Type 2 – The Complicated Diabetes

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Type 2 Diabetes
The Complicated Diabetes

Objectives:

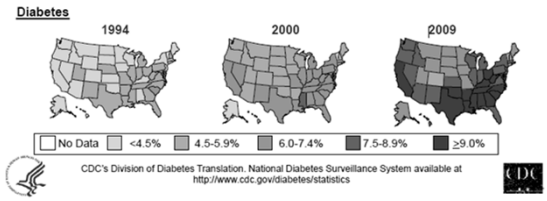
1. Type 2 – More than Hyperglycemia
2. Goals of Therapy
3. Common Meds for Type 2
4. Insulin in Type 2
5. Pumps in Type 2

Poll Question 1

- According to the CDC, what best describes the future prevalence of diabetes in the U.S.?
  a. 50% of people above the age of 20 will have type 2 diabetes.
  b. The rate of type 1 and type 2 diabetes will triple by the year 2050.
  c. 1 out of 3 persons will have type 2 diabetes by the year 2050.
  d. 1 out of 2 persons will have diabetes by the year 2050.

Diabetes in America 2015

- 29 million or > 9.3%
- 27% don't know they have it
- 37% of US adults have pre diabetes (86 mil)



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CDC Announces

35% of Americans will have Diabetes by 2050

Boyle, Thompson, Barker, Williamson
2010, Oct 22:8(1)29
www.pophealthmetrics.com

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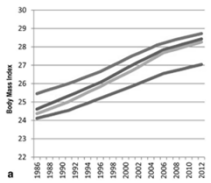
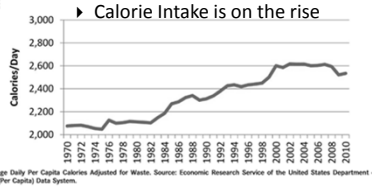
U.S. Weight - 68% overweight or obese



- ~~34% BMI 25-29~~
- 34% BMI 30 +
- 1/3 of all overwt people don't get diabetes
- We burn 100 cals less a day at work
- Overall, food costs ~ 10-15% of income
- Calorie Intake is on the rise



Average Daily Per Capita Calories Adjusted for Waste. Source: Economic Research Service of the United States Department ... ility (Per Capita) Data System.

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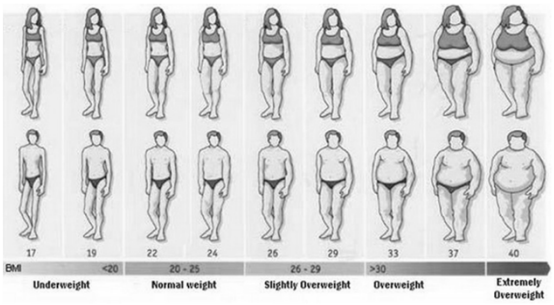
BMI Categories



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Type 2 in Kids

TODAY Treatment Options for type 2 Diabetes in Adolescents & Youth

- 7 fold increase 1990
- 1 in 6 overwt kids (age 12- 19) have prediabetes.
- ~2,500 to 3,700 new cases in U.S. annually.
- Highest risk: very obese, minority, female, low socioeconomic status, limited education
- Environmental changes to urgently needed
- Treatment options – Metformin and Insulin

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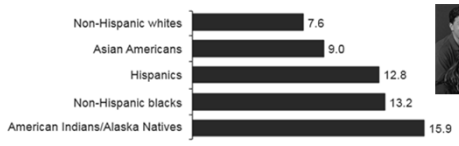
Age-adjusted Diabetes Prevalence

20 yrs or older, by race/ethnicity— U.S. 20014

Age-adjusted* percentage of people aged 20 years or older with diagnosed diabetes, by race/ethnicity, United States, 2010–2012



*Based on the 2000 U.S. standard population.
Source: 2010–2012 National Health Interview Survey and 2012 Indian Health Service's National Patient Information Reporting System.

- Among Hispanic adults, the age-adjusted rate of diagnosed diabetes was 8.5% for Central and South Americans, 9.3% for Cubans, 13.9% for Mexican Americans, and 14.8% for Puerto Ricans.
- Among Asian American adults, the age-adjusted rate of diagnosed diabetes was 4.4% for Chinese, 11.3% for Filipinos, 13.0% for Asian Indians, and 8.8% for other Asians.
- Among American Indian and Alaska Native adults, the age-adjusted rate of diagnosed diabetes varied by region from 6.0% among Alaska Natives to 24.1% among American Indians in southern Arizona.

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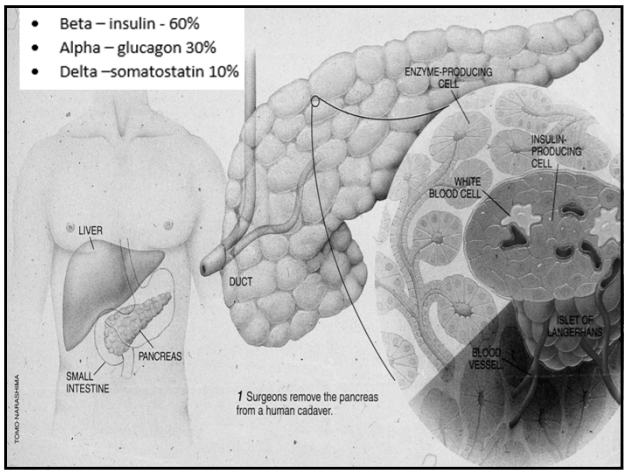

Hormones Effect on Glucose

Hormone	Effect
Glucagon (pancreas)	↑
Stress hormones (kidney)	↑
Epinephrine (kidney)	↑
Insulin (pancreas)	↓
Amylin (pancreas)	↓
Gut hormones - incretins (GLP-1) released by L cells of intestinal mucosa, beta cell has receptors)	↓

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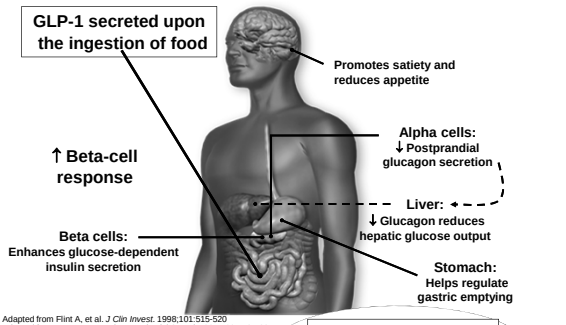
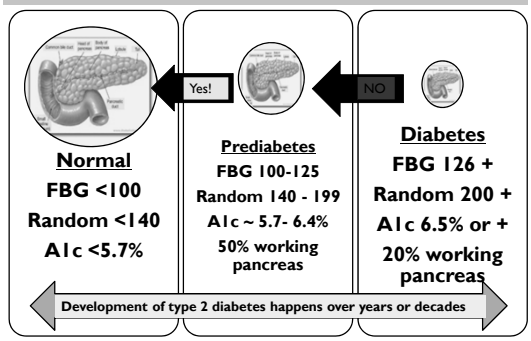
GLP-1 Effects in Humans
Understanding the Natural Role of Incretins



Adapted from Flint A, et al. *J Clin Invest.* 1998;101:515-520
Adapted from Larsson H, et al. *Acta Physiol Scand.* 1997;160:413-422
Adapted from Nauck MA, et al. *Diabetologia.* 1996;39:1546-1553
Adapted from Drucker DJ. *Diabetes.* 1998;47:159-169

Natural History of Diabetes



Diabetes 2 - Who is at Risk?

(ADA Clinical Practice Guidelines)

1. Testing should be considered in all adults who are overweight (BMI ≥ 25) and have additional **risk factors**:
   - First-degree relative w/ diabetes
   - Member of a high-risk ethnic population
   - Habitual physical inactivity
   - PreDiabetes
   - History of heart disease

Diabetes 2 - Who is at Risk?

(ADA Clinical Practice Guidelines)

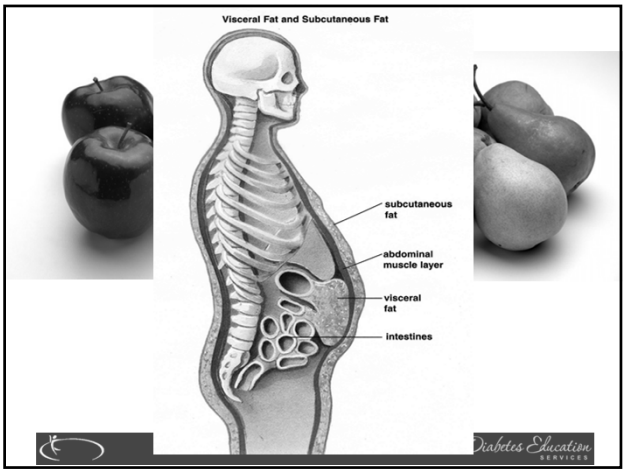
Risk factors cont'd

- HTN - BP > 140/90
- HDL < 35 or triglycerides > 250
- baby >9 lb or history of Gestational Diabetes Mellitus (GDM
- Polycystic ovary syndrome (PCOS)
- Other conditions assoc w/ insulin resistance:
  - Severe obesity, acanthosis nigricans (AN)

Life Study – Mrs. Jones

Mrs. Jones is 62 years old, overweight and complaining of feeling tired and urinating several times a night. She is admitted with a urinary tract Infection. Her WBC is 12.3, glucose 237. She is hypertensive with a history of gestational diabetes. No ketones in urine.

- What are her risk factors, signs of diabetes
- What type of diabetes does she have?
- Does she have insulin resistance?



Factors Associated with Insulin Resistance

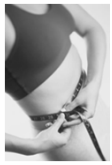
- Abdominal obesity
- Sedentary lifestyle
- Genetics / Ethnicity
- Gestational Diabetes
- Polycystic ovary syndrome
- Acanthosis Nigricans
- Obstructive Sleep Apnea
- Cancer
- Heart Disease

Poll Question 2

- Which of the following BEST describes insulin resistance?
  a. Lack of sufficient insulin receptors on fat and muscle cells.
  b. Visceral adipose tissue.
  c. A physiological condition where insulin becomes less effective at lowering blood glucose levels.
  d. Excessive triglyceride levels

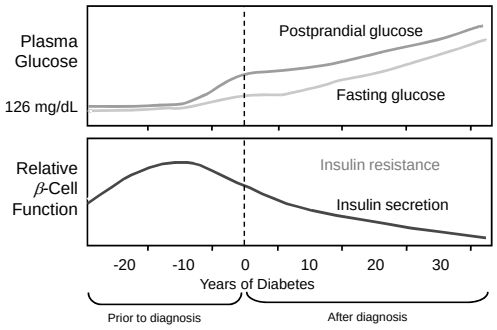
Cardio Metabolic Risk - 5 Hypers -

- Hyperinsulinemia (resistance)
- Hyperglycemia
- Hyperlipidemia
- Hypertension
- Hyper"waistline"emia (35" women, 40" men)



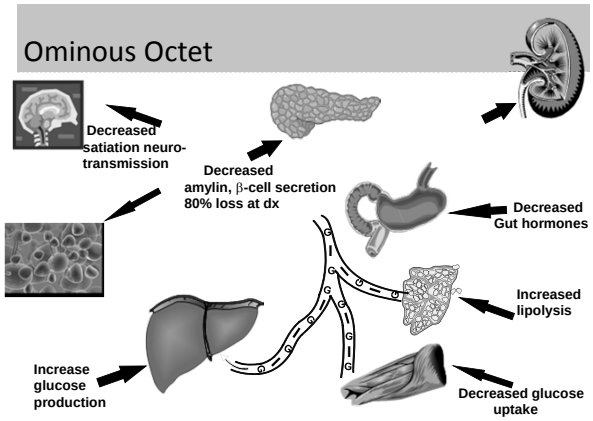
Manifestations of Insulin Resistance

Natural Progression of Type 2 Diabetes



Adapted from Bergenstal et al. 2000; International Diabetes Center.

Ominous Octet



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What kind of Diabetes?

- Pt is 58, states she has had type 1 diabetes for 18 years. Quit smoking a year ago and gained about 20 lbs. BMI 25.
- Meds
  - Humalog 18-23 units before each meal
  - Lantus 28 units at bedtime
  - Metformin 500mg TID
- What tests would you recommend?

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Double Diabetes – An Increasing Problem

- Defined as a person who presents w/ features of both type 1 and type 2 diabetes.
- Someone with type 1 diabetes gains significant weight and manifests the clinical features of insulin resistance and type 2
- or in those with type 2 who develop autoantibodies to beta cells and manifest type 1 (esp in kids)

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What type of Diabetes?

- 72 Years old
- A1c 3 months prior 6.2%
- A1c now 13.9%
- BMI 24.5
- Lost about 10 pounds over last month

Latent AutoImmunity Diabetes in Adults (LADA)

- Antibody positive to 1-2 of below
  - GAD-65 autoantibodies
  - Insulin Autoantibodies
  - Islet Cell antigen-2
- Adult Age at onset
- Usually need insulin w/in first 6 months of diagnosis
- Early insulin therapy may preserve beta cell function

Diabetes Care 26:536-538, 2003
Jerry P. Palmer, MD and Irl B. Hirsch, MD

LADA Clinical Features Compared to Type 2

Feature	LADA	Type 2
Age <50	63%	19%
Acute hyperglycemia	66	24
BMI < 25	33	13
Hx of autoimmune dx	27	12
Family hx autoimmune	46	35

Practical Diabetology March 08, Unger MD

Gestational DM ~ 7% of all Pregnancies

- GDM prevalence increased by
  - ~10–100% during the past 20 yrs
- Native Americans, Asians, Hispanics, African-American women at highest risk
- Immediately after pregnancy, 5% to 10% of GDM diagnosed with type 2 diabetes
- Within 5 years, 50% chance of developing DM in next 5 years.

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ABC's of Diabetes

A1C

Blood Pressure

Cholesterol

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Glucose and BP Control Matter

- 1% decrease in A_1c reduces microvascular complications by 35%
- 1% decrease in A_1c reduces diabetes related deaths by 25%
- B/P control (144/82) reduced risk of:
  - Heart failure (56%)
  - Stroke (44%)
  - Death from diabetes (32%)

Lancet 352: 837-865, 1998

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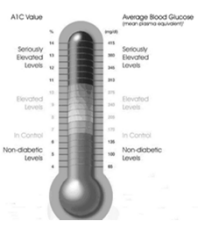
Glycemic Targets

- **Adult non pregnant A1c goals**
  - **A1c < 7%** - a reasonable goal for adults.
  - **A1c < 6.5%** - may be appropriate for those without significant risk of hypoglycemia or other adverse effects of treatment.
  - **A1c < 8%** - may be appropriate for patients with history of hypoglycemia, limited life expectancy, or those with longstanding diabetes and vascular complications.



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A1c and Estimated Avg Glucose (eAG) 2008

A1c (%)	eAG
5	97
6	126
7	154
8	183
9	212
10	240
11	269
12	298

Order teaching tool kit free at diabetes.org

eAG = 28.7 x A1c-46.7 ~ 29 pts per 1%

Translating the A1c Assay Into Estimated Average Glucose Values – ADAG Study
Diabetes Care: 31, #8, August 2008

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"Legacy Effect"

- For participants of DCCT and UKPDS
  - long lasting benefit of early intensive BG control prevents
    - microvascular complications
    - Macrovascular complications (15-55% decrease)
  - Even though their BG levels increased over time
  - Message – Catch early and Treat aggressively

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Poll 3

- What best sums up the ADA targets for those with diabetes?

A. A1c less than 7%, glucose less than 150
B. Before meal glucose 70-130
C. Post meal glucose less than 200
D. A1c less than 7%, post meal glucose <180

ABCs of Diabetes –

- A1c less than 7% (avg 3 month BG)
  - Pre-meal BG 80-130
  - Post meal BG <180
- Blood Pressure < 140/90
- Cholesterol
  - DM and 40 yrs, start statin
  - HDL >40
  - Triglyceride < 150
- E xercise, Education
- H ealthy Eating

ADA Step Wise Approach to Hyperglycemia 2015

- Start with lifestyle coaching
- Add Metformin
- Next step: Metformin and add 1-2 more meds based pt and A1c
- If A1c 9% or more
  - 3 meds (ie Metformin, glyburide and Januvia)
  - Metformin plus basal insulin / GLP-1 Agonist
  - Basal/Bolus – Multiple daily injections (MDI)

Metformin – 1st agent of choice

- **Action:** decrease hepatic glucose (glycogen)
- Metformin (Glucophage)
  - Starting dose: 500 BID, max 2500mg daily
  - Metformin XR - extended release – less GI upset
  - **Efficacy:**
    - Decrease fasting plasma glucose 60-70 mg/dl
    - Reduce A1C 1.0-2.0%
  - Benefits / Issues
    - Cheap, no weight gain; some lose weight, lowers LDL, no hypo
    - Not indicated if creat > 1.4-1.5 or GFR < 60 (cleared by kidney)

Sulfonylureas - Squirts

- Action: Increase endogenous insulin secretion throughout day
- Efficacy:
  - Decrease FPG 60-70 mg/dl
  - Reduce A1C by 1.0-2.0%
- Side Effects:
  - Weight gain, hypoglycemia
- Benefits:
  - Cheap, effective

DPP-4 Inhibitors – "Incretin Enhancers"

Januvia (sitagliptin) – Tradjenta (linagliptin)
Onglyza (saxagliptin) Nesina (alogliptin)

- **Action:**
  - Increase insulin release w/ meals
  - Suppress glucagon
- **Dosing**: Januvia – 100mg a day
  Onglyza – up to 5mg a day
  Tradjenta – 5mg a day
  Nesina – up to 25 mg a day
- **Efficacy:** Decreases A1c by 0.6 -0.8%
- **Benefits/ Issues**: weight neutral, no hypo, few side effects. Expensive

Incretin Mimetics
Byetta, Bydureon, Trulicity, Tanzeum

- **Action (synthetic gut hormone)**
  - Insulin release in response to meal
  - Slows gastric emptying
  - Causes Satiety – promotes wt loss
  - Preserves Beta Cells
- **Details:**
  - Daily and long acting version - 1x week injection
  - **Efficacy:** Decreases A1c by 0.5 – 1.6%, wt by 3lbs +
- **Benefits/Issues** – wt loss, no hyp. Expensive, N/V
  - □ Pancreatitis Warning – report signs immediately

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SGLT2 Inhibitors- "Glucoretics"

- **Action**: "Glucoretic" decreases renal reabsorption in the proximal tubule of the kidneys (reset renal threshold and increase glycosuria)

SGLT2 Inhibitors • Decrease glucose reabsorption in kidneys • "glucoretic."	Canagliflozin (Invokana) Dapagliflozin (Farxiga) Empagliflozin (Jardiance)	100–300 mg once daily 5–10 mg once daily 10–25 mg once daily

- Benefits: Lowers A1c 0.7 – 1.5%, lowers wt 1-3 lbs, no hypo
- Issues: Can initially lower GFR, monitor kidney function and lytes. Watch for hypotension/ GU infections. Expensive

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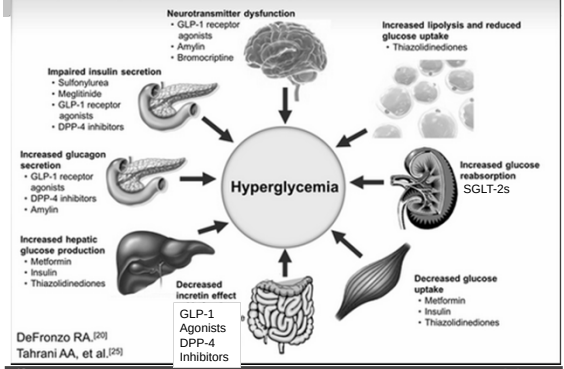
Hyperglycemia in Type 2 Diabetes



GLP-1 Agonists
DPP-4 Inhibitors

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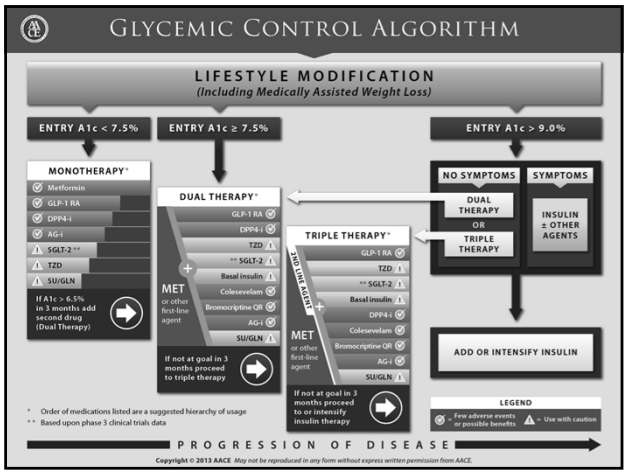
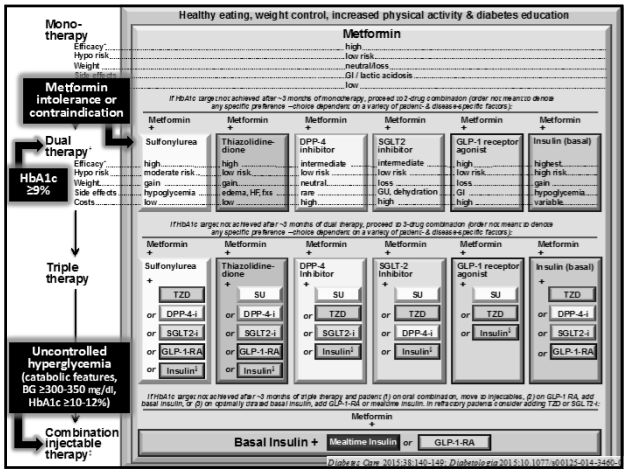
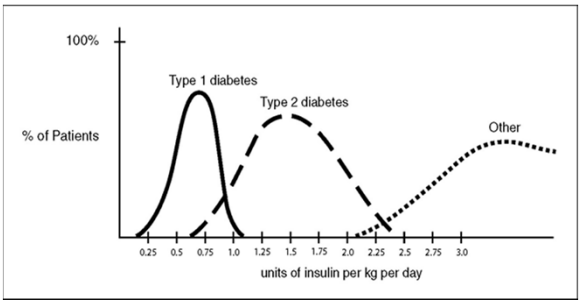




Insulin Dosing Type 1 & 2



U-500 Insulin: When More With Less Yields Success: *Diabetes Spectrum March 20, 2009 vol. 22 no. 2 116-122*

More than 200 units a day?

Medscape

Source: Am J Health-Syst Pharm © 2010 American Society of Health-System Pharmacists

Consider u-500 High Potency Insulin

5 x's the concentration of u100

- 500 units per mL vs 100 units per mL
  - How much- When converting from u100?
  - Take total daily dose and divide by 5
    - 200 units a day/5 = 40 units a day of u500
    - 300 units a day/5 = ____ units a day of u500
  - 20 mL a vial. 500 units per mL= 10,000 units/vial
  - Costs ~ ~~$400~~ $1,200 per vial – less expensive unit for unit?
  - Less volume

U-500 Insulin: When More With Less Yields Success: *Diabetes Spectrum March 20, 2009 vol. 22 no. 2 116-122*

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U-500 Insulin Caution

- High alert medication
  - Protect against hypoglycemia
- Confusing to convert dose and maintain accuracy
- Off label use for insulin pumps

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U-500 Conversion for Pump Sets using U-100 Concentration

Conversion Chart for Use of u500 Insulin in Pump Set for u100 Insulin Concentration

Setting of Basal Rates using u100 Concentration Setting for u500 insulin in Pump
u/hr

U100 insulin	3.0	3.5	4.0	4.5	5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0	9.5	10.0	10.5	11.0	11.5	12.0
U500 insulin	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4

Divide basal rate of u100 insulin by 5 to get rate using u500 insulin

Giving Boluses of u500 Insulin Using the u100 Concentration Setting in the Insulin Pump

U100 insulin	5.0	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95
U500 insulin	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10	11	12	13	14	15	16	17	18	19

Divide bolus amount using u100 insulin by 5 to get bolus amount using u500 insulin

Carbohydrate:insulin ratio using u500 insulin

Multiply gms of CHO in insulin:CHO ratio using u100 insulin by 5 to get ratio using u500 insulin, ie. 1u/2 gm CHO using u100 insulin equals 1u/10 gm CHO using u500 insulin

U100	1:1	1:2	1:3	1:4	1:5		2:1											
U500	1:5	1:10	1:15	1:20	1:25		2:5											

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Advantages of Using an Insulin Pump: ADA Website

- Eliminates unpredictable effects of intermediate- or long-acting insulin
- Allows exercise without having to eat large amounts of carbohydrate
- Flexibility with food
- Minimizes severe low blood glucose episodes
- Eliminates individual insulin injections
- Outperform MDI in improving A1C

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Disadvantages

- Hooked up to something
- Site irritation, infection
- More monitoring?
  - For type 2, avg frequency was 3.8 times a day (OpT2mise)
- Cost?
  - Break even analysis showed cost offset by ~ 2yrs through less insulin and med use.

care.diabetesjournals.org DIABETES CARE, VOLUME 36, SUPPLEMENT 2, AUGUST 2013 S219

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Type 2 Pump Candidates?

- Severe insulin resistance
- Poor glycemic control despite sufficient insulin titration and adherence to diet and exercise.
- Has ability to cope with pump with absence of cognitive or operative disability
- Personal willingness and ability to monitor blood glucose levels.

If you are already insulin resistant, why give more insulin?

- Yes, type 2 diabetes is a situation of insulin resistance, but also insulin deficiency
- When pts are glucose toxic (BG in the 300s), they may initially require higher doses of insulin, but as toxicity diminishes, insulin requirements diminish
- One strategy to overcome insulin resistance is through physiologic insulin replacement therapy.
- The pump helps to achieve glucose control with less insulin

Quality of Life - QOL

- Older adults – MDI or CSII had similar quality of life scores
- Younger Adults- CSII improved QOL scores
- Less hospitalization and ER room visits

Summary of Benefits- Opt2mise Study

- No increase rate of hypo as compared to multiple daily injections
- Insulin dose cut by ~ 20% when using pump
- A1c decreased by 0.7% compared to MDI
- Results in cost savings
- Less hospital and ER Visits

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Case Study

- 38 yr old,
- BMI 52, Weighs 200kg
- A1c – 10.2%, BG 290s for mos
- Insulin – 100 units Lantus
- Oral Meds: max dose glipizide + metformin
  - MD is contemplating starting her on insulin pump
  - Stop glipizide.
  - Continue Metformin to promote glycemic control and limit weight gain.
- Use ADA Algorithm to determine dosing

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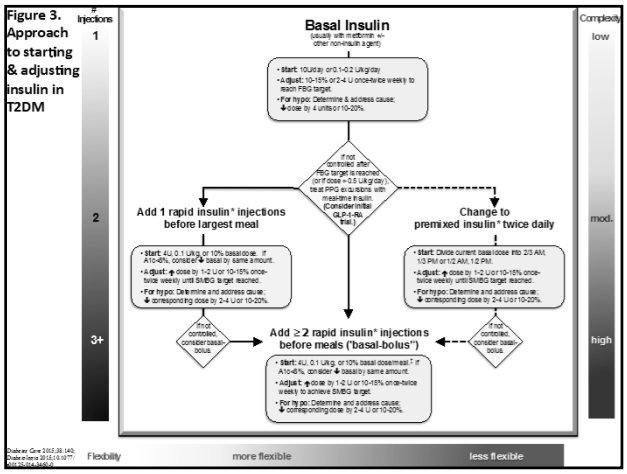

Figure 3. Approach to starting & adjusting insulin in T2DM

ADA Algorithm to determine dose

- BMI 44, Weighs 200kg
- A1c – 10.2%, BG 290s for mos
- Insulin – 100 units Lantus
- Basal 100 units of Lantus
  - For safety 100 x .75 = 75 total units (AACE)
  - 75 units/24 hours = 3.13 units per hour
- Bolus – start with largest meal
  - 10% of basal or 0.1u/kg = 10 -20 units bolus then add additional meal boluses as needed.

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Based on Body Weight

- BMI 44, Weighs 200kg
- Total daily dose options:
  - Current body weight x 0.5 = 100 units
  - Current body weight x 0.8 = 160 units
- Basal = 0.5 of daily dose / 24 hrs
  - 100 x 0.5 = 50units 50/24hrs = 2.1 units an hour
  - 160 x 0.5 = 80unts 80/24hrs= 3.3 units an hour
- Bolus = the other half/ 3 meals
  - 50/3 meals = 16.6 units per meal
  - 80/3 meals = 26.6 units per meal
- Or carb counting + correction?

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Best Approach Based on Individual

- In a French study, better glycemic control was achieved using:
  - 1 or 2 basal rates
  - Fixed bolus dosages
- Unnecessarily complex regimens may serve as a deterrent for some patients

Insulin Pump for Type 2 Diabetes

Use and misuse of continuous subcutaneous insulin infusion in type 2 diabetes

In contrast to these results, two randomized crossover studies with small

care.diabetesjournals.org DIABETES CARE, VOLUME 36, SUPPLEMENT 2, AUGUST 2013 S219

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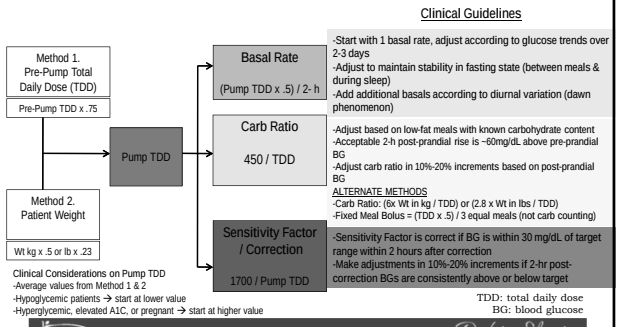
AACE Calculations for Insulin Pump Settings



No one is Unmotivated

…. to lead and long and healthy life

- **These are the 3 usual Critical Barriers**
  - Perceived worthlessness
  - Too many personal obstacles
  - Absence of support and resources

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Thank You

- Questions?
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