THE DIAGNOSIS & CLASSIFICATION OF DIABETES
HAVE WE GOT IT RIGHT?

KGMM Alberti
CLASSIFICATION
“Diabetes is an awkward affection melting down the flesh and limbs into the urine ... The patients never stop making water ... Life is short and painful ... They are affected with nausea, restlessness and a burning thirst and at no distant turn they expire.”

Arataeus of Capadocia, 130-200 AD
Mr Jacob Powell of Stebbing in Essex, who died on 6 October 1754 aged 37 years weighing almost 40 st
TYPES OF DIABETES

“Diabetes mellitus ... manifests itself in two principle clinical forms (a) acute and (b) chronic. Acute diabetes usually occurs in persons under 40 years of age ... in children and young adults. Chronic diabetes ... occurs as a rule in elderly people ... and often in those who are ... decidedly obese.

Saundby, 1907
1900s  - Juvenile onset
- Maturity onset
1979-1980 WHO/NDDG CLASSIFICATION OF DIABETES

Clinical Classes

IDDM Type 1
NIDDM Type 2: a) non-obese
b) obese
Other types IGT
Gestational diabetes
Others
1985 CLASSIFICATION OF DIABETES

- Type 1
- Type 2
- Malnutrition related diabetes
- Other types
THE RELATIONSHIP BETWEEN AETIOLOGIES (MECHANISMS) AND PATHOLOGICAL STATES (STAGES) OF DIABETES MELLITUS

<table>
<thead>
<tr>
<th>Aetiologies (mechanisms)</th>
<th>Stages</th>
<th>Normoglycaemia</th>
<th>Hyperglycaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Normal glucose tolerance</td>
<td>Borderline area</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not insulin requiring</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Insulin: for control</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Insulin: for survival</td>
</tr>
<tr>
<td>Type 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other types</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GDM</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CLASSIFICATION OF DIABETES
1997

1. Type 1 diabetes (β-cell destruction)
   a. Immune mediated
   b. Idiopathic

2. Type 2 diabetes

3. Other specific types

4. Gestational diabetes mellitus

ADA, WHO, 1997
CLASSIFICATION OF DIABETES
1997

Other Specific Types

a. Genetic defects of $\beta$-cell function
b. Genetic defects in insulin action
c. Diseases of the exocrine pancreas
d. Drug or chemical induced
e. Infections
f. Uncommon forms of immune-mediated diabetes
g. Other genetic syndromes
CLASSIFICATION OF DIABETES
1997

Major changes

• Recognition of aetiology
• Ability to re-classify as knowledge increases
• Loss of MRDM
• IGT now a risk factor not a type of DM
PROBLEMS

- Type 2, diagnosis by exclusion
- LADA
- Very Europid oriented, e.g. Periodic Insulin Dependence, Type 3
DIAGNOSIS
THE DIAGNOSIS OF DIABETES
AND HYPERGLYCAEMIC STATES
History (1)

» Ants

» Signs / symptoms

» Urine volume

» Glycosuria

» Raised blood glucose
History 2

Glucose tolerance tests

» Hofmeister, 1889
» Double load:
  Exton and Rose, 1934
» Fajans and Conn, 1959
**History 3**

**OGTT**

<table>
<thead>
<tr>
<th>Glucose Load</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA</td>
<td>40 g/m²</td>
</tr>
<tr>
<td>UGDP</td>
<td>30 g/m²</td>
</tr>
<tr>
<td>Jordo</td>
<td>100 g</td>
</tr>
<tr>
<td>Polefsky</td>
<td>1.75 g/kg</td>
</tr>
<tr>
<td>Fajans</td>
<td>1.75 g/kg TBW</td>
</tr>
<tr>
<td>BDA</td>
<td>50 g</td>
</tr>
</tbody>
</table>
## History 4

### Diagnostic Levels

<table>
<thead>
<tr>
<th>2h PG</th>
<th>Glucose Load</th>
<th>mM</th>
</tr>
</thead>
<tbody>
<tr>
<td>USPHS 1960</td>
<td>100 g</td>
<td>7.8</td>
</tr>
<tr>
<td>Fajans 1959</td>
<td>1.75 g/kg</td>
<td>7.8</td>
</tr>
<tr>
<td>BDA 1964</td>
<td>50 g</td>
<td>7.2</td>
</tr>
<tr>
<td>Japan 1970</td>
<td>100 g</td>
<td>8.9</td>
</tr>
<tr>
<td>EDESG 1970</td>
<td>50 g</td>
<td>8.3 (cap)</td>
</tr>
<tr>
<td>Bennett 1976</td>
<td>75 g</td>
<td>11.3 – 15.3</td>
</tr>
</tbody>
</table>
THE BREAKTHROUGH

WHO/NDDG 1978-80
WHAT IS DIABETES?

Hyperglycaemia

AND

increased risk of microangiopathy

AND

macroangiopathy
WHO/NDDG

1. Casual plasma glucose > 11.0 (x 2)
2. Standard glucose load - 75 g
3. Dietary preparation
4. 2-h post load value based on risk of retinopathy
5. Identification of grey zone - IGT
DIAGNOSIS OF DIABETES

1979 Criteria

Based on risk of retinopathy in:

- Bedford UK
- Pima Indians
- Nauruans

BUT: Size of glucose load
Measurement methods
## Diagnosis of Diabetes (1979)

<table>
<thead>
<tr>
<th>Condition</th>
<th>WHO</th>
<th>NDDG</th>
<th>2hPG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>≥ 8.0</td>
<td>≥ 7.8</td>
<td>≥ 11.00</td>
</tr>
<tr>
<td>IGT</td>
<td>&lt; 8.0</td>
<td>&lt; 7.8</td>
<td>8.0-10.9</td>
</tr>
</tbody>
</table>

FPG mM

WHO

NDDG
# Plasma Glucose Values for Diagnosis of Diabetes

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting:</td>
<td>8</td>
<td>7.8</td>
<td>7.0</td>
</tr>
<tr>
<td>2 hours:</td>
<td>11</td>
<td>11.1</td>
<td>11.1</td>
</tr>
<tr>
<td>Population</td>
<td>FPG mM</td>
<td>(mg/dl)</td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Pima Indians</td>
<td>6.8</td>
<td>(123)</td>
<td></td>
</tr>
<tr>
<td>Pima Indians</td>
<td>6.7</td>
<td>(120)</td>
<td></td>
</tr>
<tr>
<td>NHANES III</td>
<td>6.7</td>
<td>(120)</td>
<td></td>
</tr>
<tr>
<td>Pacific Populations</td>
<td>7.0</td>
<td>(126)</td>
<td></td>
</tr>
<tr>
<td>Tanzanian Bantu (whole blood)</td>
<td>6.2</td>
<td>(112)</td>
<td></td>
</tr>
</tbody>
</table>
## DIAGNOSIS OF DIABETES

1997: Risk of retinopathy

<table>
<thead>
<tr>
<th></th>
<th>FPG mM (mg/dl)</th>
<th>2hPG mM (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pima</td>
<td>123</td>
<td>200</td>
</tr>
<tr>
<td>Egypt</td>
<td>129</td>
<td>207</td>
</tr>
<tr>
<td>NHANES III</td>
<td>120</td>
<td>195</td>
</tr>
</tbody>
</table>
DEFINITION AND DIAGNOSIS OF DIABETES MELLITUS AND INTERMEDIATE HYPERGLYCAEMIA
WHO 2006

Conclusions: NO change!

Problem: Different IFG cutpoint from ADA
PROBLEMS WITH DIAGNOSIS

• No threshold for macroangiopathy
• Variability of OGTT (and dietary preparation)
• 2-h gold standard – tarnished!
• FPG – misses 30%
• HbA$_{1C}$ – theoretically better
• Values largely based on cross-sectional data

• ... and how should you screen?
SOLUTIONS

» Use HbA$_{1c}$?

» Use HbA$_{1c}$ + FPG

NB Not a problem in symptomatic individuals with clear hyperglycaemia - but may be too late!
THE BIGGEST QUESTION

Should the criteria include risk of macrovascular disease as well?

(which the 1964 BDA criteria DID include!)