New Paradigms of Type 2 Diabetes

“For the greatest enemy of truth is very often not the lie – deliberate, contrived and dishonest – but the myth – persistent, persuasive, and unrealistic. Too often we hold fast to the clichés of our forebears. We subject all facts to a prefabricated set of interpretations. We enjoy the comfort of opinion without the discomfort of thought.”

President John F. Kennedy
Yale University commencement address (June 11, 1962)

From: www.nusi.org
Presenter Disclosure

• Presenters – Jason Fung

• Relationships with commercial interests:
  – Grants/Research Support: None
  – Grants/Speakers Bureau/Honoraria: Consulting Fees: None
  – Consulting Fees: None
  – Other: None
Two Phases of Type 2 Diabetes

FIGURE 1 Change in fasting plasma glucose during the 13 years prior to onset of Type 2 diabetes. These data from the Whitehall II study demonstrate the elevation of plasma glucose within the normal range.

Insulin Resistance

FIG 2. Changes in fasting insulin with the progression of obesity.

Surgical treatment of obesity and its effect on diabetes: 10-y follow-up
Beta Cell Dysfunction

Surgical treatment of obesity and its effect on diabetes: 10-y follow-up
Learned Helplessness

- Fact: For most people, type 2 diabetes is a progressive disease.
- eventually oral medications may not be enough to keep blood glucose levels normal. Using insulin to get blood glucose levels to a healthy level is a good thing, not a bad one.

http://www.diabetes.org/diabetes-basics/myths
What is Insulin Resistance?

The New Paradigm
Functions of Insulin:

1. Increase glucose entry into cells
2. Turn on De Novo Lipogenesis
Metabolic Effect of Insulin

Insulin High (Fed State)

Glucose → Fat

Insulin Low (Fasted State)

Glucose → Fat
The ‘Lock and Key’ paradigm

“Internal Starvation” – Cannot drive DNL
Figure 1. Effects of Insulin Therapy.
These photographs from 1922, in a case described by Geyelin,11 show a young girl with insulin-deficient diabetes before treatment with insulin (Panel A) and after treatment (Panel B).
Internal Starvation?
If glucose cannot enter liver, how does it continue producing new fat via DNL?
The Central Paradox

Functions of Insulin (Insulin resistant cell):

1. Increase glucose entry into cells - resistant
2. Turn on De Novo Lipogenesis - supersensitive
Fatty Liver causes Insulin Resistance!

Stored Sugar

High Insulin → Food/Energy

Stored Fat

Low Insulin →
Insulin Resistance Overflow Model

Glucose

Fat

Primary defect is enlarged, fatty liver
Fatty Liver precedes T2D

18 months prior to diagnosis of DM
Long silent scream from the liver
Insulin Resistance is an Overflow Phenomenon
Insulin Resistance is an Overflow Phenomenon
How to get Fatty Liver

Effect of short-term carbohydrate overfeeding and long-term weight loss on liver fat in overweight humans

Reduction in Liver TG

Reversal of Nonalcoholic Hepatic Steatosis, Hepatic Insulin Resistance, and Hyperglycemia by Moderate Weight Reduction in Patients With Type 2 Diabetes

Diabetes 54:603–608, 2005
Improved Hepatic Insulin Sensitivity

Reversal of Nonalcoholic Hepatic Steatosis, Hepatic Insulin Resistance, and Hyperglycemia by Moderate Weight Reduction in Patients With Type 2 Diabetes
What causes Fatty Liver?
What causes Fatty Liver?

Fattening Carbohydrates → High Insulin → Obesity

Insulin Resistance → Fatty Liver

Fructose
Glucose + Fructose =
Fatty Liver =
Insulin Resistance =
Beta cell dysfunction
Burnout?
Surgery cures diabetes

Bariatric Surgery versus Intensive Medical Therapy in Obese Patients with Diabetes
Rapid Improvement of Diabetes After Gastric Bypass Surgery: Is It the Diet or Surgery?
Diabetes Care. 2013 Mar 25, Lingvay I
Decrease in Pancreatic Fat

Pancreas TG content (%)

Weeks of hypocaloric diet

Taylor R Dia Care 2013;36:1047-1055
Restoration of Beta Cell Function

![Graph showing maximal insulin response in nmol.min⁻¹.m⁻² over a period of time.](Taylor R Dia Care 2013;36:1047-1055)
Restoration of First Phase Insulin Response

Taylor R Dia Care 2013;36:1047-1055
The Sugar Bowl
The End Game
Glucose

Cell

Normal

Insulin Resistance

“Internal Starvation” Paradigm

“Overflow” Paradigm
Cumulative Incidences of Events, According to Glucose-Control Strategy

Meta-analysis of intensive glucose control in T2DM: mortality

<table>
<thead>
<tr>
<th>Number of events</th>
<th>More intensive</th>
<th>Less intensive</th>
<th>Difference in HbA1c (%)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>980</td>
<td>884</td>
<td>-0.88</td>
<td>1.04 (0.90,1.20)</td>
</tr>
<tr>
<td>CV death</td>
<td>497</td>
<td>441</td>
<td>-0.88</td>
<td>1.10 (0.84,1.42)</td>
</tr>
<tr>
<td>Non-CV death</td>
<td>476</td>
<td>432</td>
<td>-0.88</td>
<td>1.02 (0.89,1.18)</td>
</tr>
</tbody>
</table>

- Meta-analysis of 27,049 participants and 2370 major vascular events from
  - ADVANCE
  - UKPDS
  - ACCORD
  - VADT

HR, hazard ratio; CV, cardiovascular
Turnbull FM et al. Diabetologia 2009;52:2288–2298
How To Reverse Type 2 Diabetes

Type 2 diabetes is too much sugar in the body

Treatment

1. Don’t put more in – Low Carbohydrate Diet
2. Burn it off – Intermittent Fasting
HR 0.86
(95.02% CI 0.74, 0.99)
*p=0.0382*

* Two-sided tests for superiority were conducted (statistical significance was indicated if p≤0.0498)
Can We Cure Type 2 Diabetes?

No Diabetes – no diabetic nephropathy, no diabetic foot ulcers, diabetic retinopathy, reduced stroke, MI, cancers

No Drugs, No Surgery, No Cost
Time to get started...

www.IDMprogram.com
Basic Copyright Notice & Disclaimer

©2017 This presentation is copyright protected. All rights reserved. You may download or print out a hard copy for your private or internal use. You are not permitted to create any modifications or derivatives of this presentation without the prior written permission of the copyright owner.

This presentation is for information purposes only and contains non-binding indications. Any opinions or views expressed are of the author and do not necessarily represent those of Swiss Re. Swiss Re makes no warranties or representations as to the accuracy, comprehensiveness, timeliness or suitability of this presentation for a particular purpose. Anyone shall at its own risk interpret and employ this presentation without relying on it in isolation. In no event will Swiss Re be liable for any loss or damages of any kind, including any direct, indirect or consequential damages, arising out of or in connection with the use of this presentation.