

Starting or Changing Insulin Therapy For the Generalist Physician

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Dr. Dugdale - None

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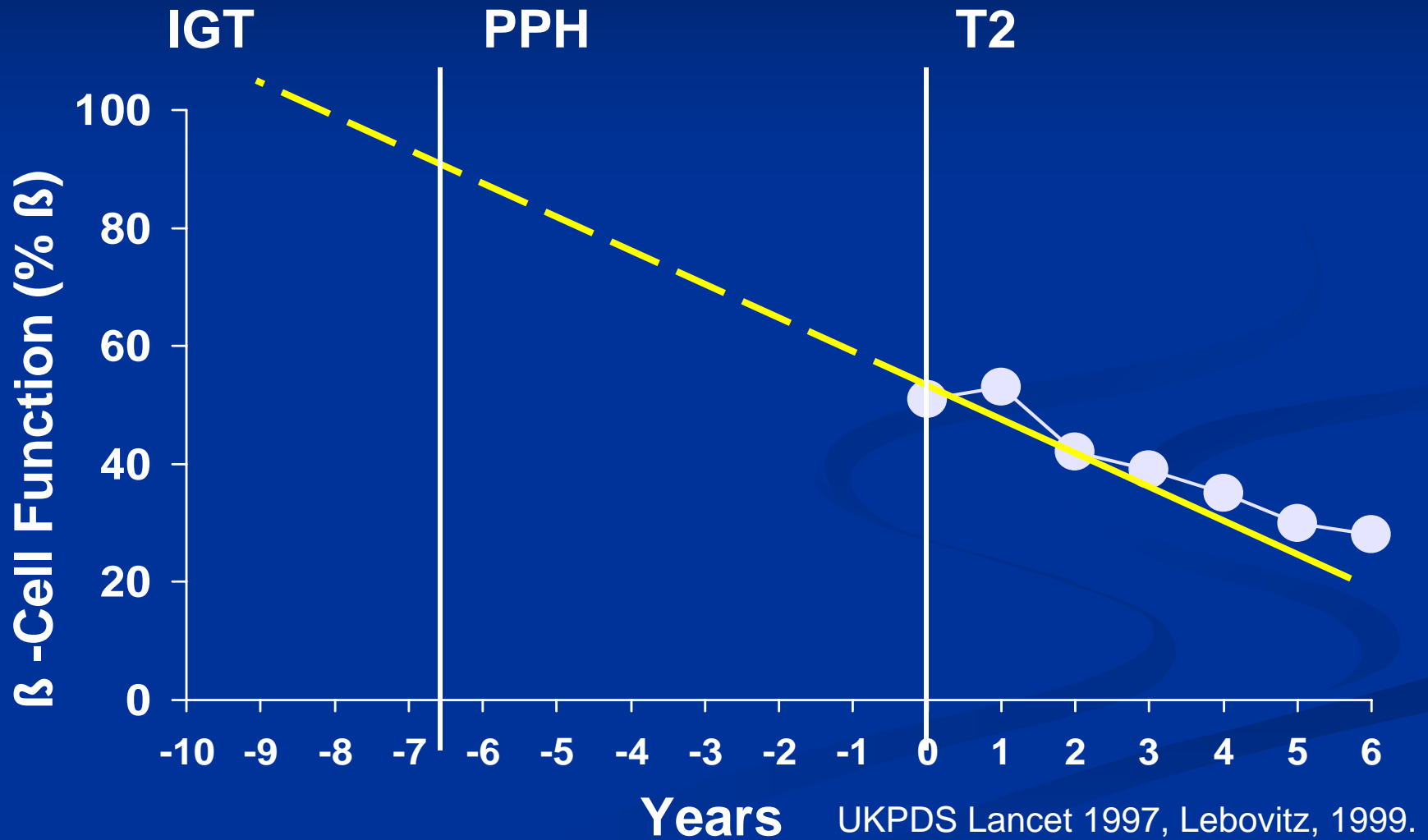
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Learning Goals

- Understand the use of new insulins including rapid acting and long acting insulins (e.g., lispro, aspart, glulisine, glargine and detemir) in outpatients.
- Know how to select appropriate patients for and transition them to using the new insulins.
- Know how to use older insulins in patients whose needs are well-served by these drugs or for whom formulary restrictions require their use.
- Review indications for new injectable agents such as exenatide and pramlintide.
- Develop strategies for teaching outpatient insulin therapy to trainees

UKPDS Extrapolated β -cell Function



Prioritizing Treatments: T2DM

- Blood pressure: $<130/80$ (ADA)
 - Usually requires 2 or more drugs; thiazide ok!
- Lipid management: statins
 - LDL target < 100 mg/dL (ADA)
- Aspirin 75-162 mg per day (ADA)
 - Age over 40 years OR other risk factors for CV disease
- Hemoglobin A1c (A1c) $< 7\%$

Diabetes Toolbox 2008

You should be able to control virtually all patients safely with these tools to A1C ~7%

1. Glucometer and A1c (HbA1c)
2. Metformin (1000 mg bid)
3. Insulin glargine (basal)- ~ 0.5-1 unit/kg
4. Insulin aspart (rapid) ~ 0.5-1 unit/kg
5. Aspart pre-mix (70/30)
6. Sulfonylurea (SU)
7. Frequent insulin adjustment by patient

Initiating Insulin: Type 2 DM

- What is the mean level of HbA1c at which insulin is started in the US:
 - A: 8%
 - B: 9%
 - C: 10%
 - D: 11%

Initiating Insulin: Type 2 DM

- CORRECT ANSWER IS:
 - C: 10% (10.4%, JAMA 1997)

Goals of Glycemic Treatment: ADA

■ Perform the A1C test

- at least two times a year in patients who are meeting treatment goals and who have stable glycemic control (Grade E)
- quarterly in patients whose therapy has changed or who are not meeting glycemic goals (Grade E)

■ The A1C goal

- *for patients in general:* <7% (Grade B)
- *for the individual patient:* as close to normal (<6%) as possible without significant hypoglycemia (Grade E)

AACE Treatment Recommendations

- Initiate SMBG (Grade A)
- Encourage patients to achieve glycemic levels as near normal without inducing clinically significant hypoglycemia (Grade B)
 - HBA1c \leq 6.5%
 - Fasting plasma glucose $<$ 110 mg/dL
 - 2 hour postprandial glucose $<$ 140 mg/dL
- Add insulin for patients on combination oral therapy if HBA1c 6.5-8.5%
- Consider initiating basal-bolus therapy when HBA1c $>$ 8.5%

The limits of A1c: ACCORD

William T. Friedewald, MD, ACCORD Steering Committee Chair

- Action to Control Cardiovascular Risk in Diabetes
- > 10,000 patients T2DM + two other CVD risk factors
- Goals: Intensive (A1C < 6%) or standard (A1C 7% - 7.9%)
- Half of the participants in the intensive treatment group achieved an A1C < 6.4%
- Half of the “standard” participants achieved an A1C < 7.5%
- 4 years: 257 intensive pts died, vs. 203 standard pts
 - 3 “excess” deaths per 1,000 participants per year
- Intensive BG arm halted early by NIH in Feb 2008

Diabetes Toolbox 2008

Alternatives to Insulins
when metformin + SU
does not reach goals

Alternatives to Insulin

- Acarbose
- TZDs
- Incretins
- NONE have the proven track record of insulin vis-à-vis safety and efficacy (including reduction of complications)

Incretins

- Gut-derived factors that increase glucose-stimulated insulin secretion
- In•Cre•Tin
- Intestine Secretion Insulin

■ *Diabetologia* 1985;28:5645

Incretin Overview

- Incretins have many actions, including increasing glucose-stimulated insulin secretion after oral intake
- Amylin and GLP-1 are incretins
- Amylin secretion is reduced in T1DM
- GLP-1 secretion is reduced in T2DM
 - GLP-1 inactivated by DPP-4 (dipeptidyl peptidase-4)
 - Inhibition of DPP-4 increases GLP-1 effect

Incretin-Related agents to treat Diabetes

- Exenatide (Byetta)
- Pramlintide (Symlin)
- Sitagliptin (Januvia)
- NONE have long term records for safety or efficacy that are comparable to metformin, SUs, and insulin

Exenatide

- A GLP-1 receptor agonist: increases glucose stimulated insulin secretion; modulates gastric emptying
- FDA approval: T2DM in pts taking 1 or 2 of MET, SU, TZD
- Given 5 or 10 mcg SC BID
 - Will not cause hypoglycemia unless given with other drug that causes hypoglycemia
- RCT of T2DM patients with mean FBG 185, A1c 8.2%, (range 7-10%), BMI 25-45, on max MET + SU x 26 weeks
- Exenatide 5 mcg BID (AC) for 4 weeks, then 10 mcg BID (AC) vs. glargine, started at 10 units q day and increased to achieve FBG < 100 mg/dl

■ Heine, Annals Int Med 2005;143:559-569

Exenatide, cont'd

- Mean final glargine dose 25 units qday
- A1c ↓ 1.1% in both groups; 46% or 48% achieved A1c ≤ 7%
- Mean BG ↓ (~183 to ~145)
- Glargine group had lower premeal BG, exenatide group had lower postprandial BG
- Weight change +1.8 kg for glargine, -2.3 kg for exenatide
- Hypoglycemia 7.3 per pt yr (exenatide) vs. 6.3 per pt yr (glargine), but severe hypoglycemia equivalent
 - Exenatide more daytime; glargine more night-time
- Nausea in 57% of exenatide, 9% of glargine
- Vomiting in 17% of exenatide, 4% of glargine

■ Heine, Annals Int Med 2005;143:559-569

Pramlintide

- Amylinomimetic: modulates gastric emptying
- FDA approval:
 - T1DM, adjunct to insulin
 - T2DM, adjunct to insulin
- Dosing
 - T1DM: 15-60 mcg SC immediately prior to major meal
 - T2DM: 60-120 mcg SC immediately prior to major meal
- Risk of hypoglycemia significant when used according to FDA indications
- Not recommended

Sitagliptin

- DPP-4 inhibitor: increases GLP-1
- FDA approval: T2DM monotherapy or combination therapy
- Dosing: 100 mg PO in AM; may need to lower SU dose
- Will not cause hypoglycemia unless given with other drug that causes hypoglycemia
- Monotherapy
 - A1c reduction ~0.5% if baseline <8%; up to ~1% if baseline >9%
 - Fasting BG reduced by 13 mg/dL; 2 hr PP BG reduced by 49 mg/dL
- Combination therapy: 24 week RCT of pts with A1c 7.5%-11%
 - A1c reductions
 - MET 500 BID: 0.82%
 - MET 500 BID + sitagliptin 50 BID: 1.4%
 - MET 1000 BID: 1.13%
 - MET 1000 BID + sitagliptin 50 BID: 1.9%
- DPP-4 ubiquitous in body, so effects on other organ systems possible

Diabetes Toolbox 2008

Helping trainees learn how to
provide good diabetes care
and use insulin therapy

Strategies for trainees

- Understand concept of “clinical inertia”, and how it can retard achieving treatment goals
- Understand limitations of HBA1c as a test
- Familiarity with BG meter and home BG testing
- Understand injection technique
- Algorithmic approach to insulin for outpatients, esp. “Treat to Target”
 - The strategies used for inpatients are not appropriate for most outpatients with T2DM

Factors that alter HBA1c

- Altered RBC turnover changes HBA1c-BG correlation
 - Affects up to 15% of patients, even after excluding those with known anemia or kidney disease
 - Shorter RBC life span lowers A1C
 - Hemolysis
 - Hemoglobinopathy
 - Liver disease
 - Kidney disease (e.g., serum creatinine > 2 mg/dL)
 - Pregnancy
 - Lowers HBA1c by inhibiting glycation: Vitamins C and E
 - Raises HBA1c
 - Hypoproliferative anemia
- National Glycohemoglobin Standardization Program web site; JAMA 2006;295:1688-1696.

HBA1c interpretation

- 6% ~ mean BG 135 mg/dL
- 1% rise ~ 35 mg/dL rise in mean BG
- **HOWEVER** these data come from “7 point” BG data collected in the DCCT, and are not as precise as one might think--Revision likely in 2008
- Total imprecision ~4% of reading (at least)
 - 7% = 6.72% - 7.28%
 - 8% = 7.68% - 8.32%
- Multiple assays with HPLC and “rapid” methods being most common

Blood Glucose Meters

- Desirable features:
 - Rapid processing (5 seconds)
 - Small sample size
 - Memory
 - Averages
 - Pre- and post-prandial flagging
 - Logbook function
- Most meters have free software that allow analysis
 - Standard deviation can assess glycemic variability
- Most physician offices **DO NOT** have this capability (>90%)

Blood Glucose Meters

- One Touch Ultra
 - Not the One Touch Mini
- Freestyle Flash
- For Medicaid patients
 - Payment for meters is fixed, so pharmacies typically dispense cheaper meter (WA state--True Track)
 - Payment for strips is not fixed, so patient with more expensive meter can get strips

Diabetes Toolbox 2008

Insulins

Case 1

- A 53 year old man presents with polyuria and fatigue for 3 months.
- PMH: MI with CHF and HTN
- BG = 478, HBA1c 9.9%.
- Random BG 4 months previously was 133

Case 1

- How would you treat this patient?
 - A. Glyburide
 - B. Glyburide and metformin
 - C. Metformin and bedtime glargine
 - D. Glyburide and bedtime glargine
 - E. Basal-prandial insulin

Initiating Insulin in T2DM

- **Metformin and bedtime glargine (NPH also reasonable)**
- Basal-prandial; Acceptable but probably overly complex
- Glyburide or Glyburide + metformin: HBA1c too high for this to be likely to work well
- Metformin has been contraindicated in CHF but stable CHF is no longer a contraindication to metformin

Case 1 Management

- Initial Rx: glyburide 5 mg qAM, and NPH insulin 10 units.
 - Increase by 2 units every 3 days if fasting BG > 120
- Over 2 months, fasting BGs went from the low to mid 200s to the mid to high 100s. Predinner BGs went down to the high 100s to low 200s.
- No hypoglycemic symptoms
- His NPH dose was 35 units hs
 - Note: “hs” usually means ~ 9 PM in clinical trials; consistent timing is the most important thing

Case 1 cont'd

- What would you recommend now?
 - A. Increase glyburide
 - B. Change NPH to glargine
 - C. Continue to increase NPH
 - D. Basal-prandial insulin
 - E. Check HBA1c

Case 1 cont'd

- **Increase NPH: A sensible choice**
- Basal-prandial Still probably overly complex
- Increase glyburide: Probably would be insufficient alone
- B, E: No clear reason for either of these

Case 1 Management, cont'd

- He was asked to increase NPH dose by 2 units every 3 days if fasting BG > 120 each time
- 2 months later
 - fasting BGs = 100 – 120
 - one fasting BG was 78
 - His predinner BGs were 96 - 154
 - Felt fatigued once when he skipped a meal
- His NPH dose was 75 units
- HBA1c was 6.3%

Case 1 cont'd

- What would you recommend now?
 - A. Decrease glyburide
 - B. Change NPH to glargine
 - C. No change
 - D. Basal-bolus insulin
 - E. Decrease NPH

Case 1 cont'd

- **Decrease NPH: A sensible choice**
- Switch to glargine: reasonable but not essential
- Basal-prandial: Not necessary
- Decrease glyburide: Less likely to decrease hypoglycemia risk
- No change: He is slightly over-treated, and some change should be made

The “Treat to Target” Trial: NPH vs. Glargine

- Randomized open-label trial of hs NPH vs hs glargine x 24 weeks in 756 overweight T2DM patients with HBA1c > 7.5%
- Duration of DM > 2 years
- Already on 1 or 2 oral agents

■ Riddle, Diabetes Care, 2003;26:3080-3086

Treat to Target Trial Protocol

If 2 day mean fasting BG is above target, increase insulin dose weekly

>141	increase insulin by 6-8 units
121-140	increase insulin by 4 units
100-120	increase insulin by 2 units
< 100	no change

If BG < 63 on more than one occasion decrease dose by 2 units

The “Treat to Target” Trial NPH vs. Glargine: Results

- ~60% attained A1C < 7% in each treatment group
- 25% fewer patients on G had nocturnal hypoglycemia (absolute risk 33% vs 26%; only difference was between 0200 and 0600)
- Symptomatic hypoglycemia was 21-48% lower with G
 - For all symptomatic events, 13.9 vs 17.7 events/pt-yr
 - For BG < 72, 9.2 vs 12.9 events/pt-yr
 - For BG < 56, 3.0 vs 5.1 events/pt-yr
 - “Severe hypoglycemia” per patient report: 2.5% with G, 1.8% with NPH

Case 2

- A 45 year old man presents with a 3 month history of fatigue and, more recently, polyuria.

- PMH notable for HTN, HIV, and gout.

- BG = 688 mg/dL

Last measured BG 15 months previously was normal.

- What information would help you choose starting therapy for his diabetes?

Case 2, cont'd

- Weight 110 kg
- Meals are “typical 3 meal per day” schedule, and consistent re: content and timing
- Serum creatinine 1.8 mg/dL
- HBA1c 11.5%

Case 2, cont'd

- What would you recommend to treat this patient?
 - A. Glipizide and metformin
 - B. Glipizide and pioglitazone
 - C. Glipizide and hs glargine
 - D. Twice daily pre-mixed insulin
 - E. Basal-prandial insulin

Initiating Insulin T2DM

- **Glipizide and hs glargine or twice-daily pre-mix are reasonable choices**
- Basal-prandial: Probably overly complex
- Glipizide and TZD: Might also work though quite high HBA1c makes it less likely
- Metformin contraindicated if Cr > 1.5 mg/dL

Case 2, cont'd

- Started on 70/30 NPH/Regular
 - 14 units pre-BF and 10 units pre-D
- *How would you choose a starting dose?*
- He was given a meter that does averages and a logbook and was trained in their use
- 1 week later, pre-BF and pre-D BGs in high 100s to low 200s

Initiating Insulin T2DM

- What would you recommend now?
 - A. Add glipizide
 - B. Add lunch time lispro
 - C. Increase dose of pre mixed insulin
 - D. Switch to basal-prandial insulin

Initiating Insulin: Type 2 DM

- **Increase pre-mix: the most logical choice**
 - Others would all help, but not the best choice
- Insulin increased to 14 units pre-BF and 14 units pre-D

Case 2, cont'd

- 1 week later, fasting BGs were 160-185. Pre-dinner BGs were more variable: 115-192 with most on the lower end.
- Insulin increased to 14 units pre-BF and 18 units pre-D

Case 2, cont'd

- 3 weeks later:
 - Fasting BG range past 2 weeks 112-147
 - 14 day mean BG 143, 30 day mean BG 169

Initiating Insulin T2DM

- What would you recommend now?
 - A. Add glipizide
 - B. Add lunch time lispro
 - C. Increase dose of pre mixed insulin
 - D. No change in regimen

Initiating Insulin T2DM

- **No change: The most logical choice**
- A, B, C: Any of these could be considered, but many patients will see further improvements at this point as they learn how to live with diabetes
- His HBA1c will not be stable for ~3 months
- Insulin continued without change
 - 3 months later HBA1c 6.7%
 - 1 year later HBA1c 7.3%

Starting premixed insulin in T2DM: INITIATE trial

- RCT of T2DM patients with A1c >8%, already on at least 1000 mg/day of metformin \pm other oral agents
- Mean diabetes duration 9 yr
- Mean baseline HBA1c 9.7%; mean fasting BG 250
- Study duration 28 weeks

Starting premixed insulin in T2DM INITIATE trial protocol

- Metformin and TZDs “optimized” (met to 1500 mg/day; pio to 30 mg/day) then **insulin added**
 - 70/30 aspart (“Novolog Mix 70/30”) 5-6 units before BF and D or
 - hs glargine 10-12 units
 - (used higher of the 2 doses if fasting BG \geq 180)

Starting premixed insulin in T2DM

INITIATE trial protocol, cont'd

- Upward insulin dose titration weekly for 12 weeks, then q 2 wk
 - For **70/30 aspart** group, change each dose based on premeal BGs (<80, decrease 2; 80-110, no change; 111-140, increase 2; 141-180, increase 4; >180, increase 6)
 - For **glargine** group, increase dose based on fasting BGs (<80, decrease 2; 80-110, no change; 111-140, increase 2-4; 141-180, increase 4-6; >180, increase 6-8)
 - Max daily increase 10 units or 10% of current total daily dose

INITIATE trial: Results

- Mean HBA1C at end of study:
 - 6.9% for 70/30 aspart (mean daily dose 77 units)
 - 7.4% for glargine (mean daily dose 51 units)
- Mean weight gain:
 - 5.4 kg 70/30 aspart
 - 3.5 kg glargine
- Hypoglycemia:
 - Minor:
 - 3.4 per pt-yr in 70/30 aspart
 - 0.7 per pt-yr in glargine
 - Major: only 1 event--in glargine group

Case 3

- A 70 year old presents with T2DM x 15 yrs
 - Rx: glipizide ER 10 mg BID for the past 10 years
 - HBA1c = 8.7%
- PMH: alcoholic cirrhosis with history of variceal bleeding and hepatic encephalopathy
- BG testing was very intermittent

Case 3, Management

- What would you do now?
 - A. Add metformin
 - B. Add hs glargine
 - C. Twice daily pre mixed insulin
 - D. Basal-bolus insulin
 - E. Get more data

Case 3, Management, cont'd

- **E: You need more data**
 - Current general medical status
 - Current HBA1c
 - Dietary and BG records: e.g. 3-5 day detailed record

Case 3, cont'd

- When seen 30 days later, HBA1c was 10.2%
- Analysis of meals showed:
 - His diet is fairly consistent
 - The patient generally eats BF. By his description, it is ~100 g of carb
 - Lunch is ~ 60 g of carb, usually beans and some salmon or meat
 - Dinner seems less consistent, ~ 30 g of carb
 - Evening snack of a sweet bread, some nights only
 - He does notice that his BG is high the next morning when he eats the sweet bread.
 - NOTE: it took about 10 minutes of clinic time to collect this information, and feel confident about it

Case 3: Management, cont'd

- What would you recommend to this patient now?
 - A: Add hs glargine
 - B: Pre meal rapid acting insulin
 - C: Twice daily pre mixed insulin
 - D: Basal-bolus insulin

Initiating Insulin: Type 2 DM

- **D: This will best address his needs, if he can deal with the complexity**
- It is OK (and often desirable) to start sequentially!
 - Even in type 1 DM
 - In patients with cirrhosis, basal dose needs are usually less than expected
 - For small doses, pen systems are more accurate

Insulin pen devices

- Portable “pen” style insulin administration devices
 - Increase compliance
 - May decrease vial wastage
 - 150 or 300 units per use vs. 1000 units per use
 - Improved ease of use vs. syringes + vial
 - More discreet for use in public
 - An option for visually or manually impaired patients

Proper insulin pen use

- Secure a needle tip to pen
 - Any size is fine though large people may need longer needle
- “Prime” the pen by wasting 2 units
 - Needs to be done before EACH injection
- Dial up dose and inject SC
- Leave needle under skin for 5 seconds then remove

“Tips” for use

- Change needle tip for each injection, or at least once daily
- Injection can be done through clothing if needed, though not ideal
- Disposable pens are easier to use than cartridges
- When calculating days supply for insurance purposes, add 6-10 extra units per day
- Refrigerate pens not in use; do not need to refrigerate pen in use

Looking at a BG log

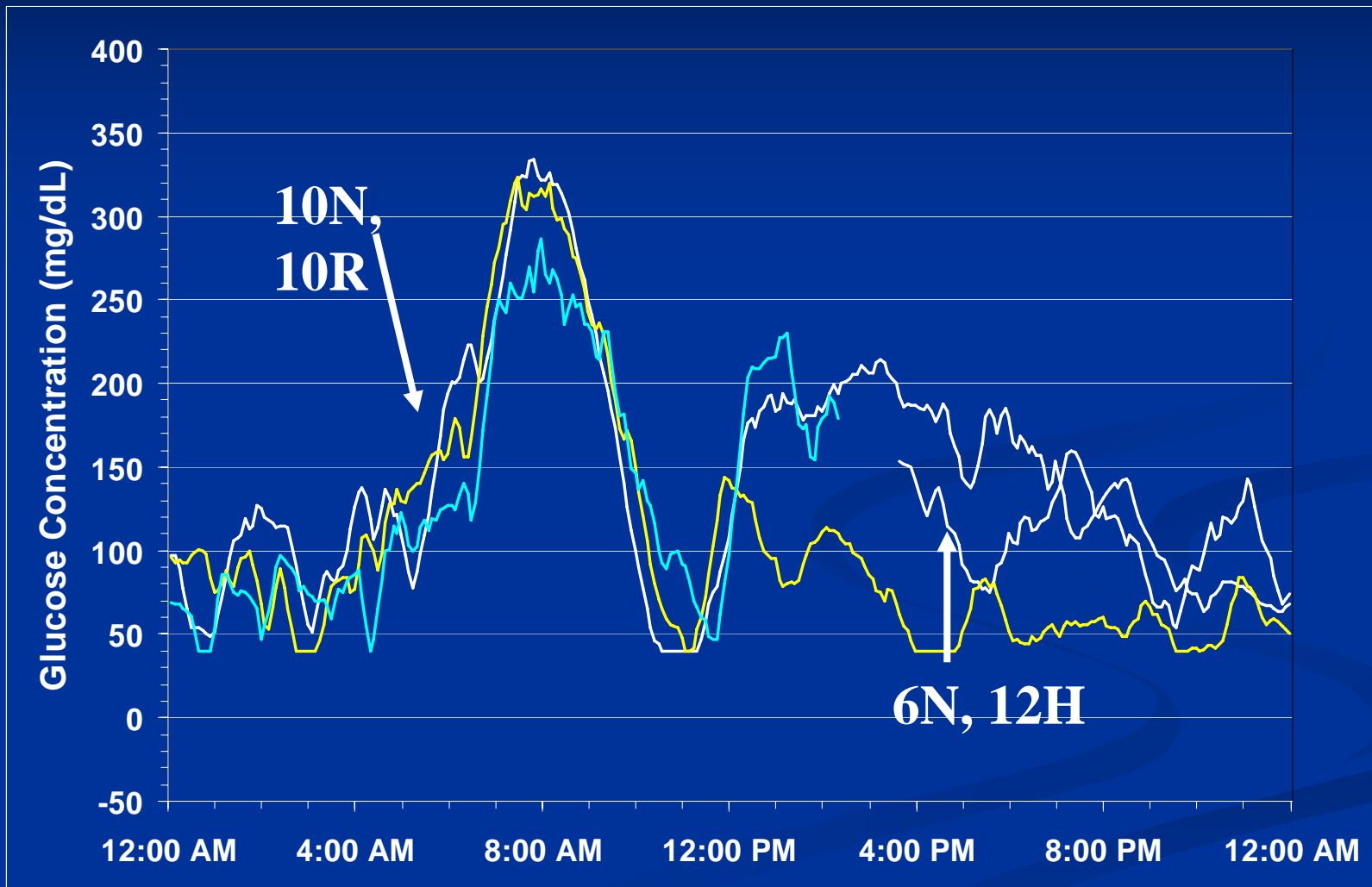
A. < 60; B. > 180; C. up or down

BB	AB	BL	AL	BD	AD
82	180	150	92	75	<i>290</i>
105	<i>224</i>	<i>205</i>	80	40!	<i>355</i>
<i>202</i>	158	<i>198</i>	103	65	<i>200</i>
100	<i>199</i>	140	66	58	<i>324</i>

- A. One hypo
- B. Almost 50% are well above target BG (< 140)
- C. Up after breakfast; down after lunch; up with dinner; down overnight

Evaluating CGMS data

58 y/o man, type 2 DM, HbA1c 7.5%



Case 3: Start Simply!

- Rx NovoLog FlexPen 4 units with BF and L
- 2 weeks later, add glargine 5 units hs
- 2 weeks after that, meter downloads show that
 - Mean pre-BF is 225 with a range 126 to 351
 - Mean pre-L is 369 with a range 266 and 472
 - Mean pre-D is 422 with a range 411 to 435
 - Aggregate mean is 266 with a range 126 to 477 (total of 41 tests in the past 30 days; most consistent was pre-BF)

Case 3, cont'd

- Increase glargine to 10 units hs
- 1 month later, based on BGs, increase aspart to 10 units before BF, 7 units before L, 3 units before D
- 1 month later, based on BGs, change aspart
 - 15 units before BF
 - 10 units before L
 - 6 units before D
 - AND increase glargine to 12 units hs

Case 3 cont'd

- 1 month later, he reports some episodes of shakiness at ~0530
- BG in clinic 299, approximately 1.5 hours postprandial
- Logbook shows
 - Pre-BF BGs in the low to mid 100s;
 - Pre-L BGs in the high 100s to mid 200s;
 - Pre-D BGs in the low to mid 200s

Case 3 cont'd

- What would you recommend to this patient now?:
 - A: Add more glipizide
 - B: Change glargine to BID
 - C: Add twice daily pre mixed insulin
 - D: Make further adjustments in basal-bolus insulin

Case 3 cont'd

- **D: Assuming he can continue to cope with the complexity, this will best address his needs**
 - Reduce glargine to 10 Units hs
 - Change aspart to
 - 15 units before BF
 - 12 units before L
 - 6 units before D

Case 3 cont'd

■ 6 weeks later he returns, still having an occasional “low” in the early AM. His pre-L and pre-D BGs are in the mid to high 100s. He is currently taking:

- glargine 10 units at hs
- aspart 15 units before BF, 12 units before L, 6 units before D

■ Recommendations:

- Stop glipizide
- Reduce glargine to 9 units at hs
- Adjust aspart upward

Case 3 cont'd

- He returns 4 months later. He has had 2 hypos, 1 in the middle of the night
- Insulin:
 - glargine 9 units hs;
 - aspart 20 - 15 - 7
- HBA1c 7.1%; 12 months later 6.8%

Case 3 cont'd

- If patients have low BGs at night on glargine:
 - Verify that the dose is right
 - Change glargine to morning dosing (1 study)
 - Switch to insulin detemir in morning only or BID with lower dose at night

Case 4

- An indigenous man with obesity, CHF, asthma, and epilepsy sees you for uncontrolled T2DM. A1c is 9% on metformin (1 gm TID) and glargine (120 units hs).
- You start him on prandial insulin.
 - 3 months later he is not willing to count carbs
 - he is frustrated with 4 shots per day and having to use 2 pens;
 - A1c 8.2%.
 - Meals are pretty predictable.
- What are your options now?

123 Trial

- Enrolled 100 pts with T2DM for ≥ 1 yr
 - HBA1c 7.5%-10% on 2 oral drugs OR 1 oral drug plus basal insulin < 60 units per day
- Open label observational study
- Used BIAsp 30, a premixed NPA/A combination, also marketed as NovoLog Mix 70/30

■ Garber. Diabetes, Obesity, and Metab 2006;8:58-66

123 trial: Phase 1

- Start insulin 12 units before dinner OR transition from basal to pre-D insulin at 70-100% of previous dose
- Increase insulin dose by 3 (111-140), 6 (141-180), or 9 units (>180), every 3-4 days based on mean fasting BG
- Maintain dose unchanged when fasting BG 80-110
- Check HBA1c at 16 weeks; if $\leq 6.5\%$, stop (N=21)

123 trial: Phase 2

- Stop oral secretagogues
- Start insulin before BF, 3 (FBG \leq 110) or 6 (FBG $>$ 110) units
- Increase pre-BF insulin dose by 3 (111-140), 6 (141-180), or 9 units ($>$ 180), every 3-4 days based on mean pre-D BG
- Hold dose when pre-D BG 80-110
- Check HBA1c at 16 weeks; if \leq 6.5%, stop (N=28)

123 trial: Phase 3

- Start insulin 3 units before lunch
- Increase pre-L insulin dose by 3 (141-180) or 6 units (>180), every 3-4 days based on mean 2 hour post lunch BG
- Hold dose when 2 hour post lunch BG 100-140
- Check HBA1c at 16 weeks; an additional 25 achieved HBA1c $\leq 6.5\%$
 - Total of 74/100 subjects met this target

Case 5

- A 59 year-old man with diet-controlled T2DM (A1c 6.9%) and a history of MI and gout develops polymyalgia rheumatica requiring prednisone.
- Random BG in the office the next week is 250 mg/dL. Cr is 1.6.
- You start him on 10 units of glargine hs
- Fasting BGs are all < 100 mg/dL, but his A1c 3 months later is 8.3%

Steroid related hyperglycemia

- The best thing to do now is:
 - A. Increase insulin glargine
 - B. Add pioglitazone
 - C. Switch to pre-mix insulin BID
 - D. Add prandial insulin

Steroid related hyperglycemia, cont'd

- Switching to pre-mix is probably the best because steroids classically worsen carbohydrate intolerance and increases post-prandial glucose >>> fasting glucose.
- Prandial insulin with metformin or low-dose pre-mix is often the best solution
- Increasing glargine is likely to increase nighttime hypoglycemia
- TZDs work but often greatly exacerbate weight gain and have risks for CHF and IHD

Adjusting once-daily basal insulin: patient instructions

- **Goal:** We want your insulin dose high enough so that all your fasting (morning) sugars are less than 100 mg/dL.
- **Why:** Controlling your diabetes (A1c < 7) helps stop nerve/foot, kidney, and eye problems.
- **Taking your Insulin**
 - Take your insulin (glargine)* at the same time every day—usually bedtime (or at breakfast or dinner)
- **Changing your dose**
 - Check and write down your blood sugar every morning before you eat**
 - If fasting sugar is > 100 mg/dL increase your insulin dose by 1 unit every day
 - If you have a “hypo” (BG < 63 mg/dL) stop increasing your dose and talk to your diabetes team
- **If you get low blood sugars (“hypos” or hypoglycemia)**
 - First check your sugar level
 - Then eat or drink something (7 jelly beans OR ½ glass soft drink)
 - Write down your sugar level and what happened
- **Call your Diabetes Care Team at (phone number) if:**
 - Your sugars are regularly high and you aren’t feeling well
 - You are sick, have gained or lost weight, or are having lots of stress, your insulin dose may need to be changed
 - You have a low blood sugar and need the help of someone else to get your sugar up

*This can also be done with protaphane or insulin detemir at bedtime.

**If giving insulin in the morning, you need to check a “fasting” sugar at the longest food-free interval later in the day.

Advancing treatment REVIEW

A patient with T2DM on metformin +
SU + insulin glargine QD titrated to
fasting glucose = < 100 mg/dL)

A1C still > 7%

Progressing from once-daily insulin glargine to basal-prandial insulin

Add small amounts of rapid pre-meal insulin (e.g. 2-4 units per meal) as needed to keep post-prandial (1-1.5 hours post meal under 140)

Changing to aspart pre-mix (NovoLog 70/30) from once-daily insulin

If post-prandial glucose is over 140 mg/dL after breakfast and tea

Use same number of units

Divide based on biggest meal and highest sugars, e.g. if tea is the biggest meal and after tea sugars are highest, you may want to give more at dinner-time (80 kg patient on 60 units glargine → 30 BID or 25 units pre-breakfast and 45 units pre-dinner)

Have patient check post-meal for several days after initiation to assess control

Adjust pre-mix insulin: beware hypos at mid-day and mid-night

if pre-dinner is high and no day-time hypos → increase breakfast insulin 2 units every 3-7 days

if pre-breakfast is high and no night hypos → increase pre-dinner insulin 2 units every 3-7 days

If post lunch and pre-dinner glucose are still high after adjustments for pre-breakfast and pre-dinner

add lunchtime rapid aspart (usually 4-6 units to start) OR

add a small injection of pre-lunch aspart pre-mix (4-6 units)

Changing from pre-mix (NovoLog mix 30) to basal-prandial insulin (glargine + rapid)

- Add up 24 hour insulin dose
 - Divide total by 2
- Use half as glargine; give once-daily at bedtime (or morning)
- Divide the other half as pre-meal rapid aspart (with each meal);
 - Divide according to meal size (especially carbohydrate, e.g. bread, potato, pasta, rice so that more would be given for high carb breakfast vs. tuna salad at lunch)

Papers that give more detail about these messages

Hirsch, IB, et al. A real world approach to insulin therapy in primary care practice. Clin Diabetes 2005;23(2):77-86.

Mooradian AD, et al. Narrative review: A rational approach to starting insulin therapy. Annals Internal Medicine 2006;145(2):125-134.