

# Advances in Diabetes Management – Philosophy to Medications to Devices

Peter Montesano, M.D.  
Anchorage, Alaska

Approach to a Patient:  
What is Type 2 Diabetes?

... It is **not** about blood sugar

It **is** about insulin resistance

Baseline patient education is very important

Deep/visceral fat around pancreas, liver, etc. prevents the body from using insulin properly.

Essentially your body is resistant to the hormone.

## Understanding Insulin Resistance

Visceral fat is directly associated with central obesity

Besides insulin resistance, obesity itself has significant implications for long-term health

## Central Obesity

## Central Obesity

For example, also associated with:

### Death from Influenza

7% increased risk of hospitalization/death with every 5 BMI increase from 22.5 Kg/M<sup>2</sup>

### Cancer risk increased 25%

40% all cancers diagnoses

Earlier onset

13 types associated with obesity

pancreatic, esophageal, gastric, breast, gallbladder, thyroid, ovarian, colorectal, liver, multiple myeloma, kidney, endometrial, meningeal

Abdominal circumference of >102cm in male and >89cm in female are independent risk factors for cardiovascular disease

Leads to cascade of metabolic derangement associated with insulin resistance

Think Metabolic Syndrome, start discussion

## Central Obesity

# Metabolic Syndrome a continuum

## METABOLIC SYNDROME

**What is Metabolic Syndrome?**  
Metabolic syndrome is a cluster of conditions that increase your risk of heart disease, stroke, and type 2 diabetes. The conditions include high blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or lipids.

**Metabolic Syndrome Risk Factors**  
**Obesity:** Excess body fat, especially around the waist, is a major risk factor for metabolic syndrome. It is associated with insulin resistance, high blood pressure, and abnormal cholesterol levels.  
**High Blood Glucose:** High blood sugar levels can lead to insulin resistance and eventually type 2 diabetes.  
**High Blood Pressure:** High blood pressure increases the risk of heart disease and stroke.  
**Abnormal Cholesterol Profile (Dyslipidemia):** This includes high levels of triglycerides and low levels of HDL cholesterol, which can lead to plaque buildup in the arteries.

**Organs Affected by Untreated Metabolic Syndrome**  
The heart, liver, and pancreas are particularly affected. The heart is at risk of coronary artery disease and heart failure. The liver can develop non-alcoholic fatty liver disease. The pancreas may become resistant to insulin, leading to type 2 diabetes.

**Medical Conditions Associated with Metabolic Syndrome**  

- Stroke
- Coronary Heart Disease
- Type 2 Diabetes

**How is Metabolic Syndrome Treated?**  
Treatment options usually include the following:  

- Weight loss
- Regular physical activity
- Healthy diet
- Medications to control blood pressure, blood sugar, and cholesterol

**Normal weight**  
Four women with a BMI of 24 but different fat distribution

Subcutaneous  
Visceral

Probability of:

|                   |                |   |       |                |
|-------------------|----------------|---|-------|----------------|
|                   | Less healthy ← |   |       | → More healthy |
| Heart disease     | ▲ High         |   | ▼ Low |                |
| Type 2 diabetes   | ▲              | ▲ | ▼     | ▼              |
| Metabolic disease | ▲              | ▲ | ▲     | ▼              |

← Less healthy → More healthy

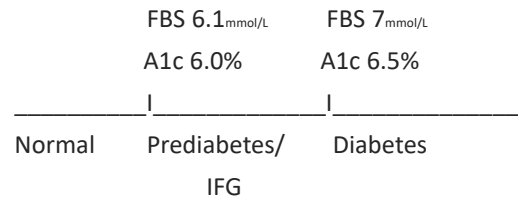
**Obese**  
Four women with a BMI of 32 but different fat distribution

**BMI, Weight: bad measures**

National Geographic Magazine, January 2019

## The Continuum

Insulin resistance takes cumulative toll  
 Overproduction of insulin wears out pancreas  
 Battle lost early, long before DM2 diagnosis



## My Goal

For the new diagnosis or new to me

“Statistically speaking, you are most likely to die of a heart attack or stroke. My goal is to have you die from something else.”



Management

Do not set people up to fail!

But be appropriately blunt.



Eating

Offer approach, telling people **what** to eat invites failure

Too much dietary advice can be overly prescriptive, all diets fail

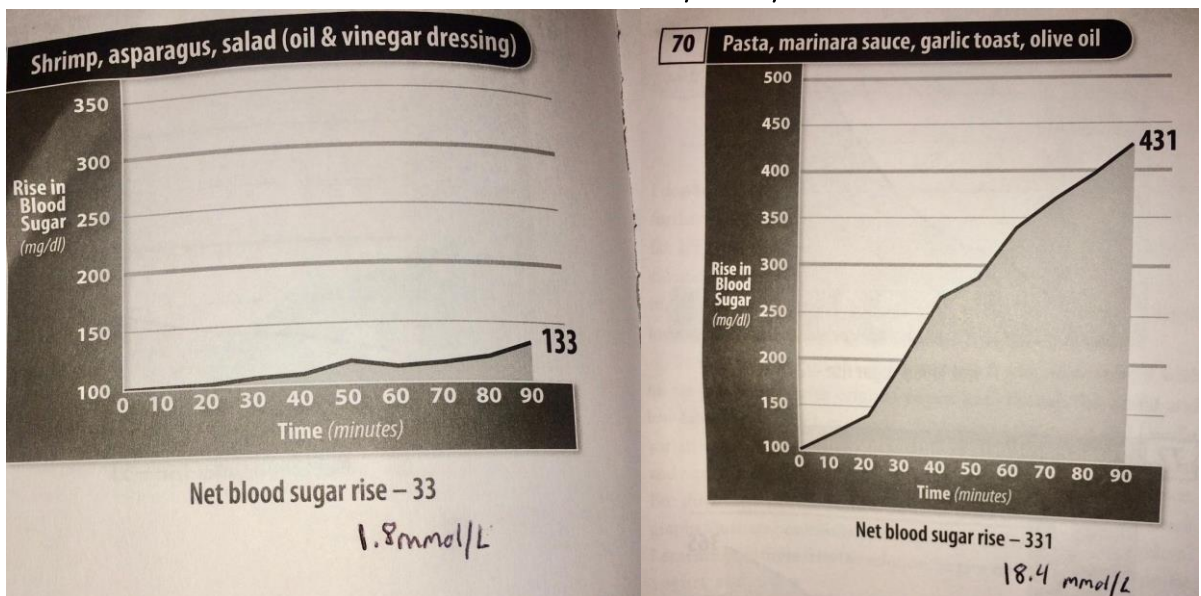
Do not assume sound approach to food, build common base beyond “low fat” mantra

## Eating: My Approach

only four things to know...

1. If it has an ingredient label, you probably should not eat it.
2. Bread, pasta, white rice, white potatoes, pasta, crackers, etc. should be considered sugar, minimized

## Book: What Should I Eat? by Rick Mystrom



Eating: My Approach  
~continued~

3. The French have it figured out.  
Eat slowly.

4. Every chain restaurant needs  
to be avoided.

Eating: My Approach







Exercise

Yes...

Exercise recommendations abound, are they realistic?

Find out where someone is and build slowly from there

Again, do not set people up to fail

But fitness at any weight has benefits (remember body scans)



The Weight Loss Discussion

A waste of time, for many reasons

Discuss weight and BMI in generalities only

I do not look at someone's weight or BMI in my diabetes appointments



## The Weight Loss Discussion

Losing weight is biologically irresponsible

The body want to be the maximum weight it has ever been

Do not set people up to fail

There is another approach



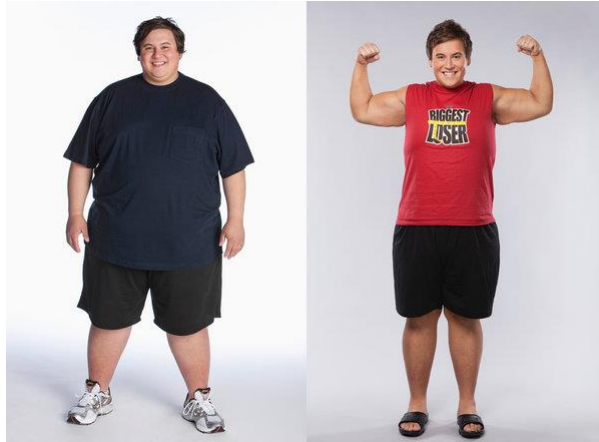
## Set Point

**Persistent metabolic adaptation 6 years after "The Biggest Loser" competition.**  
[Obesity](#) 2016 Aug;24(8):1612-9. doi: 10.1002/oby.21538. Epub 2016 May 2.

New York Times May2, 2016  
***After 'The Biggest Loser,' Their Bodies Fought to Regain Weight***

Contestants lost hundreds of pounds during Season 8, but gained them back. A study of their struggles helps explain why so many people fail to keep off the weight they lose.

Sean Algaier  
36 yo, Charlotte, NC  
Weight before show: 444 lb.  
December 2009: 289 lb.  
6 years later: 450lb...  
Burns 458cal/day less than expected



## The Other Approach

Established BMI and weight are not useful

BMI good for population, not for individual

“you must lose weight” ineffective and begs question “what weight should I be, doctor?”

## The Other Approach

Measure maximum abdominal girth, think insulin resistance

Benefits:

Allows for non-threatening goals

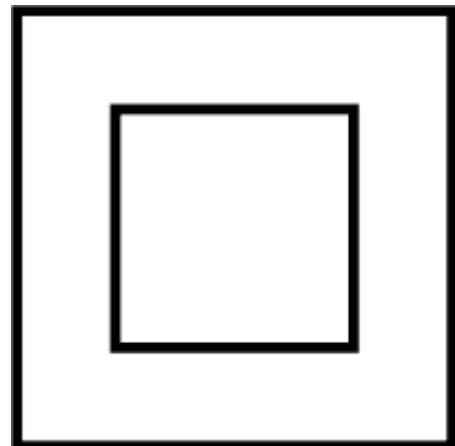
Unique to individual

Easily reproducible, tracked

Not affected by weight gain from exercising

And...

## The Other Approach



If you double the circumference, you quadruple the area---  
small decreases in maximum circumference exponentially  
decreases visceral fat.



## The Other Approach

“Sir, you are 130cm around, next year I want be 5cm less.”

“That’s all? I can do that.”

Goal: arrest growth and ultimately be able to see belt buckle

Subtle changes in approach to eating yields results

Goal is to limit insulin resistance

Fitness at whatever weight



## Sleep

Not optional...

Sleep apnea screening with all physical exams

Validated STOP BANG questionnaire

Untreated sleep apnea increases ghrelin secretion: incr. carb craving, fat storage

Decreased insulin sensitivity...in 5 days of poor sleep



## Diabetes Type 1.5

Also...

Latent Autoimmune Diabetes in Adulthood (LADA)

Possibly 20%+

onset not like Type 1

Keep this in mind...euglycemic ketoacidosis



## Medications

...it's a great time to have diabetes.

Medications can be overwhelming.

Use dichotomous approach for yourself and for patient education

“Insulin versus glucagon pathways”



## Medications

### **Insulin Pathway**

high hypoglycemia potential

weight positive

- Insulin
- Sulfonylureas-secretagogues
- Thiazolidinediones-senitzer

### **“Glucagon” Pathway**

low hypoglycemia potential

weight negative

- Metformin
- DPP-4 inhibitors
- GLP-1 agonists
- SGL-2 inhibitors\*



## Insulins

Basal and meal-time

Quick results, little increased CHF/CVD risk

Removes sugar from blood...  
So weight positive and risk of hypoglycemia

Require active monitoring

There IS a dose limit

A white rectangular box with a thin border containing the text "Sulfonylureas". The box is centered on a dark orange background, which is part of a larger slide layout with a grey vertical bar on the left.

**Secretagogues**---flog the pancreas, so must be making insulin

Need to be eating

Work quickly, cheap

Weight gain and risk hypoglycemia

Increase risk of CHF

Glimeperide and glicazide preferable to glyburide

A white rectangular box with a thin border containing the text "Thiazolidinediones". The box is centered on a dark orange background, which is part of a larger slide layout with a grey vertical bar on the left.

### Sensitizers

Must be making insulin, in effect 'decreasing' resistance,

Weeks to months to maximum effect, but effective

Weight positive and risk hypoglycemia

Associated with increased risk CHF, edema, pathological fractures and rare bladder cancer





Medications

**“Glucagon Pathway”**

low hypoglycemia potential

- Metformin
- DPP-4 inhibitors
- GLP-1 agonists
- SGL-2 inhibitors\*



Metformin

Cheap effective

For everyone and first line

decreases A1c 0.8-3.1%

Weight negative

Cardioprotective, possibly reduce cancer risk

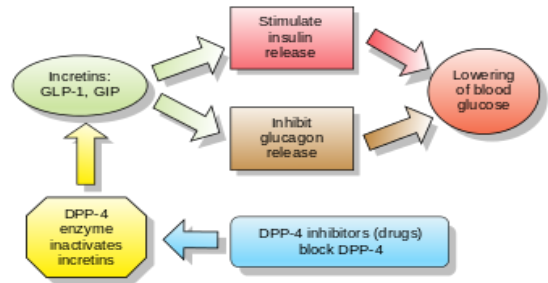
Reduces gluconeogenesis

Very rare hypoglycemia

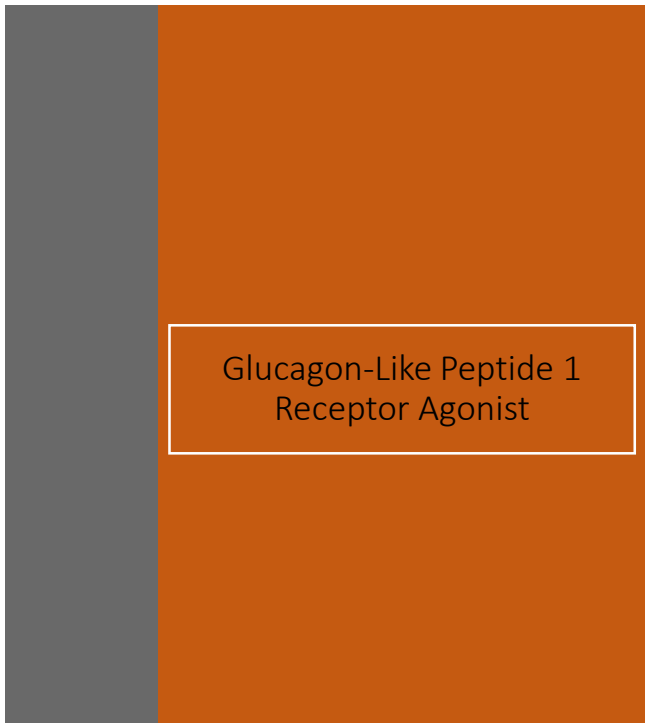
GI upset common, less with XR, titrate



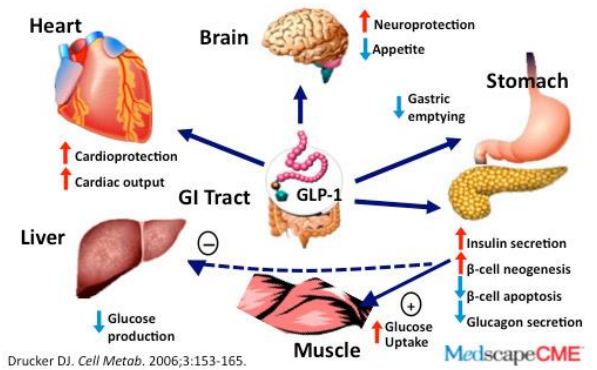
GLP-1 agonist  
 Glucose-dependent gut hormone  
 regulated by DPP-4



wikipedia.com



GLP-1 Actions in Peripheral Tissue



Drucker DJ. *Cell Metab.* 2006;3:153-165.

Glucagon-Like Peptide 1  
Receptor Agonists

Gila monster spit

Incretin released when sugar present

Safe, effective with A1c down +/- 1.5%

Hypoglycemia not an issue

Significant weight loss up to 5 kg  
without lifestyle changes

Up to 26% decrease in events

Precautions . . .

Glucagon-Like Peptide 1  
Receptor Agonist

Currently only injectable

Exanatide 2005

Liraglatide 2010-daily  
(Victoza/Saxenda)

Dulaglatide 2014-weekly

Semaglutide 2017-weekly



Dipeptidyl Peptidase-4  
Inhibitors

### DPP-4's

Inhibit the degradation of naturally occurring GLP-1, suppress gluconeogenesis

Act when sugar present-rare lows

Decrease A1c <1%

Weight negative

Daily dosing oral medication

Work in gut



Dipeptidyl Peptidase-4  
Inhibitors

Sitagliptin

Saxagliptin

Linagliptin

All come in combination with metformin

Overall safe, renal dosing

Do NOT use with GLP-1 RA's

## Sodium Glucose co-Transporter 2 Inhibitors

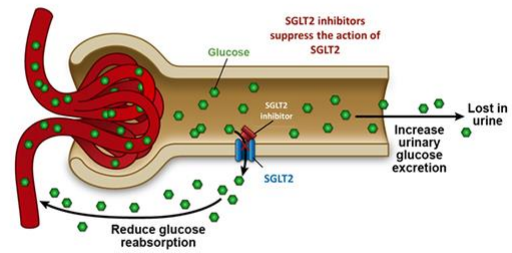
### SGLT-2's

Reversing evolution?

Primarily inhibit reabsorption of glucose

Essentially diuresis

### The Newest Antihyperglycemic Class SGLT2 Inhibitors



Wright EM, et al. *Physiol Rev.* 2011;91:733-794.

## Sodium Glucose co-Transporter 2 Inhibitors

A1c reduction 0.5-0.8%

Work when sugar present

Rare lows

Slight weight negative

## Sodium Glucose co- Transporter 2 Inhibitors

### The Downsides:

- Increased UTI's/vaginal candidiasis
- Hypotension with high BG
- Euglycemic ketoacidosis
- Monitor renal function/renal dosing
- Caution in elderly
- CHF/CVA events, data mixed

## Sodium Glucose co- Transporter 2 Inhibitors

### More Downsides:

- Increased risk fracture
- Genital/perineal gangrene?
- Amputations

#### Names:

- canagliflozin
- dapagliflozin
- empagliflozin

Devices

Glucometers  
Continuous Glucose Monitors

Glucometers

Glucometer Improvements

Allowing synchronization

Insulin tracking

Data sharing



## Continuous Glucose Monitors

“CGMs”

### Advantages:

Reduce finger sticks

Increased monitoring reduces A1c

### Disadvantages:

Interstitial, not capillary sampling

Increased cost...but maybe not over time

“CGMs”

### Freestyle Libre Pro/Libre

14 day monitoring

Relatively inexpensive

#### Libre Pro

“blind”

Placed in office/data downloaded in office

#### Libre

Show trends, programmable alarms

Data sharing

Q5min readings, need finger sticks at extremes

No calibration

Only stores data for 8 hours

Sensor Applicator



Sensor Pack



Sensor (assembled)



Reader





“CGMs”

### Eversense

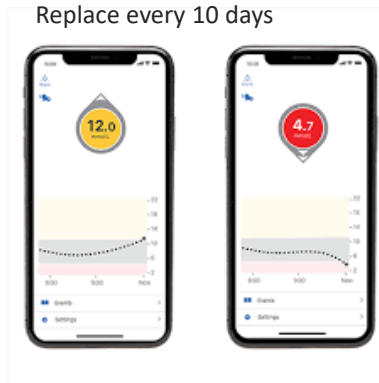
- Works for 90 days
- Need finger sticks at extremes
- Programmable alarms, shows trends
- Implantable/invasive
- Limited data sharing
- Requires twice daily calibration
- Recharge transmitter daily



“CGMs”

### Dexcom G6

- Lowered A1c decrease 0.5%, 58% decrease time in hypoglycemia (Type 1)
- Checks up to 288/day
- Shows trends with rate of change
- Programmable alarms
- Data sharing
- No calibration
- Replace every 10 days



Remember

- Goal: minimize insulin resistance
- Offer approach to eating
- Avoid weight/BMI discussions, think maximum girth
- Restorative sleep
- “Diet controlled” diabetes is vestigial
- Good monitoring options emerging
- And think longitudinally



Thank you. Questions?