The simplicity of type 2 diabetes
– and what to do about it

Roy Taylor
Type 2 diabetes is a complex, heterogeneous state
The twin cycle hypothesis

Type 2 diabetes is a simple condition caused by too much fat in liver and pancreas.

Taylor R, Diabetologia 2008; 51: 1781
The twin cycle hypothesis

Negative calorie balance in people with type 2 diabetes will:

<table>
<thead>
<tr>
<th>Liver</th>
<th>Pancreas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease fat –</td>
<td>Decrease fat –</td>
</tr>
<tr>
<td>improve insulin</td>
<td>normalise the insulin</td>
</tr>
<tr>
<td>action and</td>
<td>response to eating</td>
</tr>
<tr>
<td>normalise</td>
<td>and</td>
</tr>
<tr>
<td>overnight</td>
<td></td>
</tr>
<tr>
<td>blood sugar</td>
<td></td>
</tr>
</tbody>
</table>

Taylor R, Diabetologia 2008; 51: 1781
Effect of very low calorie diet on fasting glucose
The COUNTERPOINT study

All hypoglycaemic agents stopped

At 7 days:
- 30% fall in liver fat
- Normalisation of liver insulin sensitivity

Over 8 weeks:
- Gradual fall in pancreas fat
- Gradual return of first phase insulin response

Lim E-L et al, Diabetologia 2011; 54: 2506
The 2nd study - Counterbalance: VLCD then 6 months normal eating

Responders:

Steven et al, Diabetes Care 2016; 39:808
DiRECT – a study in routine NHS General Practice

Duration of T2DM less than 6 years; on oral agents and/or diet

INTERVENTION
15kg weight loss then maintain
149 people

CONTROL
Best management by guidelines
149 people

49 Practices
Remissions by weight-loss category at 12 months

Overall: 46% remission at 12 months

Odds Ratio (per kg weight loss): 1.32
(95% CI: 1.23, 1.41)
p<0.0001
Adherence to the Total Diet Replacement

### Behaviour-regulation strategies (examples)
- Avoidance,
- Distraction
- Drinking water
- Reminding oneself of the goals
- Removing food from environment
- Social disclosure

### Initial motivation

### Facilitators
- Emotional and cognitive barriers
  - Life events and stress
  - Lack of social support
- Environmental barriers
  - Presence of shops with food
  - Traveling
  - Going out and socializing

### Barriers
- Destabilisation
  - Re-designing of the “Foodrobe”
Non-obese cf. obese type 2 diabetes – Is the assumed difference in pathophysiology real?

Non-obese T2DM have a greater beta cell defect and less insulin resistance

Meal tests elicit similar insulin secretion (C-peptide rise of 2.5 fold in non-obese and 1.8 fold in obese) 
Reaven et al JCEM 1993; 76: 44

No greater insulin resistance in obese than non-obese T2DM relative to weight-matched control groups
Hollenbeck et al Diabetes 1984; 33: 622
BMI distribution of individuals with type 2 diabetes
Personal vs population

The Personal Fat Threshold
An index patient

54y old diagnosed with type 2 diabetes:

BMI 26.5; HbA1c 6.5%; Fasting glucose 7.2

“I do not want this. How can I get rid of it?”

Advice.
2013
Weight 126kg
HbA1c 9.2%

2014:
Weight 94kg
HbA1c 6.2%
2017
Weight 83kg
HbA1c 5.7%
Benefits to individuals

• Feeling 10 years younger
• Losing the ‘diabetic’ label
• No diabetes tablets/injections
• Outlook for long term health
• Less time at the doc’s
• No excess insurance costs

Rehovaka et al Diabetic Medicine 2018
Summary

Liver fat $↑$
Liver fat export $↑$
VLDL
Pancreas fat $↑$
Beta cell damage $↑$

Liver fat $↓$
Liver fat export $↓$
VLDL
Pancreas fat $↓$
Beta cell damage $↓$
Type 2 diabetes is a simple state of having more fat than the individual can tolerate.