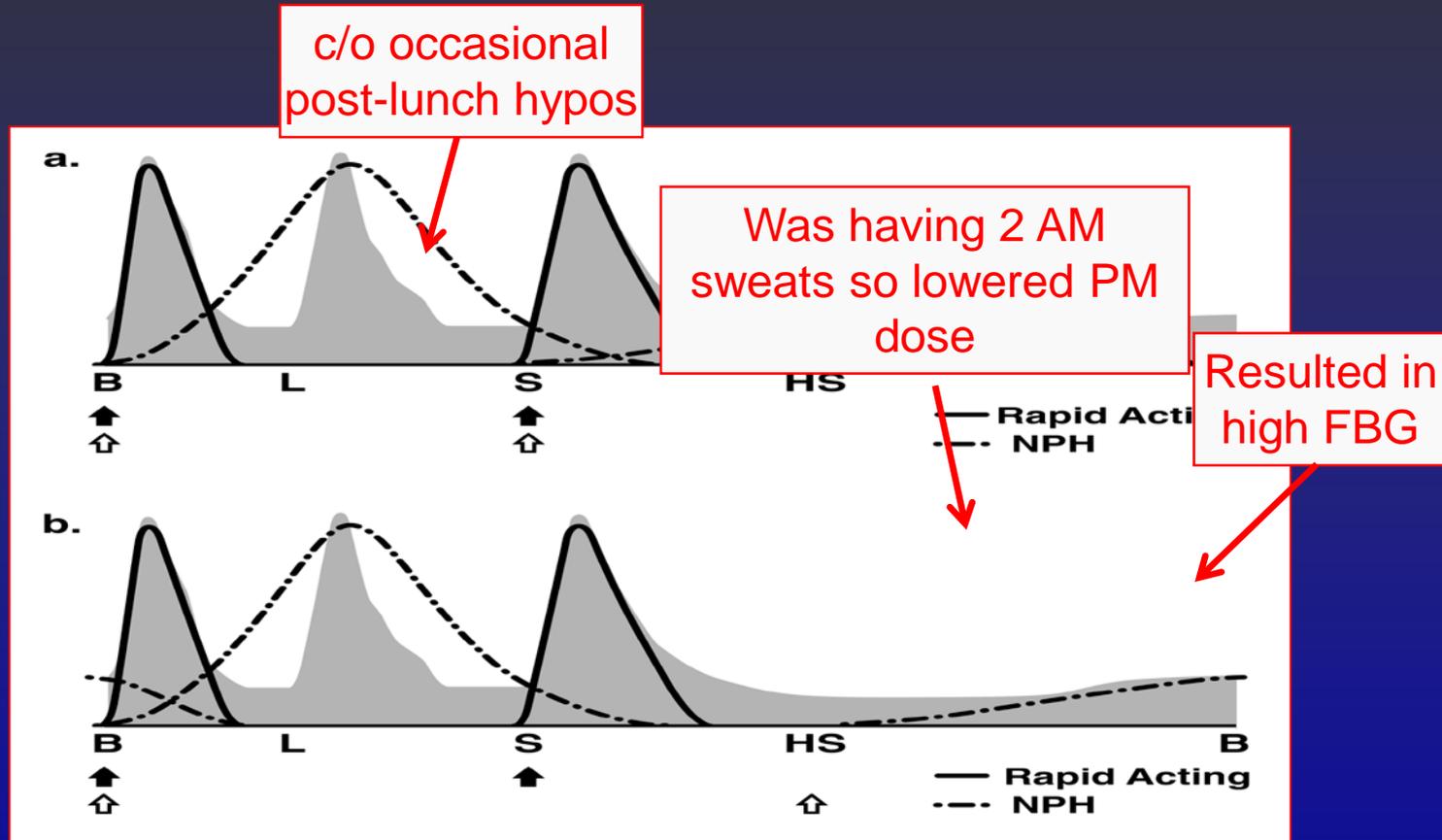
Your Visit Today

- Your first visit with him is today. He reports:
  - Still taking 45 U 75/25 AM and 35 U 75/25 PM
  - FPG values average 180-200 mg/dL
  - He experiences post lunch hypos 1 to 2 times per week "on particularly busy days or when I eat my lunch late"
  - Very frustrated... feels like it is impossible to control his diabetes
- Height and weight unchanged from diagnosis
- HbA_{1c} is 8.2%

What do you do now?

Troubleshooting the Insulin Regimen

- Get to know the patient:
  - What is his daily schedule, exercise habits, work schedule, eating habits?
  - Does his current insulin program fit his lifestyle?
- Is he over-insulinized?
- New program and doses?

Get to Know the Patient

- **Identify hypoglycemia patterns and relate to insulin peaks**
- **Look for causes:**
  - **Lifestyle issues:**
    - Exercise
    - Food
    - Alcohol
  - **Medical causes:**
    - Altered kidney or liver function
    - Hypothyroidism, Addison's, hypopituitarism
    - Gastroparesis
    - Hypoglycemia unawareness

Mr. D reports no problems

You identify no issues by history and lab testing

Troubleshooting the Insulin Regimen

- Get to know the patient:
  - What is his daily schedule, exercise habits, work schedule, eating habits?
  - Does his current insulin program fit his lifestyle?
- Is he over-insulinized?
- New program and doses?

Insulin Sensitivity Factors

Normal weight - extremely active	0.3 U/kg
Normal weight - moderately active	0.4 U/kg
Normal weight - minimally active	0.5 U/kg
	100
Obese- physically active	0.8 U/kg **kg**
Obese- minimally active	1.0 – 1.2 U/kg
Renal failure	less 0.2 U/kg
TZD usage (type 2)	less 0.2 U/kg

You estimate he needs 80 units daily, and he is taking 80 units.

Troubleshooting the Insulin Regimen

- Get to know the patient:
  - What is his daily schedule, exercise habits, work schedule, eating habits?
  - Does his current insulin program fit his lifestyle?
- Is he over-insulinized?
- New program and doses?

Outcome #1

- You start your patient on:
  - Lispro 14 U AM, 10 U Ln, 16 U PM
  - Glargine 40 U HS
  - This is 80 U = 0.8 U/kg
- 4 x daily SMBG pre-meals and bedtime telling Mr D the goal is 90 - 130 mg/dL
  - Insulin doses adjusted by *pattern management*
- Sent to a CDE and dietitian who recommend Mr D learn *carbohydrate counting*

Outcome #2

- He returns 2 months later taking:
  - Lispro 12 U AM, 8-12 U Lunch depending on activity, 16-20 U PM depending on dinner
  - Glargine 36 U PM
  - He says daytime and middle of night hypos are essentially eliminated
  - Self glucose values generally excellent
  - HbA_{1c} = 6.8%
- "My one confusion is how do I change my insulin for the occasional blood glucose reading out of my target range?"

His only confusion is... how to adjust for the occasional high PG?

AM	Ln	PM	HS	AM	Ln	PM	HS
12	8	16	36	90	115	116	108
12	10	20	36	103	72	74	128
12	11	18	36	115	123	225	137
12	11	16	36	98	98	118	104
12	12	16	36	205	130	99	154
12	10	20	36	103	108	134	135
12	10	20	36	115	194	149	165

Correction (or 'fix it') insulin

- Rule of 1800 for patients using Rapid Analogue pre-meals
  - 1800/total daily insulin dosage = expected BG lowering (mg/dL) of 1 unit of their rapid-acting analog
  - Use rule of 1500 for regular insulin based regimens
- Mr D takes (average)
  - Breakfast 12 U, Lunch 10 U, Supper 18 U, Bedtime 36 U = 76 U

1 unit of lispro should decrease his BG approximately 25 mg/dL
(conservative: round up to 30!

Pre-Meal 'fix it' Algorithm

Glucose	Insulin Dose
<80 mg/dL	Minus 1 unit
81 - 130 mg/dL	Usual dose
131 - 160 mg/dL	Add 1 unit
161 - 190 mg/dL	Add 2 units
191 - 220 mg/dL	Add 3 units
221 - 250 mg/dL	Add 4 units, etc

Designing Insulin Program

- Get to know your patient's schedule, eating and exercise habits, etc.
- Choose insulin program that best matches that schedule
  - *Basal bolus* programs typically provide most flexibility
  - *Insulin analogs* usually best for optimal glycemic control while minimizing hypos
- Calculate 24-hour insulin needs - U/kg
- Calculate starting doses - typically 50% as basal insulin and 50% spread over meals

Designing Insulin Program (cont)

- Use "team approach" when available:
  - Certified Diabetes Educators (CDEs)
  - Registered dietitian - *carbohydrate counting*
  - Diabetes Specialist
- Use home plasma glucose values to adjust starting insulin doses - *pattern management*
  - Pre-meal goals 90-130 mg/dL
  - 2-hr postprandial less than 180 mg/dL
- Then calculate algorithm for adjustments
  - Rule of 1800

From Premixed

to

Basal-Bolus

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar		**140**							
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**130**							
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**115**							
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**124**							
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**104**							
	Med		**20 u 70/30**				**10u 70/30**			

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar		140				200			
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar		130				190			
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar		115				210			
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar		124				220			
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar		104				235			
	Med		20 u 70/30				10u 70/30			

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar		**140**		**100**		**200**			
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**130**		**95**		**190**			
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**115**		**110**		**210**			
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**124**		**124**		**220**			
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**104**		**114**		**235**			
	Med		**20 u 70/30**				**10u 70/30**			
	Food									

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar		**140**		**100**		**200**		**300**	
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**130**		**95**		**190**		**300**	
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**115**		**110**		**210**		**300**	
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**124**		**124**		**220**		**300**	
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**104**		**114**		**235**		**300**	
	Med		**20 u 70/30**				**10u 70/30**			
	Food									
Date:	Blood Sugar		**125**		**130**		**160**		**300**	

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar	65	140		100		200		300	
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar	70	130		95		190		300	
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar	55	115		110		210		300	
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar	80	124		124		220		300	
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar	100	104		114		235		300	
	Med		20 u 70/30				10u 70/30			
	Food									
Date:	Blood Sugar	92	125		130		160		300	

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar	65	140		100		200		300	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	70	130		95		190		300	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	55	115		110		210		300	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	80	124		124		220		300	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	100	104		114		235		300	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar	80	140		60		200		210	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	150	155		95		130		140	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	60	115		120		160		150	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	80	124		124		185		165	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	100	104		164		95		135	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar	80	140		60		200		210	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	150	155		95		130		140	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	60	115		120		160		150	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	80	124		124		185		165	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									
Date:	Blood Sugar	100	104		164		95		135	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		7 u NPH	
	Food									

		3:00 AM	Bef. B	Aft. B	Bef. L	Aft. L.	Bef. D.	Aft. D.	Bed	Notes
Date:	Blood Sugar	80	140		85		160		150	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		6 u Glar	
	Food									
Date:	Blood Sugar	150	135		95		130		140	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		6 u Glar	
	Food									
Date:	Blood Sugar	90	115		120		160		150	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		6 u Glar	
	Food									
Date:	Blood Sugar	100	124		124		185		165	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		6 u Glar	
	Food									
Date:	Blood Sugar	100	104		124		140		135	
	Med		6 u Rapid		6 u Rapid		5 u Rapid		6 u Glar	
	Food									

Other emerging treatments

- New long acting insulins
  - Deglutide
  - Peg-Lyspro
- New Pre/Peri transplant protocols
- Inhaled insulin (came/ went/ coming back?)
- Closed loop pumps/ Sensors
- Glucagon Receptor blockers

For now……

- Individualize glycemic goals
- Physiologic approach to both insulin and non-insulin meds
  - Consider:
    - mechanism
    - Side effects

Questions

You are welcome to email me:

Jhone@AIHScorp.org

Or call me:

805-681-7356 ext 211 (o)

303-921-6740 (c)