

Management Tips – Insulin Regulation



CDA Diabetes Educator Section
Calgary DES Chapter
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Disclosure

- Book sales – all pump companies
- Instructor – J&J Diabetes Institute
- Advisory Board Member – Agamatrix, Medingo, Tandem Diabetes, Unomedical
- Royalties – Roche, Abbott
- Consultant – Bayer, Roche, Tandem Diabetes
- Speakers Bureau – Smiths Medical, Tandem Diabetes
- Sub-Investigator – Glaxo Smith Kline, Animus, Sanofi-Aventis, Bayer, Biodel, Dexcom, Novo Nordisk
- Web Advertising – Sanofi-Aventis, Sooil, Medtronic, Animas, Accu-Chek, Abbott, etc.

Outline

- Insulin Overview
- Insulin Dosing
- Find TDD, Basals, Boluses
- Change Doses Carefully
- Insulin Tips



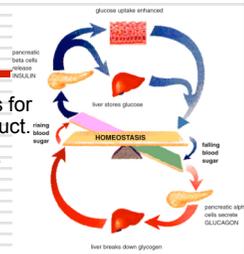
Terms To Know

- **TDD** – total daily dose of insulin (all basals and boluses)
- **Basal** – background insulin released slowly through the day
- **Bolus** – a quick release of insulin
 - Carb bolus – covers carbs
 - Correction bolus – lowers high readings that arise from deficits in basal rates or carb boluses
- **Bolus On Board (BOB)** – bolus insulin still active from recent boluses, aka Unused Insulin Rule for MDI
- **Duration of Insulin Action (DIA)** – time that a bolus will lower the BG – used to measure BOB



What Insulin Does

- Aids glucose entry into cells for energy storage & heat product.
- Enhances protein synthesis and cell growth
- Enhances fat storage and reduces fat mobilization
- Inhibits glucose release from liver and from glycogen stores in muscle
- Inhibits glucose formation from amino acids



Impact Of Insulin Deficit

- Glucose elevation from decreased cell uptake (loss of energy)
- Glucose loss in urine (weight loss)
- Excess glucose produced by liver & released from muscle glycogen (increased urination and thirst)
- Muscle used for energy (weight loss)
- Excess fat used for energy ----> ketones (DKA)
- Complications (multiple mechanisms)

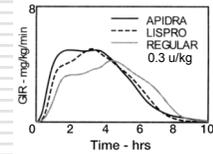
Who Needs Insulin?

- All Type 1s
- Type 2s not in control with meds, diet, exercise
- Women with gestational diabetes if MNT or oral agents don't work
- With parenteral nutrition
- Acute MI (keep BG under 110mg/dl)
- S/P pancreatitis, pancreatectomy, or other loss of beta-cell function

Insulin Varieties – Injection

Rapid / Short

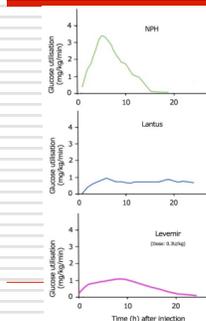
- Apidra, Humalog, Novolog / Regular
 - Covers meal intake
 - Used for elevated BG



Intermediate / Long acting

- NPH / Lantus, Levemir
 - Used for basal insulin needs
 - Not intended to cover meals

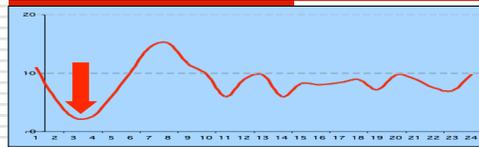
Even Long-Acting Insulins Peak



- NPH has a pronounced peak that can be useful for a Dawn Phenomenon, etc.
- Lantus has an action time of 18 to 26 hours – those with shorter action times get more peaking
- Lantus and Levemir may not sustain activity for full 24 hrs

Take Home: the more injections the flatter the action

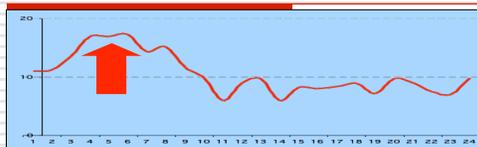
Somogyi Phenomenon



Body's counter-regulatory response to hypo causes a followup high

- | Cause: | Treatment: |
|--|--|
| • Counter-regulatory hormone release | • Decrease evening intermediate/LA insulin |
| • Increase in hepatic glucose production | • Switch NPH dose to bedtime |
| • Insulin resistance from release of counter-regulatory hormones | • Increase or start bedtime snack |

Dawn Phenomenon



Growth hormone rises in early morning and causes high fasting BGs

- | Cause: | Treatment: |
|---------------------------------|---------------------------------------|
| • Too little insulin at bedtime | • Increase or don't forget night dose |
| • Excess food at bedtime | • Less bed time snack or low GI food |
| • Skipping evening LA insulin | • Give NPH before supper |

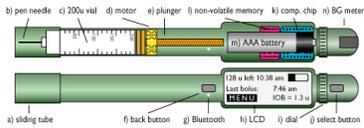
Insulin Varieties – Injection

Mixed – rapid and intermediate insulins

- 50:50 (50% NPH and 50% insulin Lyspro)
- 75:25 (75% NPH and 25% insulin Lyspro)
- 70:30 mixtures (70% NPH, 30% insulin aspart)
- 70:30 (70% NPH, 30% Regular)

Insulin Pens

- Convenience, flexibility, accuracy
- Used for over 90% of insulin delivery in most European countries and Japan
- Rising use in U.S. but still only about 20%



Mixed Insulin Pens

Best for:

- Older person with regular meal and activity patterns
- Diminished vision
- Trouble with dexterity
- Just starting insulin therapy

Mixed insulin pens

- 50/50
- 70/30

Insulin Varieties – Pumps

Uses only Rapid (Novolog, Humalog, Apidra) or Short (U100 or U500 Regular) insulin

- Basal: delivered all day to cover the normal needs of the body when not eating
- Carb Bolus: On demand insulin to cover food
- Correction Bolus: extra insulin to cover hyperglycemia



Goals For Insulin Use

Goals For Insulin Use

Control:

- HbA1c < 6.5% or 7%
- Pre-meal BG 80-120 mg/dl (4.4-6.7 mmol/l)
- 2 hr PP < 160 mg/dl (8.9 mmol)
- Bed time SMBG 100-140 mg/dl (5.6-7.8 mmol/l)
- No ketonuria
- Mean blood glucose level 120-160 mg/dl (6.7-8.9 mmol/l)

Clinical:

- Eliminate hyperglycemia and ketosis
- Prevent chronic complications

Other:

- Maintain desirable weight
- Maintain normal growth and sexual development
- Maintain mental and social well-being

Set Clear Goals For Self-Management

- Set glucose and A1c targets
- Bring records to clinic
- Look for patterns
- Adjust basals and boluses from glucose patterns



Insulin Education

- Address fears and myths
- Review insulin action
- Demonstrate insulin administration
- Site rotation
- Storage
- Needle disposal
- Glucose monitoring
- Handling hyper and hypoglycemia
- Referrals

Barriers To Insulin Use

DAWN Study by NovoNordisk and International Diabetes Federation sought psychosocial issues related to poor outcomes.

Results:

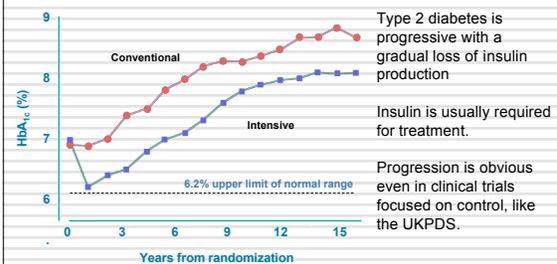
- 50% report insulin use means they failed to manage their disease
- Only 27% believe insulin would help them better manage their DM
- 43% of MDs postpone meds and insulin until absolutely essential

M. Funnell: The Diabetes Attitudes, Wishes, and Needs (DAWN) Study, *Clinical Diabetes* 24:154-155, 2006

Other Barriers

- Fear of needles
- Fear of the unknown
- Cost
- Inconvenience
- Weight gain
- Using insulin, especially multiple injections, means you have "bad" diabetes and it's getting worse

Type 2 Is Progressive



UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998; 352:837-853.

Why Insulin Causes Weight Gain

- Less glycosuria with improved control
 - Reduce calorie intake at start if avg BG > 10 mmol
- Anabolic effect of insulin
- Over-treatment of hypoglycemia
 - Avoid lows with accurate dosing
- Defensive eating to avoid hypoglycemia
 - Avoid lows with accurate dosing
- Consider metformin, Symlin, GLP-1 agonist

How To Avoid Weight Gain

- If starting average BG is above 180 mg/dl, current diet intake needs to be reduced to avoid gaining weight
- Avoid foods that raise the glucose
- Set and test insulin doses to avoid hypoglycemia and the need to overeat
- Advise that only 15 to 20 grams of carb are usually needed for lows and it takes 20 minutes to feel better
- Treat lows with glucose tabs or other fast carbs

Insulin Dosing

Starting Insulin – Type 2

Dose timing for start depends on whether highest readings occur fasting or after meals

High fasting BGs

- Start with once daily long-acting insulin and continue oral agents (except sulfonylureas)

High postmeal BGs

- Start with meal coverage for largest meal of day and continue oral agents (except sulfonylureas)

Insulin Dose – How Much?

Consider weight, age, level of insulin resistance, and lifestyle

- Starting dose (adults):
 - Starting dose: 0.5-1.0 units/kg/day
 - Average dose 0.8-1.2 u/kg
- Starting dose (children):
 - Starting pre-puberty 0.2-1.0 u/kg
 - Average dose 0.5-1.0 u/kg
 - Starting puberty 0.3-1.2 u/kg
 - Average dose 0.8-1.5 u/kg

Insulin Dose – How Much?

Determine glucose target range

Start with small dose based on weight

Gradually learn to adjust both rapid and long insulin doses from glucose readings

Individualize

Realize that gradual increase in doses is normal due to gradual loss of beta cells

Begin Self-Management Right Away

Rapid Insulin Adjustments			
	Current Units	Lows at next meal	Highs at next meal
	< 10u / meal	- 1u	+ 1u
	11-19u / meal	- 2u	+ 2u
	> 20u / meal	- 3u	+ 3u
Long Acting Insulin Adjustments			
Avg FBG	Add	Every	Till Below
> 180 mg/dl	+ 4u	3 days	180 mg/dl x 2 days
> 140 mg/dl	+ 2 u	3 days	140 mg/dl x 2 days
> 90 mg/dl	+ 1u	3 days	90 mg/dl x 2 days

Lantus / Levemir

- Are clear solutions
- Don't confuse with rapid insulin !!!
- Don't use in pump
- Don't give IV (it precipitates)
- Don't mix with a rapid insulin (pH rises and changes absorption)

Long-Acting (LA) Insulin Tips

- Flatten LA insulin action (& avoid insulin gaps)
 - Give NPH (mixed) TID
 - Give Lantus or Levimir BID
- Best measures of LA insulin dose
 - Breakfast BG
 - Presence of lows 4 or less hrs before breakfast

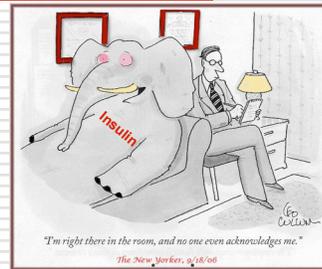
Causes For Lows

- "Stacking" insulin
- Eating fewer carbs than expected
- Insulin-to-carbohydrate ratio number is too low
- Excessive basal insulin
- Delayed eating after taking mealtime insulin
- Increased activity or exercise
- Delayed stomach (gastric) emptying
- Fear of complications
- Taking the wrong insulin by mistake
- Drinking alcohol
- Increased insulin sensitivity
- "Covering" snacks for exercise or lows with insulin
- Use of an incretin based therapy or an amylin analog

Causes For Highs

- | | |
|--|---|
| ■ Incorrect carb counting | ■ Fear of lows |
| ■ "Out-eating" the insulin | ■ Needle phobia |
| ■ Insufficient insulin for carbs | ■ Meds that cause insulin resistance |
| ■ Inadequate insulin dose | ■ Inactivity |
| ■ Rebound from low glucose | ■ Weight gain |
| ■ Delayed stomach (gastric) emptying | ■ Increase in stress hormones |
| ■ Under-insulinization because of fear of lows | ■ Bad (spoiled) insulin |
| ■ Not checking glucose levels | ■ Incorrect insulin injection technique |
| | ■ Taking wrong insulin by mistake |

The Elephant In The Room

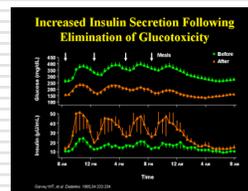


Prevent Progression Of Type 2

- GLP-1s
- Glitazones
- Insulin

See Dr. Ralph DiFronzo's presentation at the 2008 ADA meeting.

Beta Cell Preservation



WT Garvey, Diabetes 1995, 34, 222-234

In Type 2 diabetes, MANY studies show long-term benefit after short-term use of insulin pumps to normalize glucose levels.

Benefits may arise from:

- Decreased glucose toxicity
- Decreased oxidative damage
- Increase in 1st phase insulin release

In new onset Type 1 diabetes, the honeymoon phase also appears to be extended with early and aggressive insulin use.

Ilkova H, Glaser B, Tunckale A, et al; *Diabetes Care* 20:1353-1356, 1997
Weng J, Li Y, Xu W, et al.; *Lancet* 371: 1753-1760, 2008

Get Basals & Boluses From TDD

To dose insulin well:

- Select starting basal rate and correction factor from Optimal TDD
- Select starting carb factor from Optimal TDD and weight

To get a fresh start for major control problems, do this over again

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Easy Basal Rates & Correction Factors

10.4 Starting Basal Rate And Correction Factor

Find your starting TDD in the first column. Then look across that row to find your starting hourly basal rate and correction factor.

Starting TDD	Total Basal Per Day	Average Basal Rate ¹	Correction Factor ² (u lowers BG)
18 units	9 units	0.38 u/hr	111 mg/dl (6.1 mmol)
22 units	11 units	0.46 u/hr	91 mg/dl (5.0 mmol)
26 units	13 units	0.54 u/hr	77 mg/dl (4.2 mmol)
30 units	15 units	0.63 u/hr	67 mg/dl (3.7 mmol)
35 units	18 units	0.75 u/hr	56 mg/dl (3.1 mmol)
40 units	20 units	0.83 u/hr	50 mg/dl (2.8 mmol)
45 units	23 units	0.96 u/hr	45 mg/dl (2.4 mmol)
50 units	25 units	1.04 u/hr	38 mg/dl (2.2 mmol)
60 units	30 units	1.25 u/hr	33 mg/dl (1.8 mmol)
70 units	35 units	1.46 u/hr	29 mg/dl (1.5 mmol)
80 units	40 units	1.67 u/hr	25 mg/dl (1.3 mmol)
90 units	45 units	1.88 u/hr	22 mg/dl (1.2 mmol)
100 units	50 units	2.08 u/hr	20 mg/dl (1.1 mmol)

¹ Avg Basal Rate = Total Basal Per Day divided by 24 hrs
² Corr Factor = 2000/TDD in mg/dl, 110/TDD in mmol

Basal ~50% of TDD
Corr. Factor = 2000/TDD*

*The better the control,
the higher the correction factor

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J Walsh and R Roberts: *Pumping Insulin (5th ed)*, 2010

Easy (Safe) Basal Adjustments

11.3 Adjust Your Basal Rates From Your Basal Test

mg/dl (mmol)	If your glucose falls				If your glucose rises			
	-100 (-5.5)	-80 (-4.1)	-60 (-3.3)	-40 (-2.2)	+40 (+2.2)	+60 (+3.3)	+80 (+4.1)	+100 (+5.5)
and your TDD is:	Lower your basal by a TOTAL of				Raise your basal by a TOTAL of			
20 u	-0.5 u	-0.3 u	-0.1 u	retest	retest	+0.1 u	+0.3 u	+0.5 u
30 u	-0.8 u	-0.5 u	-0.2 u	retest	retest	+0.2 u	+0.5 u	+0.8 u
40 u	-1.2 u	-0.8 u	-0.4 u	retest	retest	+0.4 u	+1.8 u	+1.2 u
50 u	-1.5 u	-1.0 u	-0.5 u	retest	retest	+0.5 u	+1.0 u	+1.5 u
60 u	-1.9 u	-1.3 u	-0.7 u	-0.1 u	+0.1 u	+0.7 u	+1.3 u	+1.9 u
80 u	-2.6 u	-1.8 u	-1.0 u	-0.2 u	+0.2 u	+1.0 u	+1.8 u	+2.6 u
100 u	-3.2 u	-2.3 u	-1.3 u	-0.3 u	+0.3 u	+1.3 u	+2.3 u	+3.2 u

For safety, these adjustments may be slightly less than you need but will improve readings.
Example: If a 0.5 unit total basal reduction is needed, try lowering your basal rates by 0.1 u/hr over 5 hrs between 3 and 8 hrs before the low reading occurs.

These basal adjustments provide about 1/3 to 1/2 of the full basal adjustment that may be required.

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J Walsh and R Roberts: *Pumping Insulin (5th ed)*, 2010

Easy And Accurate Carb Factors

10.5 Easy Carb Factors

TDD	Carb Factors For Various Wts and TDDs					
	100 lb	120 lb	140 lb	160 lb	180 lb	200 lb
120		3.03	3.47	3.90	4.33	
110		3.31	3.78	4.25	4.73	
100		3.12	3.64	4.16	4.68	5.20
90		3.47	4.04	4.62	5.20	5.78
80	3.25	3.90	4.55	5.20	5.85	6.50
70	3.71	4.46	5.20	5.94	6.69	7.43
60	4.33	5.20	6.07	6.93	7.80	8.67
50	5.20	6.24	7.28	8.32	9.36	10.40
45	5.78	6.93	8.09	9.24	10.40	11.56
40	6.50	7.80	9.10	10.40	11.70	13.00
35	7.43	8.91	10.40	11.89	13.37	14.86
30	8.67	10.40	12.13	13.87	15.60	17.33
25	10.40	12.48	14.56	16.64	18.72	20.80
20	13.00	15.60	18.20	20.80	23.40	26.00
15	17.33	20.80	24.27	27.73		
Wt =	100 lb	120 lb	140 lb	160 lb	180 lb	200 lb

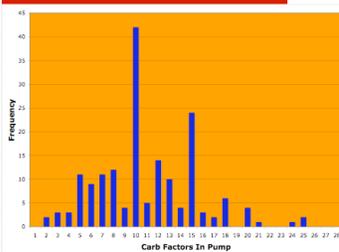
$$\text{Carb Factor} = \frac{10.4 \text{ g/u} \times \text{Wt (kgs)}}{\text{TDD} \times 1.8}$$

Carb factor = an average carb factor times the individual's insulin sensitivity
Replaces old 450/500 Rule

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J Walsh and R Roberts: *Pumping Insulin (5th ed)*, 2010

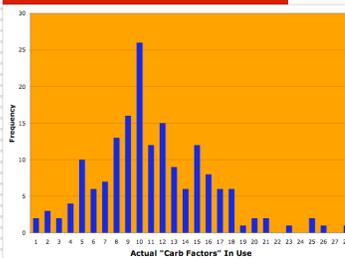
Carb Factors Found In Pumps



Carb factors in 183 complaint-free pumps from US and Canada user in good control (avg BG 145 mg/dl, 4.45 tests/day over 73.9 days)*

* Author's unpublished data

Carb Factors Actually Used For Meals



Pump users in good control adapt despite incorrect Carb Factors in pump*

Unfortunately, to do this, they must change carb count or ignore the bolus recommendation from their pump

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* Author's unpublished data

Verify Carb & Correction Factors

Carb factor = avg. carb factor times insulin sensitivity:

$$\text{Carb Factor} = 10.4 \text{ g/u} \times \frac{\text{Weight (lb)}}{\text{TDD} \times 4}$$

Check: Does result match current Carb Factor?

Correction factor closely estimated with the 2000 Rule:

$$\text{Correction Factor} = 2000 / \text{TDD}$$

Check: Does Corr Factor X TDD = 1800 to 2400?

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Change Doses Carefully

Know BG Impact Before Changing Doses

How a dose change affects glucose.

- A 5% change in the TDD changes the glucose about 25 mg/dl through the day.
 - 5% TDD increase (ie, from 40 to 42 u/day) = fall in avg BG from 175 to 150 mg/dl
- A 5% change in the carb factor changes the glucose about 20 mg/dl* per meal.
 - 5% = an increase from 10 to 10.5 g/u or 6 to 6.3 g/u, for a postprandial BG fall from 160 to 140 mg/dl.

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* Varies by weight and insulin sensitivity

How Change In Carb Factor Affects BG

Table shows avg fall in glucose after each meal when carb factor is reduced from 10 to 9 g/u and from 5 to 4 g/u (for appr. wt & TDD).

How A 1-Step Reduction In Carb Factor Impacts Avg. Meal BG					
Change in CarbF	Weight (~TDD)	Carb/day	Carb/meal	Units/meal	Impact on BG per meal*
1/10 to 1/9	160 lb (~40 u)	220 gr	73 gr	+ 1.44 u (CorrF = 50)	- 73.3 mg/dl
1/7 to 1/6	240 lb (~100 u)	330 gr	110 gr	+ 3.62 u (CorrF = 20)	- 72.4 mg/dl

B * Calculated as $\left[\frac{\text{carbs/day}}{\text{new carb factor}} - \frac{\text{carbs/day}}{\text{old carb factor}} \right] \times \frac{1}{3} \times \frac{2000}{\text{TDD}}$

Remember

Raise the carb factor for frequent postmeal lows
Lower the carb factor for frequent postmeal highs

AFTER checking basal / carb bolus balance

Insulin Tips

Most TDDs Need To Rise

The average glucose on a pump is 196 mg/dl*
Most pump users need a higher TDD

Roughly 75% of Type 1s and 50% of Type 2s are above loose BG target goal of less than 7%

* Cozmo Data Analysis 2 Study (CDA2)

Control Guides

$$\text{TDD (nl insulin sensitivity)} = \frac{\text{Wt (kg)}}{1.8}$$

$$\text{Individual's Insulin Resistance} = \frac{\text{TDD} \times 1.8}{\text{Wt (kg)}}$$

1 g Carb raises BG =	~8 mg/dl	~4 mg/dl	~2 mg/dl
	80 lbs	160 lbs	320 lbs

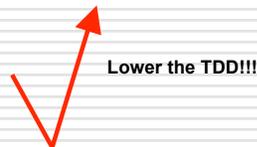
$$\text{Max allowable carbs in a meal}^1 = \text{Wt (lb)} \times 0.38$$

¹ J. Bondia, E. Dassau, H. Zisser, R. Calm, J. Vehi, L. Jovanovic, F.J. Doyle III, Coordinated basal-bolus for tighter postprandial glucose control in insulin pump therapy. JDST, 3(1), 89-97, 2008

Stop Lows First

Better control, less variability

- Release of stress hormones raises glucose for hours
- Avoids overtreatment and skipped boluses
- Preventing lows improves accuracy of all doses
- Lows may be treated with no test (NO RECORD! – ASK!)



* Low overtreated? Count the wrappers and bolus right away for excess carbs

Things To Watch To Improve Control Look For These On Pump's Analysis Screens

- Average 7 to 14 days
- # of carbs per day – are carbs counted & covered?
- Avg. total daily dose (TDD)
- % of TDD as basal
- % of TDD as carb boluses
- % of TDD as correction boluses

- # of BG tests
- Avg BG
- BG standard deviation

Sweet Spots For Control

- Night basal – BGs middle of the night to breakfast
- Day basal – start with average of night basals
- Carb bolus doses – premeal to premeal BGs
- Correction bolus doses
 - Should bring high BG to target 4-5 hrs later with no lows
 - If highs are frequent, raise basal or carb bolus doses
 - % of TDD devoted to correction boluses should be less than 8%

Questions That Guide Treatment

Look at recent glucose results for trends and patterns:

- Does the blood sugar fall or rise overnight? (basal)
- Is the blood sugar controlled after most meals? (carb factor/bolus)
- When a high blood sugar is treated, does the blood sugar end up at target 4-5 hours later without going low? (correction factor/bolus)
- Are lows often followed by highs? (overtreatment)
- What percent of TDD is used for corrections?

Bolus Early – Stop PP Spikes

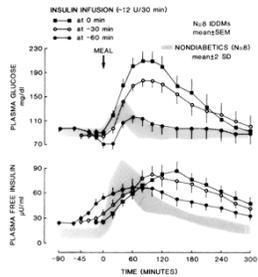
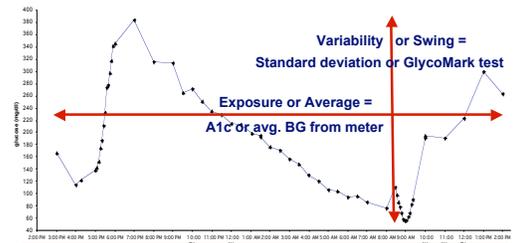


Figure shows rapid insulin injected 0, 30, or 60 min before a meal
Normal glucose and insulin profiles shown in the shaded areas
Best glucose profile when bolus given 60 min ahead, but this is too risky to recommend!!!

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Evaluate Glucose Exposure And Variability



One day – BG checks every 30-60 min.

Insulin / Carb Bolus Balance

When the glucose goes high or low, a quick insulin analysis helps determine the cause.



** Pump can show exact insulin and carb excess or deficit

Check The 5 Hour Insulin Window

When a low or high reading occurs, check:

- how much basal and
- how much bolus
- was active over the previous 5 hours

Lows – usually caused by the larger insulin amount
Highs – usually caused by the smaller insulin amount

Assume that boluses work for 5 hours!

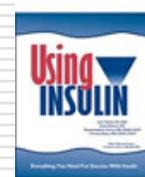
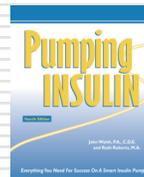
Examples – 5 Hour Window



1
BG = 54 mg/dl (3 mmol)
at 1:00 am
In previous 5 hours:
Boluses = 9.2 u
Basal = 4.6 u

2
BG = 252 mg/dl (14 mmol)
at 4:30 pm
In previous 5 hours:
Boluses = 6.5 u
Basal = 2.4 u

For Answers To Your Questions



Available at www.diabetesnet.com or 800-988-4772