

**JACK L. SNITZER, D.O.**

Internal Medicine Board Review Course

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**ENDOCRINE PANCREAS**

# JACK L. SNITZER, D.O.

Peninsula Regional Endocrinology

1415 S. Division Street

Salisbury, MD 21804

Phone:410-572-8848

Fax:410-572-6890

E-Mail: DSNITZER1@COMCAST.NET

# DISCLOSURES

- Speaker bureau for:  
BI-Lilly  
Janssen

# Endocrine Pancreas

- n Alpha Cells: Glucagon
- n Beta Cells: Insulin
- n Delta Cells: Somatostatin
- n D1 Cells: Vasoactive intestinal Polypeptide (VIP)
- n F Cells: Pancreatic Polypeptide (PP)
- n G Cells: Gastrin

# GLUCAGONOMA

-Glucagonoma

Causes increased glucose production.

Rare, often malignant tumors.

Classic Rash: Necrolytic Migratory  
Erythema

Painful glossitis, angular stomatitis.

Tx: Surgery, Octreotide

# INSULINOMA

-Insulinoma

Spontaneous hypoglycemia. 80% are benign. Usually very small tumors. Second most common pancreatic tumor found in MEN 1.

# INSULINOMA

-Insulinoma

Dx: elevated insulin and C-peptide level with simultaneously low glucose and symptoms.

-Fasting glucose <50 mg/dl.

Tx: Surgery. Octreotide to palliate.

# Hypoglycemia: other causes in non-diabetics

- Reactive hypoglycemia (generally in obese patient with metabolic syndrome)
- Malnutrition (celiac disease, eating disorder, etc.)
- Cortisol insufficiency (adrenal or pituitary cause)
- Nesidioblastosis (for instance: post-gastric bypass: islet cell hyperplasia)



# Hypoglycemia: other causes in non-diabetics

- Liver disease
- Surreptitious, malicious or inadvertent use of insulin. In this case, when the BG is low, insulin level will be high and C-peptide level will be low. Need to obtain these levels before treating with glucose or glucagon.
- Surreptitious use of insulin secretagogue. Insulin and c-peptide levels will be high when BG is low.
- Glucometer error (glucose meters are inaccurate when the BG is low); or hypoperfusion of the fingers

# Hypoglycemia: other causes in non-diabetics

- Remember: early hypoglycemia symptoms (shakes, sweats, anxiety, hunger) are due to catecholamine release.
- Conditions that can mimic hypoglycemia Sx's but no consistent proof of low BG at the time of symptoms:
  - NMH (Neurologically Mediated Hypotension); POTS (Postural Orthostatic Tachycardia Syndrome); Seizures; panic attacks/anxiety; cardiac arrhythmia; hunger; mastocytosis; monoclonal gammopathy; medication side effect, pheochromocytoma, etc.

# SOMATOSTATINOMA

-Somatostatinoma

Rare.

Somatostatin inhibits release of many substances.

No specific syndrome.

Often malignant.

Tx: Surgery

# VIPoma

-VIPoma

Vasoactive Intestinal Peptide secretion.

Severe watery diarrhea.

Rare.

Often malignant.

Tx: Surgery

# PANCREATIC POLYPEPTIDE

## -Pancreatic Polypeptide

Inhibits gall bladder contraction and pancreatic enzyme secretion.

No syndrome or symptoms.

Rare.

May be used in future as marker for pancreatic tumors.

# GASTRINOMA

## -Gastrinoma

Gastrin stimulates gastric acid secretion.  
Most common pancreatic tumor associated with MEN 1.

Zollinger-Ellison Syndrome: peptic ulcer disease, increased gastric acidity.

Secretin test to confirm Dx.

Octreotide scan. Can be malignant.

Tx: Surgery, Proton-pump inhibitors.

# DIABETES MELLITUS

- FROM LATIN:
- DIABETES: URINE
- MELLITUS: HONEY SWEET
  
- Insulin aids in conversion of carbohydrate into energy for intracellular energy. It is an anabolic hormone with salt retention properties.

# NORMAL BLOOD SUGAR LEVELS

- FBS:<100
- 2 Hour Post-challenge or post-prandial: <140
- A1c: 5.5% or less



# DIABETES MELLITUS: diagnosis

## -DIABETES MELLITUS - Diagnosis

- FBS 126 or higher (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours. Result might need to be confirmed by repeat testing.
- 2 hour plasma glucose 200 or higher (11.1 mmol/L) during an OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose 200 or higher.
- A1c: 6.5% or higher.

# Pre-Diabetes

- Fasting hyperglycemia:

  - FBS: 100-125 mg/dl

- Glucose intolerance:

  - 2 hour post-challenge: 140-199 mg/dl

- A1c: 5.6% to 6.4%

# DIABETES COMPLICATIONS

Complications: Fatigue, infections, blindness (retinopathy), atherosclerotic cardiovascular disease, nephropathy (proteinuria, microalbuminuria, macroalbuminuria), neuropathy (peripheral and autonomic), erectile dysfunction, etc.

(microalbuminuria: 30-300 mcg/mg)

(macroalbuminuria: over 300 mcg/mg)

# **TYPE 1 DIABETES MELLITUS**

## **TYPE 1 DIABETES MELLITUS**

Autoimmune attack on islet cells.

Often:

GAD-65 antibody positive (glutamic acid decarboxylase) (formerly islet cell ab)

and/or

Insulin Auto-Antibody (IAA) positive

# TYPE 1 DIABETES MELLITUS

-Type 1 Diabetes mellitus

Treatment:

-Insulin (BID, TID, QID). MDI: multiple daily injections.

Mealtime rapid-acting insulin (for carbs) plus high glucose correction dose of rapid-acting insulin; plus basal insulin (to counteract the hepatic production of glucose).

-Insulin pump.

# DCCT

- n **Diabetes Control and Complications Trial (DCCT)** showed that tight glycemic control in patients with type 1 DM can reduce complications as much as 70%. This effect is long-lived (“legacy effect”)

# INSULIN: NPH

NPH: Human insulin.

intermediate acting; relatively  
inexpensive; peaks and troughs.

# INSULIN: Basal

Glargine (Lantus) and Detemir (Levemir);  
Glargine U-300 (Toujeo); Degludec U-200  
(Tresiba):

Basal, peakless insulin.

Analogue insulin.

Once or twice daily.

Basic function is to counteract hepatic glucose  
production.

Should be titrated to maintain stable BG overnight (i.e.:  
FBS should roughly equal the prior night's HS  
BG, assuming no food or rapid-acting insulin at  
nighttime).



# INSULINS: rapid-acting

Human Regular (R): (U-100 or U-500).

Longer-acting and later peak than rapid-acting insulin analogues.

Function is to prevent carbohydrate intake from raising glucose level and to treat elevated glucose levels.

Relatively inexpensive.

The only insulin used intravenously.

# INSULIN: rapid-acting analogues

Lispro (Humalog), Aspart (Novolog), and Glulisine (Apidra)

Relatively expensive.

Onset more rapid than Regular insulin.

Effect is gone sooner than Regular insulin.

# TYPE 2 DIABETES MELLITUS

Insulin resistance caused by genetics and abdominal obesity.

Adipokine dysfunction.

Hyperinsulinemia years before diagnosis

HAIR-AN (hyperandrogenism, insulin resistance, acanthosis nigricans)

Polycystic Ovary Syndrome

Metabolic Syndrome

Insulin Resistance Syndrome

# METABOLIC SYNDROME

- Metabolic Syndrome (Insulin Resistance Syndrome)
  - Insulin Resistance
  - Hyperinsulinemia
  - Low HDL; Small, dense LDL, Elevated triglycerides
  - Glucose intolerance
  - Elevated uric acid
  - Hyperandrogenism in females
  - Anovulation (PCOS)
  - Obesity

# METABOLIC SYNDROME

## **ATP III classification**

Abdominal obesity

Waist circumference: men >40 inches;  
women >35 inches

Triglycerides: 150 or higher

HDL: men <40; women <50;

BP: 130/85 or higher

FBS: 110 or higher

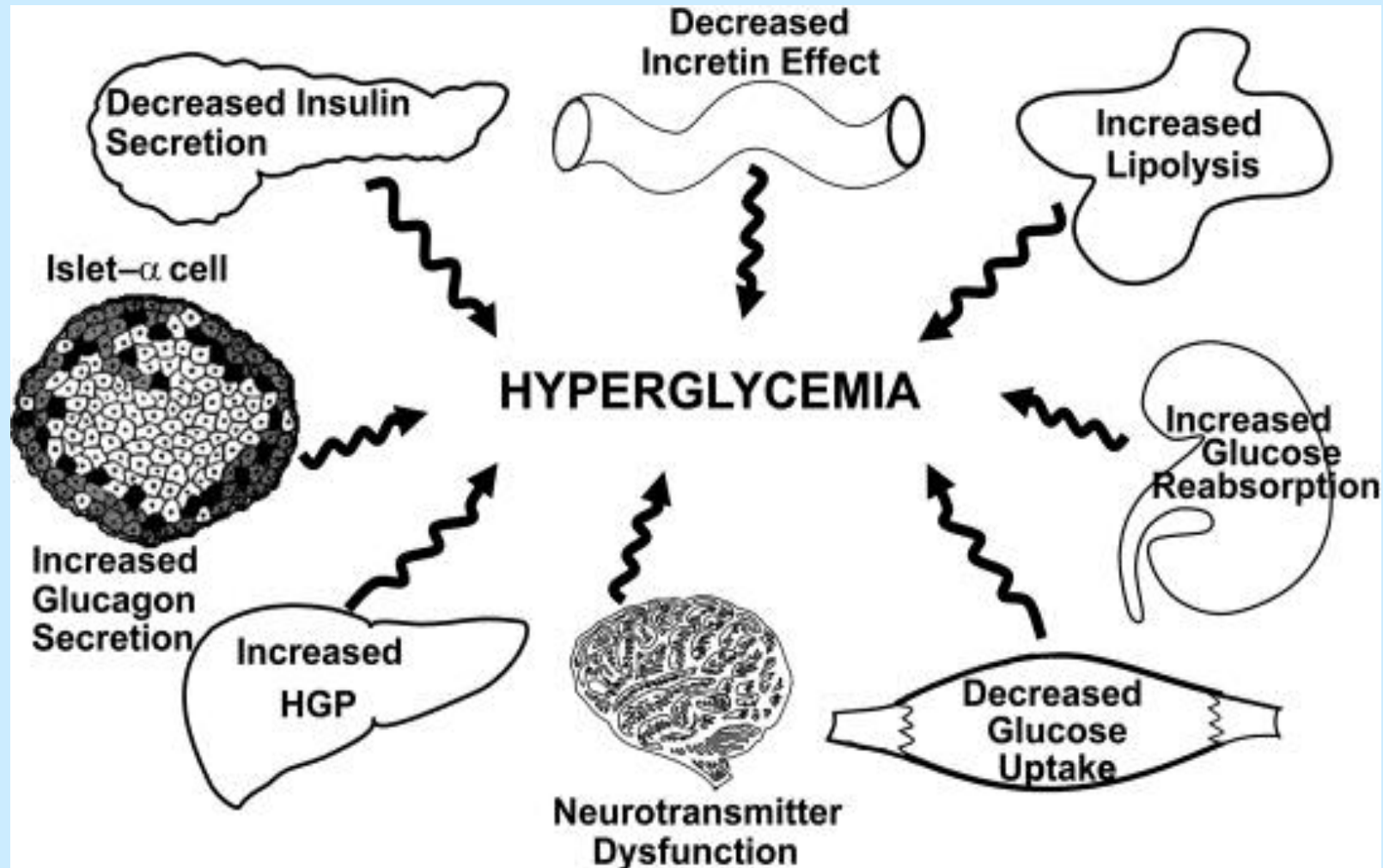
# ACANTHOSIS NIGRICANS



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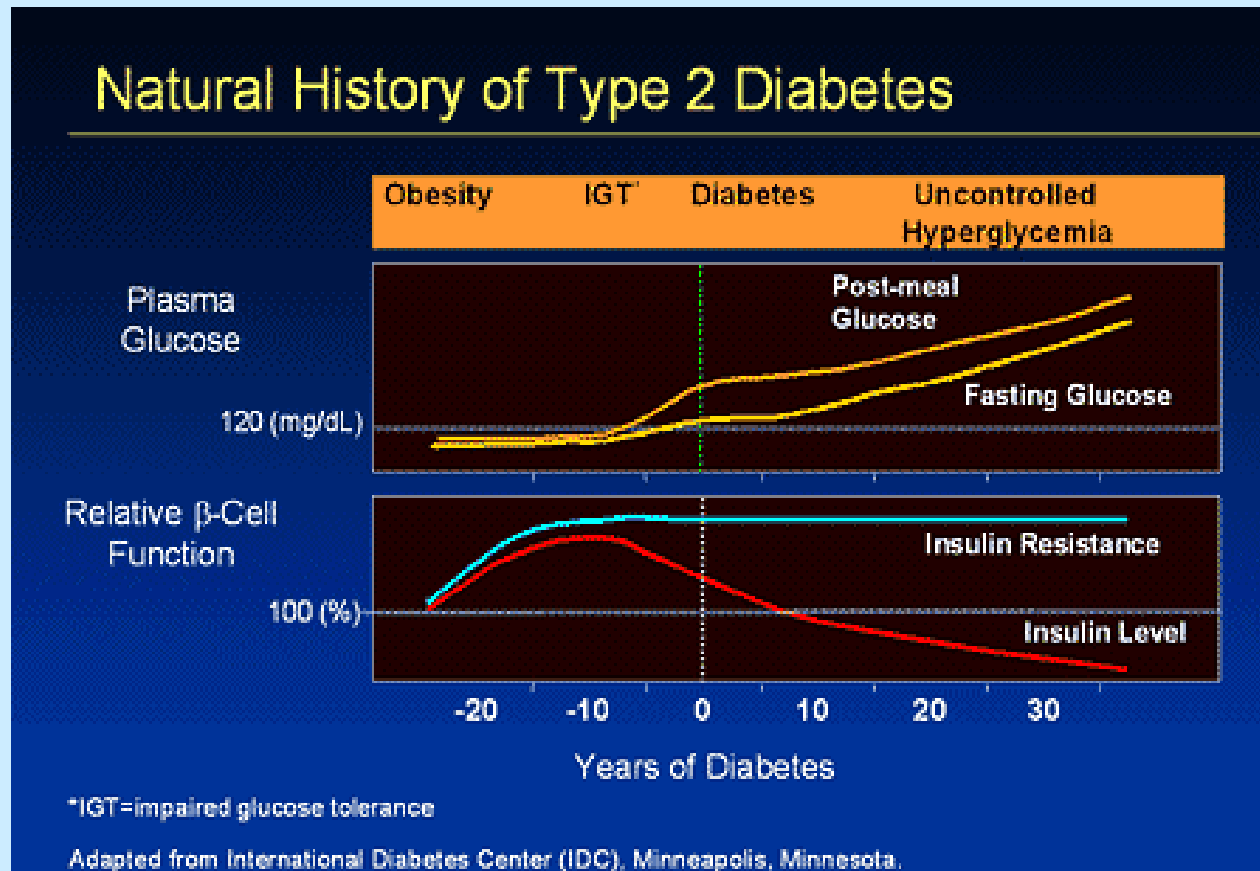
- Acanthosis nigricans is the finding most pathognomonic for insulin resistance

# OMINOUS OCTET in Type 2 Diabetes (DeFronzo)





# Natural History of Type 2 Diabetes



# ADA RECOMMENDATIONS

- Yearly dilated eye exam
- Evaluate feet each visit
- Check sensation in feet (10 gram filament)
- Dental exam regularly
- A1c 2-4 times yearly
- Urine microalbumin **RATIO (mcg/mg or mg/g)** yearly (Note: LabCorp code 140285: use this code or LabCorp will do the test without a ratio, which is a useless test); normal range is <30 mg/g (mcg/mg).
- Aspirin use if not contraindicated
- ACE inhibitor or ARB, especially if microalbuminuria or if hypertensive

- Lipid goals

# A1c

- Goals of therapy  
AAACE: A1c: 6.5% or better if can achieve this safely. Less tight control in the young, elderly and those with hypoglycemia unawareness and marked co-morbidities probably advisable due to risk from low blood sugars
- ADA: A1c <7% if can achieve safely

# TYPE 2 DIABETES STUDIES

United Kingdom Prospective Diabetes Study (UKPDS) showed reduced microvascular complications with tighter control. (Macrovascular complications were lower, but not significantly.) There was a “legacy effect”, however.

DIABETES PREVENTION PROGRAM (DPP):  
Exercise and metformin delayed development of type 2 diabetes from pre-diabetes. Exercise did better than metformin.

# DIABETES miscellaneous

- CONCEPTS
  - Post-prandial hyperglycemia
  - Hepatic Glucose production
  - Endothelial dysfunction
  - Inflammation
  - Free fatty acids
  - Cytokines and adipocytokines (adiponectin, Leptin, TNF, IL-6, resistin, ghrelin, etc.)
  - Incretins (intestinal hormones- GLP-1, GIP, oxyntomodulin, etc.)

# T2DM MEDICATIONS: metformin

1. Biguanides (metformin)-decrease hepatic glucose production.

Side effects: Lactic acidosis; B12 deficiency; GI upset; Diarrhea (less with extended release).

Contraindicated if Creatinine 1.4 or higher (females) or 1.5 or higher (males) or if significant hepatic dysfunction or in CHF.

Might decrease risk of some cancers.

Delays conversion of pre-diabetes into diabetes (DPP study).

# METFORMIN

New guidelines:

Can start metformin if eGFR is  $>45$ .

Can continue metformin if eGFR is 30 or higher.

Stop metformin if eGFR is under 30.



# METFORMIN

- Guidelines recommend stopping metformin if contrast is given (for two days) since contrast might worsen renal function, thereby increasing the risk of metformin induced lactic acidosis.
- Guidelines suggest that you might need to check creatinine after two days to see if can resume metformin.

# METFORMIN

- **NOTE: FIRST DRUG TO USE IN A PATIENT WITH TYPE 2 DIABETES IF NO CONTRA-INDICATIONS.**
- Use at diagnosis of type 2 diabetes

# Metformin ER

- Ghost pill will be in the stool, but this is expected and the active ingredient is none-the-less absorbed.

# TYPE 2 DM MEDICATIONS

## 2. Sulfonylureas-insulin secretagogues

(glipizide, glimepiride, glyburide):

stimulate insulin production; avoid glyburide;

main side effects: hypoglycemia;

black box warning: ?increase cardiovascular morbidity/mortality;

Note: avoid glyburide (too much hypoglycemia, especially as one ages, and possible adverse cardiovascular effects)

# TYPE 2 DM MEDICATIONS

## 3. Alpha-glucosidase inhibitors

(acarbose: Precose, miglitol: Glyset):

delay absorption of carbohydrates;

side effects: gas

# TYPE 2 DM medications: TZD's

## 4. Thiazolidinediones (pioglitazone: Actos; rosiglitazone: Avandia):

Improve insulin resistance;

PPAR-gamma receptor agonist;

Side effects: edema, CHF, weight gain

Worsen bone density

Actos: 10/100,000 risk of urinary  
bladder cancer: recent studies  
question any risk

# TZD's

- **CONTRA-INDICATED IN NYHA CLASS 3 AND 4 CHF**

# **TYPE 2 DM MEDICATIONS**

5. Meglitinides (repaglinide: Prandin,  
nateglinide: Starlix): short-acting  
insulin secretagogue;

side effects: hypoglycemia



# TYPE 2 DM MEDICATIONS

## 6. DPP-4 inhibitors.

Sitagliptin (Januvia); Saxagliptin (Onglyza); Linagliptin (Tradjenta); Alogliptin (Nesina);

increase GLP-1 and GIP levels; Insulin production “on demand”. Suppress inappropriate post-prandial glucagon production;

Precautions: ?pancreatitis; ?pancreatic cancer (recent studies show no link to pancreatic cancer); increased hospitalization for CHF in some studies. Not sure if true or if class effect.

# TYPE 2 DM MEDICATIONS

## 7. GLP-1 agonists (SC)

Exenatide (Byetta) twice daily; Liraglutide (Victoza) once daily; Bydureon: extended release exenatide (once weekly); Trulicity (dulaglutide) weekly.

Effects: insulin secretion on demand; suppress post-prandial glucagon production. Suppress appetite. Cause earlier satiety. Weight loss.

Side effects: Nausea, vomiting, ?pancreatitis;  
?medullary thyroid cancer/C-cell hyperplasia;  
?pancreatic cancer

# Victoza

- Recent study (LEADER) showed decrease in cardiovascular mortality (primary prevention)

# Type 2 DM MEDICATIONS

- 8. SGLT2 (sodium-glucose co-transporter 2) inhibitors:

Invokana (canagliflozin)

Farxiga (dapagliflozin)

Jardiance (empagliflozin)

MOA: Increase urine excretion of glucose.

Side effects: dehydration, vaginal or penile yeast infections; UTI's, hyperkalemia (Invokana); ?bladder cancer (Farxiga)

# SGLT-2 inhibitors

- Jardiance study (EMPA-REG OUTCOME) showed a decrease in cardiovascular mortality (in patients with cardiovascular disease). This was a secondary prevention trial.
- Invokana Study (CANVAS) showed a decrease in cardiovascular mortality in primary prevention. Also showed increase in lower extremity amputations.

# T2DM MEDICATIONS

9. Combination therapy (pills plus insulin)
10. Symlin (approved to be used in a patient on insulin (see discussion later)
11. Insulin (side effects: hypoglycemia, weight gain [muscle or fat], injection site lipodystrophy)
13. Intensive insulin therapy (MDI: multiple daily injections)
14. Insulin Pump therapy

# TYPE 1 DM MEDICATIONS

1. Insulin
2. Amylin
3. Intensive insulin therapy (MDI)
4. Insulin pump therapy

# TYPE 1 DM MEDICATIONS

4. Pramlintide (Symlin)- This is Amylin.  
Amylin is normally co-secreted with insulin by the islet cells.  
Suppresses post-prandial glucagon production. Suppresses appetite. Weight loss.  
Approved to be used in type 1 diabetes or type 2 diabetes if patient is on insulin.  
Side effects: Nausea



# INSULINS

-BASAL (analogue)

Levemir (detemir); Lantus (glargine);

Toujeo (glargine U-300); Tresiba (degludec U-200).

-Intermediate acting insulin (Human)

NPH

-Rapid-acting insulin (Human)

Regular (U-100)

Regular (U-500)

# INSULINS

-Rapid-acting insulin analogues

Novolog (aspart)

Humalog (lispro): U-100 and U-200.

Apidra (glulisine)

-Pre-mixed: Humalog mix 75/25; Humalog mix 70/30; Humalog mix 50/50; Novolog mix 70/30; Humulin or Novolin or Reli-On 70/30; Humulin 50/50;

# INSULINS

- Humulin R U-500

five times concentrated Regular insulin.  
used in patients who require very large  
doses of insulin.

This actually has a longer  $T_{1/2}$  than R U-100  
insulin.

Comes as a pen or vial.

U-500 syringes now available.

# INSULINS

- INHALED INSULIN

Afrezza: rapid acting inhaled Human R insulin.

Cartridges: 4, 8 and 12 units.

# Inhaled insulin



# Inhaled insulin



# INTENSIVE INSULIN THERAPY

- MDI (Multiple Daily Injections)
- Basal insulin once or twice daily and rapid-acting insulin analogues with each meal
- Important to estimate if patient is severely insulin deficient
- Important to know if patient's BG is highest fasting, after meals, or both.
- Important to determine if patient is insulin resistant or sensitive.

# INTENSIVE INSULIN THERAPY

- Intensive insulin therapy
  - DCCT found intensive insulin therapy much more effective at reducing A1c and complications in patients with type 1 DM
  - 3, 4, or more injections daily or insulin pump
  - Basal/Bolus concept
  - Basal insulin once (or twice) daily and rapid-acting insulin with meals
  - NPH at HS (and probably in AM) and rapid-acting insulin with meals: Not considered our usual intensive regimen.
  - Insulin pump therapy (uses rapid-acting insulin analogue only)



# INTENSIVE INSULIN THERAPY

- We have a better understanding of how to use basal/bolus insulin based on what we have learned from insulin pump therapy
- Carbohydrate counting
- Matching rapid-acting insulin to carbs and blood sugar level (labor intensive, but must try to teach patient these concepts if possible)
- Diabetes education; MNT (Medical Nutrition Therapy)
- Fingerticks at various times in the day (for instance, before and 2 hours after meals)

# BASAL INSULIN

- Glargine (Lantus) and Detemir (Levemir) and Toujeo and Tresiba.
- Function is basically to control hepatic glucose production
- Generally over-dosing these, particularly since we tend to keep increasing the dose until the morning BG is good, ignoring the HS (post-meal) blood sugar
- Should be titrated to maintain stable FBS compared to bedtime BG, assuming no food or rapid-acting insulin at nighttime.

# BASAL INSULIN

- *If the Basal insulin dose is correct, the HS BG should roughly equal the FBS, assuming no food in between and no rapid-acting insulin at nighttime; i.e.: the BG should not rise or drop much overnight; and the BG should be stable in a fasting state throughout the day, assuming no exercise.*

# BASAL INSULIN

- Whenever we start a patient on basal insulin, we need to think about what is be done doing to control their BG after meals, since basal insulin does not effectively do this.
- 80% of patients on basal insulin will need rapid-acting insulin before one or more meals.
- **DON'T TITRATE THE BASAL INSULIN JUST BASED ON THE FASTING BLOOD SUGAR OR THE A1C.**

# BASAL INSULIN

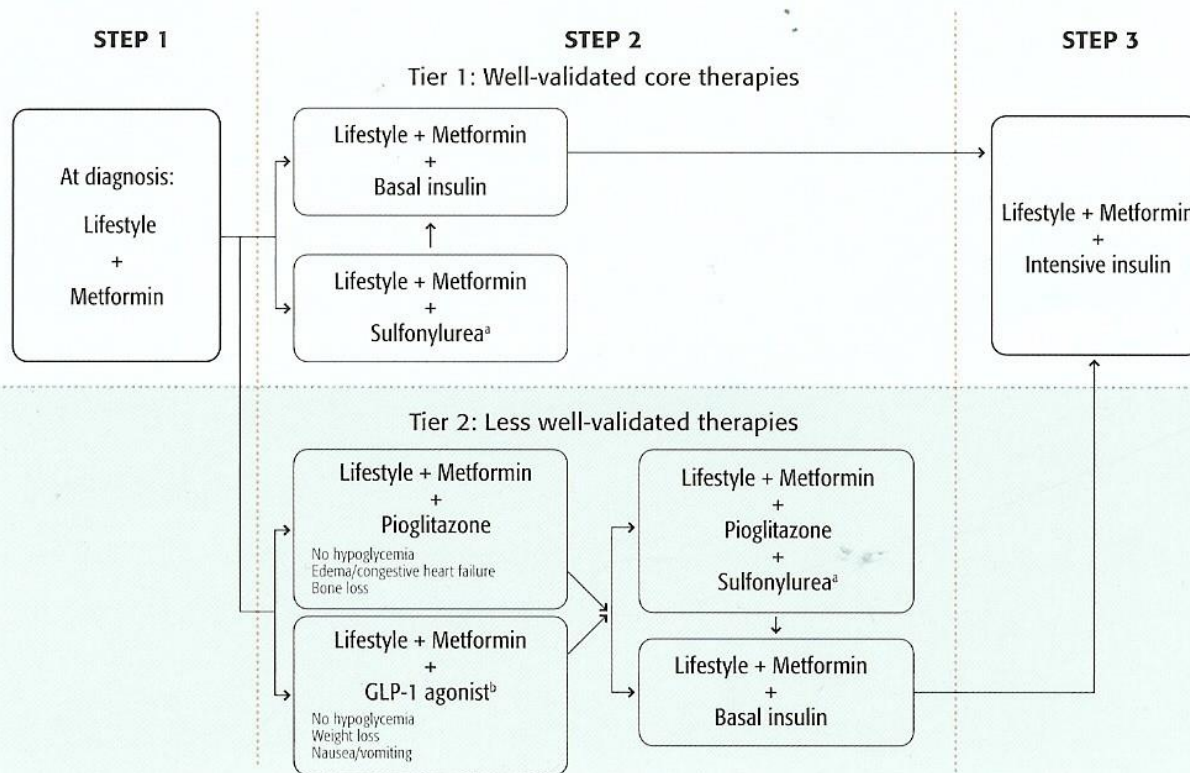
- In order to effectively use, need to have patient check BG at HS and the next AM regularly (and eventually several times daily)
- Many individuals, particularly very insulin deficient patients, will not be able to be on just basal insulin. They will need basal/bolus insulin. So, when we start a patient on basal insulin, we need to assume that they might need MDI (multiple daily injection) therapy with basal and bolus insulin

# Intensive Insulin Therapy (MDI)

- Results are very user dependent, labor intensive, data driven
- Therefore, using the diabetes education resources (CDE's, nutritionists, etc.) is often important to enhance the patient's understanding and in becoming a partner in their own DM care

# 2008 ADA-EASD CONSENSUS ALGORITHM

## Algorithm for the management of type 2 diabetes<sup>1</sup>



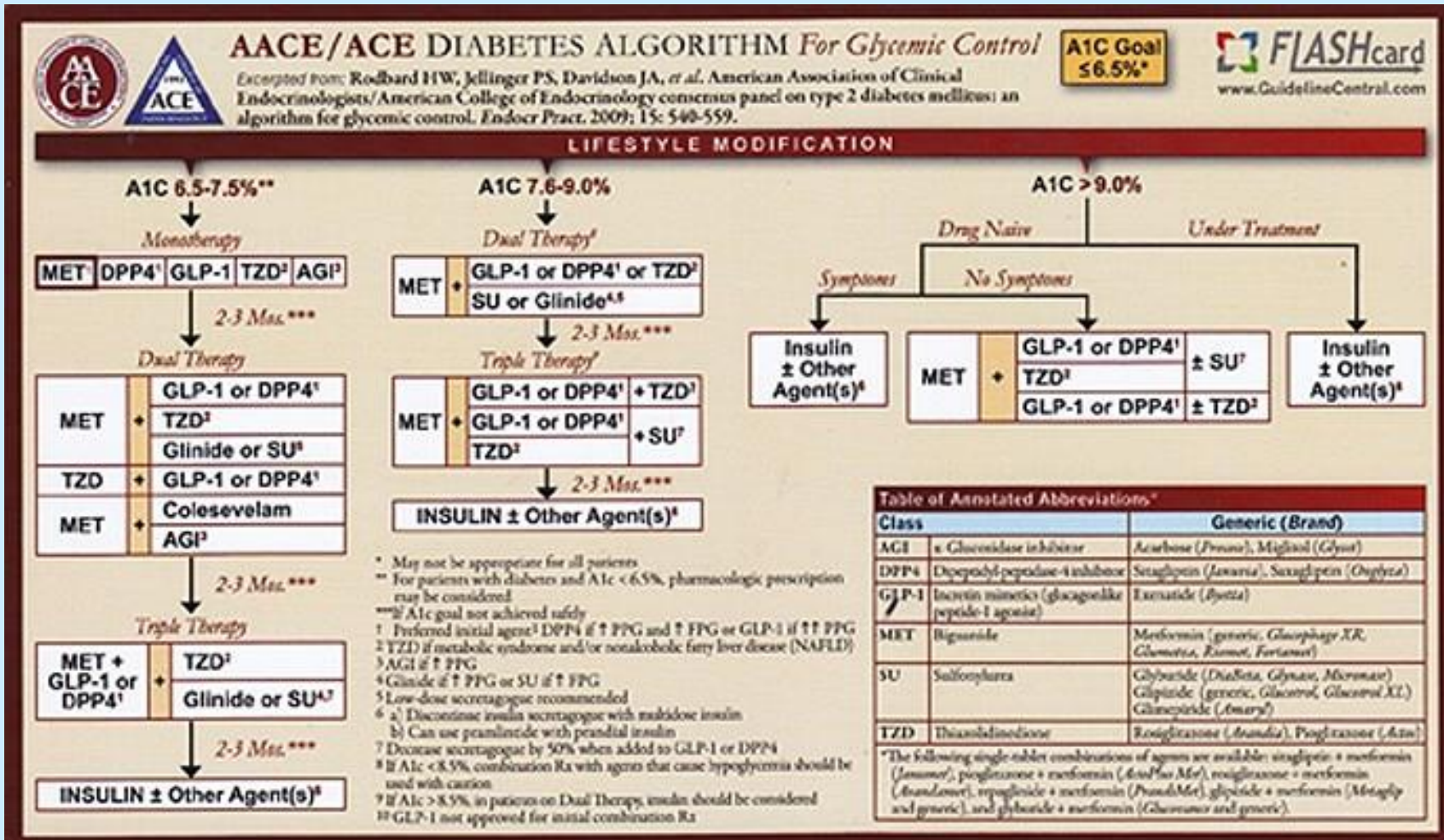
<sup>a</sup>Sulfonylureas other than glybenclamide (glyburide) or chlorpropamide.

<sup>b</sup>Insufficient clinical use to be confident regarding safety.

Abbreviation: GLP-1, glucagon-like peptide-1.

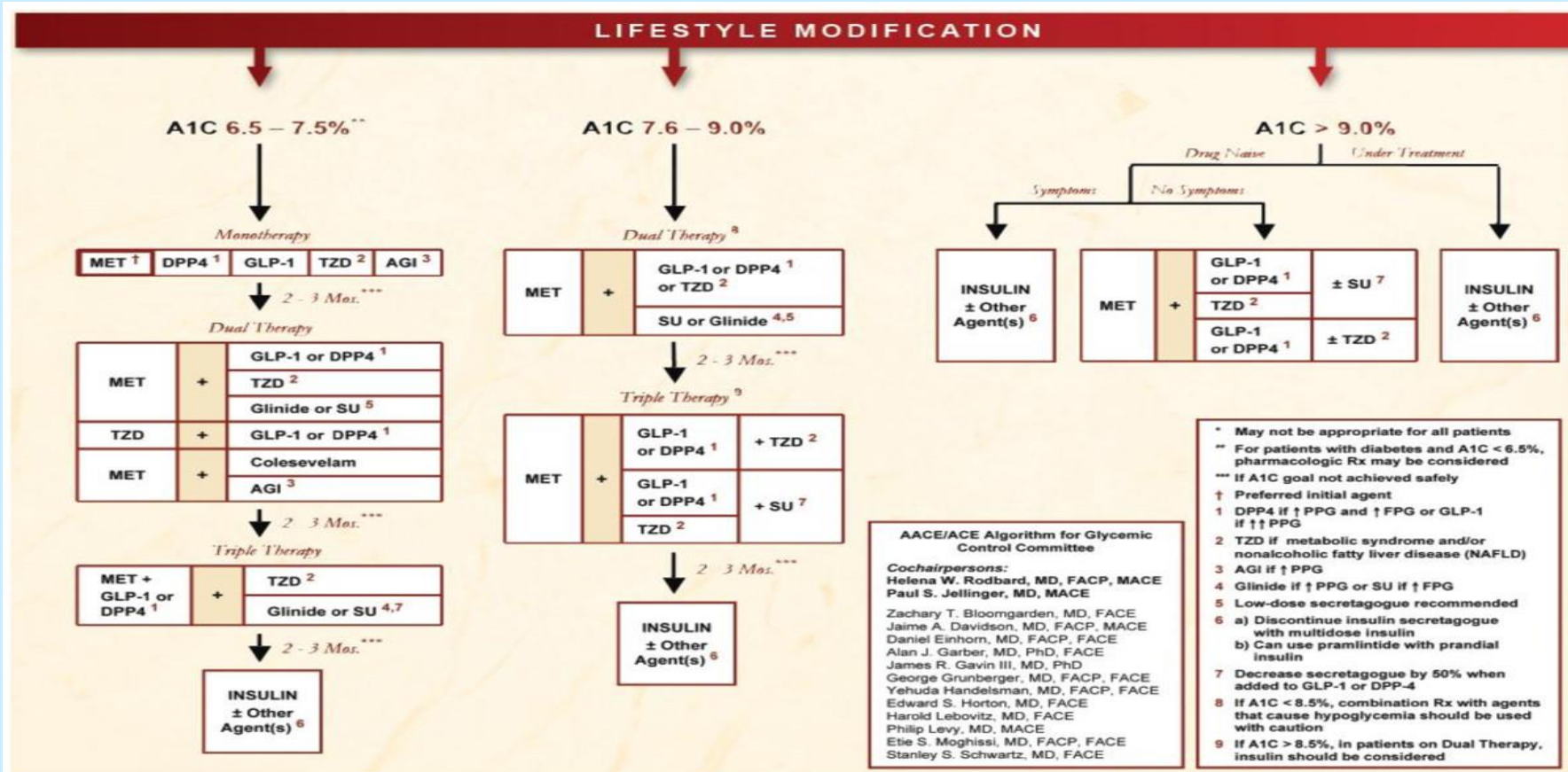
Adapted from *Diabetes Care*. 2008;31(12):1-11.

# AACE/ACE DM algorithm





# AACE/ACE DM algorithm



# Profiles of anti-DM medications

	MET	DPP-4i	GLP-1 RA	TZD	AGI	COLSVL	BCR-QR	SU GLN	INSULIN	SGLT-2	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/ Severe Mild	Moderate to Severe	Neutral	Neutral
WEIGHT	Slight Loss	Neutral	Loss	Gain	Neutral	Neutral	Neutral	Gain	Gain	Loss	Loss
RENAL/ GU	Contra- indicated Stage 3B,4,5	Dose Adjustment May be Necessary (Except Linagliptin)	Exenatide Contra- indicated CrCl < 30	May Worsen Fluid Retention	Neutral	Neutral	Neutral	More Hypo Risk	More Hypo Risk & Fluid Retention	Infections	Neutral
GI Sx	Moderate	Neutral	Moderate	Neutral	Moderate	Mild	Moderate	Neutral	Neutral	Neutral	Moderate
CHF	Neutral	Neutral	Neutral	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
CVD	Benefit	Neutral	Neutral	Neutral	Neutral	Neutral	Safe	?	Neutral	Neutral	Neutral
BONE	Neutral	Neutral	Neutral	Moderate Bone Loss	Neutral	Neutral	Neutral	Neutral	Neutral	? Bone Loss	Neutral

Few adverse events or possible benefits
  Use with caution
  Likelihood of adverse effects

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# DM VARIANTS

## OTHER VARIANTS OF DIABETES

- MODY (Maturity Onset Diabetes of the Young):  
monogenic diabetes
- LADA (Latent Autoimmune Diabetes of Adults)  
(GAD-65 antibody positive): really type 1  
diabetes

others

# SECONDARY DM

- Drugs: glucocorticoids, atypical anti-psychotics; statins; pentamidine, thiazides, OCP's, dilantin, HIV drugs
- Alcohol;
- Pancreatic disease;
- Cushing's syndrome;
- Hemochromatosis ("bronze diabetes")
- Lipodystrophy disorders

# OTHER DIABETES TRIALS

- HOPE Trial
- Micro-Hope

Ramipril 10 mg reduces cardiovascular complications in diabetics

# ACCORD STUDY

- ACCORD: Initially reported as intensive A1c lowering led to increased mortality in patients with coronary artery disease; however, then reported that the patients with better A1c control in the intensive group did not have an increase in mortality. Also, hypoglycemia was not the cause of increase in mortality.

# NICE-SUGAR STUDY

- NICE-SUGAR

Intensive insulin therapy in ICU patients to maintain  $BG < 120$  was associated with more mortality than therapy to keep  $BG$  120-180. (Increase in the risk of death by 10%)

# VADT

- Decreased risk of cardiovascular events in adults who initiated intensive glucose control in the first 15 years after a diagnosis of type 2 diabetes.



# OTHER DIABETES TRIALS

- Intensive insulin management post-CABG:  
insulin drip for 3 days to maintain  
normoglycemia yielded improved outcomes.  
(FURNARE, VAN DEN BERGHE)

# INSULIN PUMPS

- Have to be motivated and possess a reasonable diabetic knowledge-base to make pump therapy optimally effective.
- All types of intensive insulin regimens are labor intensive and user dependent to be optimally effective.
- Use only rapid-acting insulin analogues in pumps; no basal insulin needed.
- Basal rates (units/hour)
- Boluses: carbohydrate ratio; high sugar correction dose (sensitivity);

# CONTINUOUS GLUCOSE MONITORING

- Monitors glucose every 5 minutes
- Has alarms for high or low blood sugar levels and for rate of change in BG
- Change sensor site every 3-7 days
- Mini-Med;
- Dexcom G4/G5
- Glucose sensors can send the BG data to receivers or pumps or mobile phones.

# MEDTRONIC MINIMED PUMP



# MINIMED 670 G PUMP AND GUARDIAN CGM



# Dexcom G4 (and G5)



# TANDEM T-SLIM PUMP



# OMNIPOD PUMP

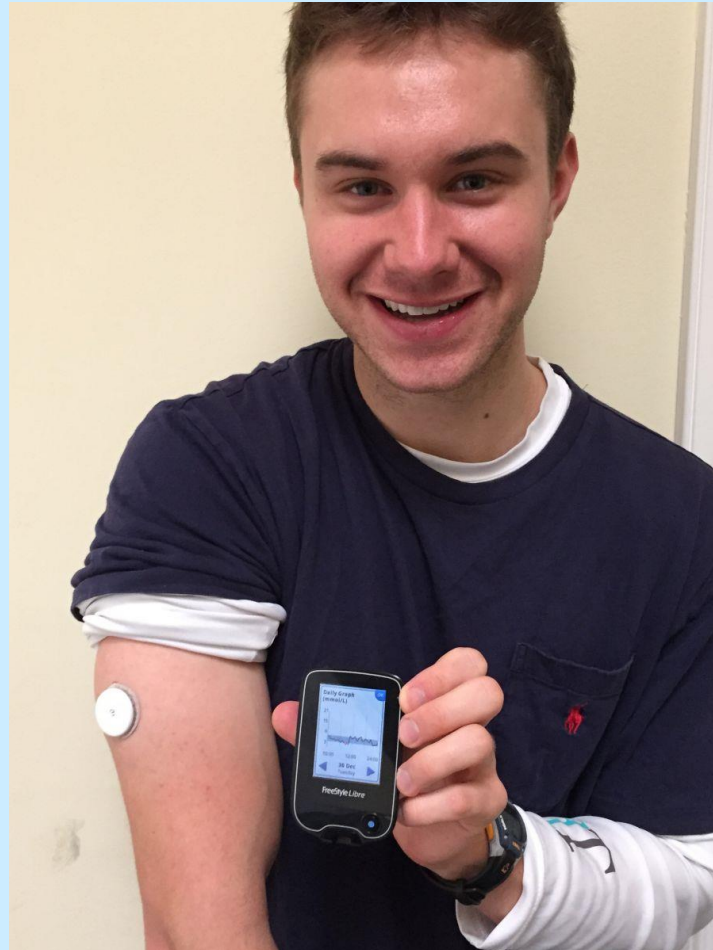




# OMNIPOD PDM



# FREESTYLE LIBRE CGM



# Total Estimated daily insulin dose

- Remember that most people need a total daily dose of insulin of about 0.5-1 unit/kg per day.
- Patients on insulin generally need about  $\frac{1}{2}$  of their insulin as basal insulin and  $\frac{1}{2}$  as rapid-acting insulin.
- This, of course, can be affected by insulin resistance, DM medications they are taking, activity, food intake, etc.

# Formulae for estimating rapid-acting insulin doses

- Total Daily Dose (units) of insulin (TDD): weight in pounds x 0.23 (or weight in kg x 0.5-1).
- 
- Carbohydrate ratio (Insulin to carb ratio; I:C ratio):  $500/\text{TDD}$
- For example: if TDD is 50 units, the carb ratio would be 10 (i.e.: 1 unit insulin for every 10 grams of carbs).

- MINIMED 670 G PUMP AND  
GUARDIAN CGM WITH HYBRID  
ARTIFICIAL PANCREAS FUNCTION



# Formulae for estimating rapid-acting insulin doses

- Insulin Sensitivity Factor (ISF):  $1,700/\text{TDD}$   
(How much 1 unit of insulin drops the BG over 1-2 hours)
- For example: if TDD is 50 units, the ISF would be 34 (i.e.: 1 units of insulin drops the blood sugar by 34 mg/dl).
- Then we calculate the correction dose of insulin as follows:
- $(\text{current blood sugar level} - \text{target blood sugar level})/\text{ISF}$

# Formulae for estimating rapid-acting insulin doses

- These are good approximations and we also we have to keep in mind that many patients have different ISF and I:C ratios at different times in the day.
- Also, morbidly obese patients might be so insulin resistant and very thin type 1 patients, for example, might be very sensitive to insulin that we might have to make some initial adjustments in these formulae to be safe. Then if they don't work, we just change the formulae based on what seems to be needed.



# Basal Insulin calculation

- For Basal Insulin:
- Rough daily Basal insulin requirement would be:  $TDD/2$ .
- Of course we generally start with the recommendations per the package insert for basal insulin of 0.1-0.2 units/kg /day; but this equation at least lets us estimate what the eventual basal dose might be. I generally titrate the basal insulin so that the HS BG roughly equals the FBS (assuming no food in between). If the HS BG is much higher than the FBS, then I add or adjust rapid-acting insulin before dinner (and possibly each meal), or possibly add an agent that particularly targets food intake (GLP-1 agonist, DPP-4 inhibitor, sulfonylurea, etc.)

# CASE 1

22 year old female. Glucose 400. 3+ urine ketones.

n No family history of DM.

n Not overweight.

# CASE1

- Needs an insulin drip first.
- Then likely would use basal/bolus insulin
- DM education and MNT consults
- Likely has positive GAD-65 antibodies and possibly insulin antibodies as she likely has type 1 diabetes

# CASE 2

## n Case 2

65 year old female with type 2 diabetes mellitus for 4 years. Has CAD.

Tingling/burning feet at night. Bed sheets hurt. Urine:2+ proteinuria. A1C:9.1%. On NPH 58 units BID.

## CASE 2

- Likely has significant post-meal hyperglycemia.
- Need to intensify the insulin by adding rapid-acting insulin before one or more meals.
- Consider changing the NPH to Lantus or Levemir, etc.
- DM education and MNT
- Must be cognizant of hypoglycemia issues
- A1c goal is probably 7% in her

# CASE 3

## n Case 3

34 year old with "hypoglycemic" symptoms. Occur 2 hours post-prandial. Does not awaken to eat. On Oral contraceptives.

# CASE 3

- Note:
  1. glucose meters inaccurate for low sugar levels
  2. symptoms of hypoglycemia are catecholamine symptoms, and many things can cause these symptoms (including just hunger)
  3. it is difficult to get a patient to go to the lab for a venous glucose level at the time of symptoms; it is critical to confirm low sugar with venous lab at time of symptoms

# CASE 3

4. A high percentage of normal people, especially females, have low blood sugars as a normal finding without symptoms
5. If a patient is ill or has low BP, they might not perfuse their fingertips well, thereby lowering their fingerstick glucose level



# CASE 3

- If hypoglycemia truly present:
  - rule out reactive hypoglycemia (obese & FHx DM)
  - nesidioblastosis post-gastric bypass (islet cell hyperplasia): post-prandial hypoglycemia
  - insulinoma (fasting hypoglycemia);
  - surreptitious insulin or sulfonylurea use;
  - cortisol deficiency;
  - malnutrition (celiac disease)/anorexia
  - if obese, FHx of DM, r/o reactive hypoglycemia

# CASE 3

- Rule out non-glucose causes of “spells”:

- CARDIAC:

- NMH (neurologically mediated hypotension): probably the most common mimicker

- POTS (postural orthostatic tachycardia syndrome)

- Cardiac dysrhythmia

- NEUROLOGIC: seizures

- Psychiatric: anxiety/panic attacks

- Hunger itself

- Side effect of meds or withdrawal from meds (narcotics, others)

- OTHER: MGUS/Myeloma; Mastocytosis; Pheochromocytoma, etc.