What’s new in diabetes monitoring?

Ronda Greaves
Overview

- Prevalence

- Diagnostic Criteria – glucose

- Monitoring Diabetes – HbA1c
  - Harmonisation: New HbA1c units

- The Diabetes Clinic at RCH
Prevalence
Prevalence of diabetes

- Worldwide 246 million people have diabetes

- AUSTRALIA population 21+ million
  - Diabetes is Australia’s fastest growing chronic disease
  - An estimated 2.1 million Australians are at risk of diabetes
  - One person is diagnosed every seven minutes
  - About 1 million Australians are diagnosed with diabetes. However, for every one diagnosed, another is undiagnosed
  - By 2014 the expected number of people with diabetes will be 4.5 million
  - Type 2 diabetes costs Australia $3+ billion per year

- VIETNAM population 86+ million
  - “With 5 million sufferers, Vietnam is one of the countries which have the highest rates of diabetes in the world”
  - 67% of people only discover they have the disease because of complications
  - One of the four fastest developing diseases (next to cancer, cardiovascular disease and obesity)
  - Expected to reach 10 million in next decade.

Increasing prevalence of diabetes in UK

![Bar chart showing the increasing prevalence of diabetes in the UK from 1995 to 2010. The chart compares Type 1 and Type 2 diabetes, with a significant increase in Type 2 diabetes over the years.]
<table>
<thead>
<tr>
<th><strong>Type 1 diabetes</strong></th>
<th><strong>Type 2 diabetes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>autoimmune destruction of insulin</td>
<td>insulin resistant condition with</td>
</tr>
<tr>
<td>producing pancreatic beta islet cells</td>
<td>inadequate insulin secretion</td>
</tr>
<tr>
<td>Australian prevalence 1% and rising</td>
<td>Australian prevalence 8% (4% overt)</td>
</tr>
<tr>
<td></td>
<td>and rising (2-4 x higher in indigenous</td>
</tr>
<tr>
<td></td>
<td>population)</td>
</tr>
<tr>
<td>typical onset &lt; 30 years</td>
<td>typical onset &gt; 20 years</td>
</tr>
<tr>
<td>sudden onset</td>
<td>gradual onset</td>
</tr>
<tr>
<td>severe symptoms</td>
<td>may be no symptoms</td>
</tr>
<tr>
<td>usually thin</td>
<td>usually obese</td>
</tr>
<tr>
<td>spontaneous ketosis</td>
<td>not ketotic</td>
</tr>
<tr>
<td>insulin low or absent</td>
<td>insulin low, normal or high</td>
</tr>
<tr>
<td>absent C-peptide</td>
<td>detectable C-peptide</td>
</tr>
<tr>
<td>islet cell antibodies</td>
<td>no islet cell antibodies</td>
</tr>
</tbody>
</table>
Type 2 diabetes mellitus

- usually insulin resistant with inadequate insulin production to maintain normal glucose levels
- onset (usually gradual) at any age, usually >20 years
- usually overweight or obese but not ketotic and often no symptoms at presentation
- worldwide very high prevalence in rural to urban migrant communities

Underlying insulin resistance
- genetic and ethnicity
- obesity
- inactivity / low physical fitness
- intrauterine & childhood factors
- smoking & drugs

Impaired insulin secretion
- worsens with time (β-cell exhaustion)
Syndrome of insulin resistance

AKA syndrome X, metabolic syndrome

- microalbuminuria
- high blood pressure
- hyperuricaemia
- PAI-1 ↑
- fibrinogen ↑
- factor VII ↑
- abdominal obesity
- insulin resistance
- hyperinsulinaemia
- glucose intolerance
- diabetes
- HDL cholesterol ↓
- VLDL triglyceride ↑
- small dense LDL ↑
Diabetes in pregnancy

- Increased risk of neonatal morbidity with maternal diabetes

- Gestational diabetes
  - normal pregnancy associated with increased insulin resistance
  - GD develops if failure to increase insulin secretion
  - Screening at 24-28 weeks with 50g OGGT

- Pre-existing diabetes
  - Excellent glycaemic control required to reduce risks
Diagnosing Diabetes: Glucose
2 hour Glucose Tolerance Test

DIAGNOSES

- Diabetes Mellitus if:
  - Fasting plasma glucose is $\geq 7.0$ mmol/L
  - and/or
  - 2 hour plasma glucose is $\geq 11.1$ mmol/L

- Impaired glucose tolerance
- Impaired fasting glucose
Impaired Fasting Glucose

DIAGNOSED if:

- Fasting plasma glucose is 5.6 to 6.9 mmol/L
  According to the American Diabetes Association

  Or

- Fasting plasma glucose is 6.1 to 6.9 mmol/L
  According to NHMRC, WHO, IDF, ADS, RCPA and AACB
The 2 tests (GTT v Fasting glucose) do not define identical populations (i.e. do not give same results)

- GTT – More abnormals in older, heavier population
- Fasting glucose – more abnormals in younger, thinner population
Monitoring diabetes: HbA1c
Monitoring diabetes - why

- Improving blood glucose control reduces risk of microvascular complications in Type 1 and Type 2 DM

- Complications include:
  - Neuropathy
  - Retinopathy
  - Nephropathy
  - CVD

http://www.stlukeseye.com/Conditions/DiabeticRetinopathy.asp

[medicine.ucsd.edu/clinicalmed/extremities.htm](http://medicine.ucsd.edu/clinicalmed/extremities.htm)
Glycated Haemoglobin

- Haemoglobin A (97%) $\alpha_2\beta_2$
- Haemoglobin A$_2$ (2.5%) $\alpha_2\delta_2$
- Haemoglobin F (0.5%) $\alpha_2\gamma_2$

6% of HbA is HbA$_1$

- HbA$_{1a}$ fructose-1,6-diphosphate 0.2%
- HbA$_{1b}$ glucose-6-phosphate 0.2%
- HbA$_{1b}$ pyruvate 0.4%
- HbA$_{1c}$ glucose 5%

© Fleshandbones.com Baynes: Medical Biochemistry
HbA$_{1c}$ methods in use in Australia

From RCPA QAP Glycated Hb 2010

- Total labs = 288
  - Immunoassay = 158
  - HPLC
    - Cation exchange = 93
    - Affinity = 32
  - 12 labs also reporting new IFCC units
1970: Routine testing of glycated Hb began

1981: First immunoassay

1993: DCCT Type 1 diabetes 9 year study

1995: JDS

1996: NGSP

1998: Mono S

2000: JDS

2007: International consensus committee recommended HbA1c should be reported in new units

2010: May 2011: UK new units
Comparison of HbA1c measured with nationally designated methods


NGSP HbA$_1$c = 0.915 (IFCC HbA$_1$c) + 2.15
JDS HbA$_1$c = 0.927 (IFCC HbA$_1$c) + 1.73
Mono S HbA$_1$c = 0.989 (IFCC HbA$_1$c) + 0.88
HbA1c: Reporting of results

- NGSP/DCCT/UKPDS - Report as a percentage of total haemoglobin
- IFCC - Report as mmol/mol
- Denominator is HbAo + HbA1c

IFCC HbA₁c (mmol/mol) = 10.93 * NGSP HbA₁c (%) – 23.5

<table>
<thead>
<tr>
<th>NGSP %</th>
<th>IFCC mmol/mol</th>
</tr>
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<tbody>
<tr>
<td>3.0</td>
<td>9</td>
</tr>
<tr>
<td>4.0</td>
<td>20</td>
</tr>
<tr>
<td>5.0</td>
<td>31</td>
</tr>
<tr>
<td>6.0</td>
<td>42</td>
</tr>
<tr>
<td>7.0</td>
<td>53</td>
</tr>
<tr>
<td>8.0</td>
<td>64</td>
</tr>
<tr>
<td>9.0</td>
<td>75</td>
</tr>
<tr>
<td>10.0</td>
<td>86</td>
</tr>
<tr>
<td>11.0</td>
<td>97</td>
</tr>
<tr>
<td>12.0</td>
<td>108</td>
</tr>
<tr>
<td>13.0</td>
<td>119</td>
</tr>
<tr>
<td>14.0</td>
<td>130</td>
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<tr>
<td>15.0</td>
<td>140</td>
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<tr>
<td>16.0</td>
<td>151</td>
</tr>
<tr>
<td>17.0</td>
<td>162</td>
</tr>
<tr>
<td>18.0</td>
<td>173</td>
</tr>
<tr>
<td>19.0</td>
<td>184</td>
</tr>
<tr>
<td>20.0</td>
<td>195</td>
</tr>
</tbody>
</table>
2010 Diabetes UK booklet

HbA$_{1c}$ in Diabetes
case studies using IFCC units

Edited by Stephen Gough, Susan Manley and Irene Stratton
### Case Example 14 – Diabetes UK

<table>
<thead>
<tr>
<th>Case notes</th>
<th>IFCC HbA$_1$c mmol/mol</th>
<th>NGSP%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presentation:</strong> Previously well controlled 14yo girl with T1 DM had lost 3 kg over 3 months</td>
<td>59 to 81</td>
<td>7.5 – 9.6%</td>
</tr>
<tr>
<td><strong>Insulin regime:</strong> Pre-prandial rapid acting insulin analogue + once daily long acting analogue given in the evening.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment plan:</strong> Change insulin regime, gentle enquiries about weight and mental assessment</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3 weeks later:</strong> She was admitted to hospital with DKA pH=6.9; glucose = 33.5 mmol/L; ketones 5.6 mmol/L</td>
<td>96</td>
<td>10.9%</td>
</tr>
<tr>
<td><strong>Post recovery:</strong> Weight drop and admitted to skipping insulin doses for weight control</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Next two years</strong></td>
<td>92 – 111</td>
<td>10.6-12.3%</td>
</tr>
<tr>
<td><strong>Age 17</strong></td>
<td>72</td>
<td>8.7%</td>
</tr>
</tbody>
</table>
# GLYCOHAEMOGLOBIN PROGRAM 2010

## RESULT SHEET

<table>
<thead>
<tr>
<th>DUE DATE FOR RESULTS</th>
<th>SAMPLE NUMBER</th>
<th>UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mmol/mol</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HAEMOGLOBIN A1c</th>
<th></th>
<th></th>
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<tbody>
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<td></td>
<td></td>
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## CHANGE OF METHOD CLASSIFICATION

**IMPORTANT!**
PLEASE COMPLETE IF YOU HAVE ALTERED OR DELETED A METHOD.

**CHANGE EFFECTIVE FROM:**

<table>
<thead>
<tr>
<th>CYCLE No.</th>
<th>SAMPLE No.</th>
<th>ANALYTE</th>
<th>NEW METHOD CODE</th>
<th>ADDITIONAL INFORMATION IF REQUIRED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HAEMOGLOBIN A1c</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ADAG Study

- ADAG = A1c Derived Average Glucose
- Equating Haemoglobin A1C results with estimated average glucose concentrations
- ADAG Study
  - 507 participants, each with about 2700 glucose measurements
  - e.g. HbA1c 6% = 42 mmol/mol = average glucose of 7.0 mmol/L
- Some consensus statements recommend reporting both % and mmol/mol, as well as estimated average glucose!
- Case Study 30 from Diabetes UK booklet:
  - Example of a 66 y.o. women with type 2 DM for 11 years without complications.
  - “The patient’s GP was aware that although the mean glucose (eAG) for a patient with an IFCC HbA1c of 53 mmol/mol (NGSP 7.0%) was around 8.6 mmol/L it can vary between individuals from 6.8 – 10.3 mmol/L.”
The Diabetes Clinic at RCH