Diabetes – Is It Worth Talking About?

Greg Stewart

2019 CAMLT Annual Meeting
30.3
Agenda

- Overview of Diabetes
- Overview of HbA1c
- Hemoglobin Variants
- Testing Types and Methods
Diabetes

What is it?

Source: American Diabetes Association (ADA)
Diabetes

Group of diseases marked by high levels of blood glucose

Defects in:
insulin production, insulin action or both

Source: American Diabetes Association (ADA)
Why should we care?
Complications

1st cause of kidney failure, lower-limb amputations and adult blindness

Source: ADA and CDC
Complications

Kidney failure
- Kidneys filter too much blood leading to loss of protein in the urine

Amputation
- More likely to have a foot or leg amputated than other people
- Peripheral arterial disease (PAD) reduces blood flow to the feet
- Combined with infections the outcome is amputation

Blindness

Glaucoma
- The longer one has diabetes, the more likely they will have glaucoma
- The pressure pinches blood vessels that carry blood to retina and optic nerve leading to retina and nerve damage

Cataracts
- Presence of diabetes means it’s more likely that cataracts will occur

Source: ADA and CDC
Complications

Source: ADA and webmd
If that’s not enough...
7th cause of death in the United States

Source: ADA and CDC
Risk Factors

Source: https://sites.psu.edu/educatedm/2015/09/08/pre-diabetes-care-guide/
What is Insulin?

- A hormone made by the pancreas
- Allows your body to use glucose for energy or to store glucose for future use
When things are good then…
Insulin

Helps to keep your blood sugar level from getting too high (hyperglycemia) or too low (hypoglycemia)
Insulin
Insulin
When things are *not so good*

then...
Types of Diabetes

**TYPE 1 DIABETES**
Body does not produce enough insulin

**TYPE 2 DIABETES**
Body produces insulin but can’t use it well

**GESTATIONAL DIABETES**
A temporary condition in pregnancy

Source: www.who.int/diabetes/global-report
Type 1- Deficiency

~1.25 million in US (5% of population)

Previously known as juvenile diabetes but present in both adults and children

Source: ADA
Type 2 - Resistance

Most common type

~29 million in US (90-95%)

Source: ADA
Gestational - Temporary

2-10% of annual pregnancies

In women who don’t already have diabetes

Insulin resistance caused by hormone interference

Source: ADA
Prediabetes

A condition of higher than normal blood sugar that if not treated, often leads to type 2 diabetes within five years

Source: CDC
Testing Guidelines

Screening methods for Diabetes

Fasting plasma glucose

HbA1c

Plasma Glucose (blood sugar)

First test physician orders

Immediate answer at any time

Result affected by food, stress, illness, physical activity
Plasma Glucose (blood sugar)

Measured by a glucose meter or continuous glucose monitor
Plasma Glucose (blood sugar)

Measured by a glucose meter or continuous glucose monitor
Glucose Levels
HbA1c
What is HbA1c or A1c?

(aka Glycated Hb)
Develops when hemoglobin, a protein within red blood cells that carries oxygen, joins with glucose to become ‘glycated’
HbA1c is measured to identify a 3 month average plasma glucose concentration

Testing limited to a 3 month average because lifespan of a red blood cell is 3-4 months
HbA1c Advantages

Standardized Testing
Diagnosing Diabetes

A1c Test Results

Diabetes
6.5% or higher

Prediabetes
5.7 to 6.4%

Normal
Below 5.7%

Source: Webmd
### A1c and Blood Sugar

<table>
<thead>
<tr>
<th>A1c (%)</th>
<th>Average Blood Sugar (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>68</td>
</tr>
<tr>
<td>5</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>126</td>
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<td>7</td>
<td>152</td>
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<td>8</td>
<td>183</td>
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<td>13</td>
<td>326</td>
</tr>
<tr>
<td>14</td>
<td>355</td>
</tr>
</tbody>
</table>
IS THERE ANY HOPE?
Food
Fitness
Hemoglobin - Structure

Source: https://medium.com/impossible-foods/heme-health-the-essentials-95201e5aaffa
Hemoglobin - Structure

Love meat? Eat meat. Impossible™ delivers all the flavor, aroma and beefiness of meat from cows. But here's the kicker: It's just plants doing the Impossible.

Source: https://medium.com/impossible-foods/heme-health-the-essentials-95201e5afffa
Hemoglobin Variants

Abnormalities in the synthesis of hemoglobin can occur leading to specific blood disorders

Hemoglobinopathy - change of a globin chain

Thalassemia - reduced production of a globin chain
Hemoglobinopathies

Globin Chains
# Common Hemoglobinopathies

<table>
<thead>
<tr>
<th>Hb</th>
<th>Distribution</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>Africa, India, Middle East, Mediterranean</td>
<td>Hemolytic anemia</td>
</tr>
<tr>
<td>C</td>
<td>Western Africa</td>
<td>Hemolytic anemia</td>
</tr>
<tr>
<td>E</td>
<td>Southeast Asia</td>
<td>Hemolytic anemia</td>
</tr>
</tbody>
</table>
Clinical Issues

Sickle cell disease

Hemolytic anemia

Red blood cells (RBC) are destroyed faster than they can be made

Less RBCs = Less oxygen being carried to the body's cells

# Common Thalassemias

<table>
<thead>
<tr>
<th>Hb</th>
<th>Distribution</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Thalassemia</td>
<td>Mediterranean, N Africa, Middle East</td>
<td>Mild to severe anemia</td>
</tr>
<tr>
<td>Alpha-Thalassemia</td>
<td>Southeast Asia, Indian, Chinese</td>
<td>Asymptomatic or anemia</td>
</tr>
</tbody>
</table>
Testing Methods for HbA1c
Testing Methods for HbA1c

Charge

Structure
National Glycohemoglobin Standardization Program
• HbA1c assays to those of the DCCT and UKPDS

• ADA and IEC recommend use of HbA1c to screen and diagnose
High Performance Liquid Chromatography (HPLC)
HPLC
HPLC - Ion Exchange

• Used in key landmark studies for glycemic control

• Detects most common Hb variants in presence of HbA1c
HPLC - Ion Exchange

• Separation of hemoglobin molecules based on ionic charge (positive or negative)
  
  o Analytical cartridge (also called column) with a negative charged resin
  
  o Buffers have varying ionic strengths of positive charge
Addition of Buffer B

Analytical Cartridge - resin with negative charge

Detector

Chromatogram
HPLC - Ion Exchange

<table>
<thead>
<tr>
<th>Peak Name</th>
<th>RT</th>
<th>Area</th>
<th>Area%</th>
<th>Concentration (% NGSP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1a</td>
<td>5.83</td>
<td>2141.92</td>
<td>1.37</td>
<td>---</td>
</tr>
<tr>
<td>F</td>
<td>7.59</td>
<td>6884.66</td>
<td>4.41</td>
<td>---</td>
</tr>
<tr>
<td>Unknown</td>
<td>9.49</td>
<td>2259.72</td>
<td>1.45</td>
<td>---</td>
</tr>
<tr>
<td>LA1c</td>
<td>10.97</td>
<td>5438.04</td>
<td>3.49</td>
<td>---</td>
</tr>
<tr>
<td>HbA1c</td>
<td>13.26</td>
<td>10516.24</td>
<td>---</td>
<td>8.5</td>
</tr>
<tr>
<td>P3</td>
<td>18.15</td>
<td>37849.81</td>
<td>24.26</td>
<td>---</td>
</tr>
<tr>
<td>A0</td>
<td>23.97</td>
<td>90923.79</td>
<td>58.28</td>
<td>---</td>
</tr>
</tbody>
</table>

Total Area: 156014

Status: Released
HPLC - Ion Exchange Instruments

Bio-Rad

Tosoh
Capillary Electrophoresis
Another separation technique method

Instead of using

Now using
Capillary Electrophoresis
Capillary Electrophoresis
Capillary Electrophoresis Instrument

Sebia
Method - Structure

HPLC - Boronate Affinity
HPLC - Boronate Affinity

Glycated

Non-Glycated

Hemoglobin

Glucose

Hemoglobin is bound to glucose

Hemoglobin is not bound to glucose
HPLC - Boronate Affinity

Column with Boronate

Blood Sample & Buffer A

Chromatogram
HPLC - Boronate Affinity

Column with Boronate

Blood Sample & Buffer A

Detector

Chromatogram
HPLC - Boronate Affinity

Column with Boronate

Buffer B

Detector

Chromatogram
HPLC - Boronate Affinity Instrument

Trinity
Method - Structure

Immunoassay
This method uses a chemical process that measures the presence or concentration of an analyte.
Immunoassay

A1c = 8.00%
Immunoassay Instruments

Siemens

Roche
Point of Care

Closer to the patient
Results while waiting
Point of Care

Siemens

Abbott
Conclusion

- Diabetes is worth talking about
- People should be tested for HbA1c
- Testing technology has improved and is more accurate
- Manage your own health and care
  - Diet and Exercise
“It’s not the load that breaks you down, it’s the way you carry it.”
~ Lou Holtz