Diabetes Mellitus

Classification, Diagnosis, and Monitoring

Dr. Morris Pudek

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Objectives

- Learn classification of DM
- Learn major characteristics of Type 1 and 2 DM
- Learn the criteria for diagnosis of and screening for DM
- Describe pathogenesis, clinical features and lab findings of acute complications of DM
- Describe role of HbA1c and albumin excretion rate in long term monitoring of DM
- Review the latest recommendations for diagnosis now using HbA1c
- Outline therapeutic goals for DM
DIABETES MELLITUS: SOME RECENT FACTS

- More than 25 million North Americans affected; 25% have the disease but are not yet diagnosed.
- Recent estimate 1 in 7 health care dollars spent on the complications of DM. In Canada $15 billion/yr.
Onset of disease occurs on average 4 - 7 years prior to diagnosis (for Type 2)

Major cause of death prior to insulin was diabetic ketoacidosis

Now major problems are chronic complications: vascular, myocardial infarction, pregnancy complications, neuropathy, renal disease, retinopathy, infections, peridontal disease, hypertension etc

About 80% of diabetics die of heart disease or stroke, about 75% will develop retinal damage, >1in 3 develop renal problems, 10% foot ulcers (amputation may be required)

GI problems in up to half of diabetics

Average annual cost for meds and testing supplies is $5000/pnt
Diabetes Statistics: BC

Now:
- 220,000 known diabetics in our province
- Cost of medical management > $1 Billion

10 years from now:
- 350,000 diabetics
- Cost $2 Billion

*Shocking statistic: 1 in 3 NAs born today will develop DM sometime during their lifetime.
Prevalence of DM in Canada by Age

The chart shows the prevalence of DM in Canada by age group. The prevalence increases with age, with the highest rates observed in the age group 75-79 and ≥85 years. The prevalence is higher for males compared to females across all age groups. The total prevalence ranges from 0.3% in the 1-19 age group to 6.8% in the ≥85 age group.
Classification of Diabetes Mellitus

I  Type 1 (beta cell destruction)
   A. autoimmune
   B. idiopathic

II  Type 2 (insulin resistance and rel.def.)

III  Other specific types (see handout)

IV  Gestational diabetes mellitus

V  Impaired fasting glucose or IGT
## Major characteristics of type 1 and type 2 diabetes mellitus

<table>
<thead>
<tr>
<th>Feature</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>typical age of onset</td>
<td>childhood, young adult</td>
<td>middle-age, elderly</td>
</tr>
<tr>
<td>onset</td>
<td>acute</td>
<td>gradual</td>
</tr>
<tr>
<td>habitus</td>
<td>lean</td>
<td>often obese</td>
</tr>
<tr>
<td>weight loss</td>
<td>usual</td>
<td>uncommon</td>
</tr>
<tr>
<td>ketosis-prone</td>
<td>usually</td>
<td>usually not</td>
</tr>
<tr>
<td>serum insulin conc.</td>
<td>low or absent</td>
<td>often normal</td>
</tr>
<tr>
<td>family history of diabetes</td>
<td>uncommon</td>
<td>common</td>
</tr>
<tr>
<td>HLA association</td>
<td>DR3, DR4</td>
<td>none</td>
</tr>
<tr>
<td>Autoantibodies (islet, GAD)</td>
<td>Present prior to onset</td>
<td>Absent</td>
</tr>
</tbody>
</table>
Incidence of Type 1 Diabetes in Different Countries

Risk per Year/100,000:
- Finland: 28.6
- Sweden: 22.6
- Norway: 17.6
- United States: 14.2
- Scotland: 13.8
- Denmark: 13.7
- Netherlands: 10.9
- New Zealand: 10.4
- Canada: 9.0
- England: 7.7
- Kuwait: 5.6
- Israel: 4.3
- France: 3.7
- Japan: 0.8
Pathogenesis of Type 1 Diabetes

Immune dysregulation

Environmental triggers and regulators

IAA, GADA, ICA +

Loss of first-phase insulin response

Variable insulitis β-cell sensitivity to injury

Pre-Diabetes (IGT)

Glucose intolerance

Absence of C-peptide

Overt Diabetes

Time

Mechanisms Involved in Type 2 Diabetes

- Increased Glucose Production
- Impaired Insulin Secretion
- Receptor + Postreceptor Defect
Signs/Symptoms of DM

- Persistent thirst
- Frequent urination
- Weight gain or loss
- Extreme fatigue or lack of energy
- Blurred vision
- Frequent or recurring infections
- Cuts and bruises slow to heal
- Tingling or numbness of hands and feet
- Difficulty maintaining an erection
Diagnostic Criteria for Diabetes Mellitus

Normal

1. Fasting glucose < 6.1 mmol/L (in US < 5.7 mmol/L)
2. Two hour oGTT value < 7.8 mmol/L
Diagnostic Criteria for Diabetes Mellitus 2007

Diabetes mellitus in non-pregnant patients

1. Symptoms plus FPG ≥ 7.0 mmol/L or;
2. Symptoms plus random glucose ≥ 11.1 mmol/L or;
3. Symptoms plus 2 h post 75 g oGTT ≥ 11.1 mmol/L

*In the absence of symptoms repeat testing is required to confirm the diagnosis.*
Diagnostic Criteria for Diabetes Mellitus

Impaired fasting glucose or impaired glucose tolerance

1. FPG between 6.1 and 6.9 mmol/L (lower limit is 5.7 in the US)
2. Two hour value in oGTT between 7.8 and 11.1 mmol/L
Protocol for Glucose Tolerance Test

- Patient should be fasting between 8 - 12 hours prior to test
- Normal carbohydrate diet prior to test
- At rest during test
- Patient given 75 gm glucose (glucola) to ingest
- Plasma glucose measured prior to glucose load (0 hr) and 2 hour post ingestion.
- For gestational diabetes, 75 gm load given and glucose measured at 0, 1, and 2 hr post load.
Criteria for Screening for DM in Asymptomatic Individuals 2007

1. Test all individuals at age 40 and above. Repeat at 3 year intervals if normal.

2. Test at younger age or more often if:
   - obese
   - family history
   - high risk ethnic group (Aboriginal, Hispanic, Asian, African)
   - previous history of GDM
   - hypertensive
   - low HDL and/or high triglyceride
   - previous IFG or IGT
   - Others: polycystic ovary syndrome, acanthosis nigricans, schizophrenia

*preferred test was a FPG, do oGTT if between 5.7 and 6.9
Latest guideline HbA1c has become a diagnostic test
Diagnosis of Gestational DM

- Optional initial screen with 1 hour glucose post 50 gm oral glucose load. Normal response <7.8 mmol/L. Usually carried out at 24 - 28 weeks (no fasting required).

- Now recommend 2 hr glucose tolerance test following 75 g of oral glucose (pre test fasting required).

- *Normal criteria:

<table>
<thead>
<tr>
<th>Fasting</th>
<th>1 hour</th>
<th>2 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>mmol/L</td>
<td>&lt;5.1</td>
<td>&lt;10.0</td>
</tr>
</tbody>
</table>

*One or more results exceeding these limits is diagnostic of GDM
Consequences of GDM for Neonate

- Macrosomia
- Respiratory distress syndrome
- Hypoglycemia
- Hypocalcemia
- Polycythemia
- Intrauterine death
- Congenital malformations
- Hyperbilirubinemia
Acute Complications of Diabetes Mellitus

- Diabetic Comas: diabetic ketoacidosis (DKA)*, hyperglycemic hyperosmolar state (HHS)*, hypoglycemia
- Myocardial Infarction
- Infections: poorly controlled diabetics have impaired phagocytic function
- Stroke: more common in diabetic because of hypertension and other factors
Pathogenesis of DKA

Hyperglycemia → Glycosuria → Loss of calories
- Hunger
- Polyphagia
- Weight loss
- Mobilization of fat and protein
  - Acidosis
  - Hyperpnea
  - Negative nitrogen balance
  - Loss of electrolytes
  - Polyuria
  - Dehydration
  - Polydipsia
  - Coma & Death
## Causes of Hyperglycemic Ketoacidotic Coma

<table>
<thead>
<tr>
<th>Absolute Insulin Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newly presenting Type I diabetes with β-cell depletion</td>
</tr>
<tr>
<td>Incorrect insulin dosage (omitted or decreased)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative Insulin Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress states: infection</td>
</tr>
<tr>
<td>myocardial infarction</td>
</tr>
<tr>
<td>trauma</td>
</tr>
<tr>
<td>cerebrovascular accident</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs/endocrine disorders:</th>
<th>steroids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>adrenergic agonists</td>
</tr>
<tr>
<td></td>
<td>hyperthyroidism</td>
</tr>
<tr>
<td></td>
<td>pheochromocytoma</td>
</tr>
<tr>
<td></td>
<td>thiazide diuretics</td>
</tr>
</tbody>
</table>

Clinical Features of DKA

- Thirst
- Polyuria
- Dehydration
- Hypotension, tachycardia
- Ketosis
- Hyperventilation
- Vomiting and abdominal pain
- Drowsiness and coma
Lab tests in DKA

- Glucose
- Urea / creatinine
- Ketones (beta hydroxybutyrate)
- Electrolytes / Osmolality
- Urinalysis
- Blood gases
- CBC and differential
- Others: HbA1c, ECG, chest radiograph, culture
Metabolic Features of DKA

- Hyperglycemia
- Glycosuria
- Metabolic acidosis
- Ketonemia and ketonuria (B-OH butyrate)
- Acute pre-renal failure (increased urea)
- Hyperkalemia
- Hemoconcentration
<table>
<thead>
<tr>
<th>Element</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>5-6 liters</td>
</tr>
<tr>
<td>Sodium</td>
<td>500 mEq</td>
</tr>
<tr>
<td>Chloride</td>
<td>350 mEq</td>
</tr>
<tr>
<td>Potassium</td>
<td>300-1000 mEq</td>
</tr>
<tr>
<td>Magnesium</td>
<td>25-50 mEq</td>
</tr>
<tr>
<td>Phosphate</td>
<td>50-100 mEq</td>
</tr>
</tbody>
</table>
Main Elements of Treatment of DKA

- Fluid replacement (normal saline)
- Insulin
- Potassium
- Alkali (bicarbonate) only if pH < 7.0
- Monitor patient, clinical and lab parameters
- Treat underlying precipitating factor if identified
Case History: Diabetic Ketoacidosis

- An 18 year old female presents to the emergency department with drowsiness, recent weight loss, polyuria, and vomiting. Physical examination revealed a blood pressure of 95/60 and a pulse rate of 112/min. The patient was also hyperventilating and there was a smell of acetone on her breath.

- Lab results:
  - Na 130 (135-145)
  - K  5.8 (3.5-5)
  - HCO3 5 (21-28)
  - Urea 18 (2-8)
  - Cr 140 (40-90)
  - Gluc 32 (3.5-11)
  - pH 7.05 (7.35-7.45)
  - pCO2 15 (35-45)
Pathogenesis of Hyperglycemic Hyperosmolar State (HHS)
Osmolality and Mental Status in HHS

Ranges in Osmolality

( ) = number of patients

Mean Osmolality (mOsm/Kg)

Alert (51)  Drowsy (48)  Stupor (17)  Coma (6)

MENTAL STATUS
Case History: Hyperglycemic Hyperosmolar State

- A 64 year old female who lived on her own was discovered by her son in a semi-conscious state at home. In the ER she was found to be very dehydrated with a normal respiritory rate.

- Lab results

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Normal Range</th>
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</thead>
<tbody>
<tr>
<td>Na</td>
<td>149</td>
<td>(135-145)</td>
</tr>
<tr>
<td>K</td>
<td>4.9</td>
<td>(3.5-5)</td>
</tr>
<tr>
<td>HCO3</td>
<td>18</td>
<td>(21-28)</td>
</tr>
<tr>
<td>Urea</td>
<td>35</td>
<td>(2-8)</td>
</tr>
<tr>
<td>Cr</td>
<td>180</td>
<td>(40-95)</td>
</tr>
<tr>
<td>Gluc</td>
<td>54</td>
<td>(3.5-11)</td>
</tr>
<tr>
<td>Tot. Pr.</td>
<td>90</td>
<td>(60-80)</td>
</tr>
<tr>
<td>Osm.</td>
<td>380</td>
<td>(275-295)</td>
</tr>
</tbody>
</table>

Ketones Negative
The Major Chronic Complications of Diabetes

- Eyes (retinopathy)
- Brain and cerebral circulation (cerebrovascular disease)
- Heart and coronary circulation (coronary heart disease)
- Kidney (nephropathy)
- Lower limbs (peripheral vascular disease)
- Peripheral nervous system (neuropathy)
- Diabetic foot (ulceration and amputation)
Chronic Complications of Diabetes Mellitus

- Leading cause of visual impairment (retinopathy and cataracts)
- Diabetic nephropathy
- Diabetic neuropathy (peripheral and autonomic)
- Diabetic dermopathy
- Cardiovascular disease
- Gangrene (peripheral vascular disease)
- Infection (candida and other unusual infections)
Do we have proof that good glucose control reduces chronic complications?
One of Jean Chretien's finer moments.

"The proof is the proof and when you have a good proof it's proven."

— Jean Chretien on the standard of truth required for deciding Canada's involvement in the US war on Iraq.

Has there EVER been a better time for pie??
Studies That Proved Glucose Control Important

- Diabetes Control and Complications Trial (DCCT) 1993. Looked at Type 1 DM patients for 10 years. Intense glucose (avg HbA1c 7.2%) control reduced retinopathy, nephropathy, and neuropathy by 60% compared to standard treatment (avg HbA1c 8.9%).

- United Kingdom Prospective Diabetes Study (UKPDS) 1998. Looked at Type 2 DM patients. Showed that glucose control and blood pressure control significantly reduced microvascular complications.
Monitoring Patients with Diabetes Mellitus

- Glucose control: home glucose meters, HbA1c
- Diabetic nephropathy: albumin excretion rate, serum creatinine
- Physical examination: blood pressure, opthamological, cardiovascular, neurological exam
- Lipids
Newer glucose meter

- Results in just 5 seconds
- Clinically proven to help significantly reduce average blood glucose levels
- Tiny blood sample of only 1.0 µL which can mean a less painful test
- At the push of a couple of buttons, easily see trouble spots, hypos, impact of meals
- Compatible with OneTouch® Diabetes Management Software
New continuous monitoring device
A Step Towards Closing the Loop

The MiniMed® Paradigm® Veo™ Insulin Pump and Continuous Glucose Monitoring (CGM) System*

The first insulin pump and CGM system with an automatic low glucose suspend feature.

Live More, Worry Less
HbA1c

- Essential test for assessment of long-term glucose control
- How is it formed?
- How do we use it?
- How can we use it in the future?
Non-enzymatic glycosylation of N-terminal valine of beta chain of HbA leads to formation of HbA1c.
Aldimine

Ketamine

Amadori rearrangement

amino-terminal valine of β chain
Interpretation of HbA1c (A1C)

- Reference interval 4 - 6 %
- A 1% rise in HbA1c reflects an average glucose concentration increase of 1.6 mmol/L
- Target HbA1c is 7% (lower is desirable)
- Poor control > 8.0%
- When glucose control therapy changed it takes at least 6 weeks to be reflected in HbA1c values.
Future Applications of HbA1c

- Report estimated average glucose concentration based on HbA1c level
- Use HbA1c as the initial diagnostic test for diabetes mellitus (Decision level > 6.5%) Advantage: No patient prep req’d. Stable, unlike glucose values. CDA has recently approved this test for diagnosis along with traditional tests (i.e. FPG).
DCCT: Relationship of A1C to Risk of Microvascular Complications

DCCT Experience: Tight Blood Glucose Control Allows Reduction of Retinopathy but is Associated With an Increase of Severe Hypoglycemia
Implications of Non-enzymatic glycosylation of proteins

- Any protein exposed to high concentrations of glucose may be glycosylated irreversibly which in turn may alter the function of this protein (collagen, lens crystallin, basement membrane proteins, etc.)

- In addition “advanced glycosylation end-products (AGE)” may form

- These changes may account for some of the long term complications of diabetes.
Fasting Plasma Glucose (FPG) for Diagnosis revisited

Advantages

1. Easy

2. Single blood sample

3. Single cutoff - 7.0 mmol/L
Fasting Plasma Glucose (FPG)

Disadvantages

1. Patient must fast $\geq 8$ h

2. Repetition of FPG on different days reveals large biological variability:
   - Intraindividual CVs 4.6-8.3%
   - Interindivdual CVs 7.5-12.5%

3. Less sensitive than OGTT

4. Sample stability (cell metabolism)
OGTT Lacks Reproducibility

1. 524 subjects had 2 OGTTs 2-6 weeks apart
   198 had IGT initially: repeat testing;
   39% normal, 13% DM

3. Other studies show only about 50% OGTTs reproducible
HbA1c for Diagnosis of Diabetes

Advantages

1. Indicates chronic hyperglycemia
2. Low intra-individual variability (<2%)
3. Single test for diagnosis and monitoring is attractive
4. Evidence suggests that diagnostic accuracy similar to FPG
5. Fasting not necessary. Stable analyte
DISADVANTAGES OF HbA1c

1. Variety of methods used. Standardization issue?

2. Many patients do not understand the name or the units

3. Does not reflect glucose variability during the day

4. What should the decision level be for diagnosis? (present suggestion 6.5%)

5. Other conditions may alter the relationship between glucose and HbA1c (Hgb variants, rbc life span, uremia, transfusion, anemia)
<table>
<thead>
<tr>
<th>Factor</th>
<th>Increased A1C</th>
<th>Decreased A1C</th>
<th>Variable change in A1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythropoiesis</td>
<td>Iron deficiency</td>
<td>Use of erythropoietin, iron or B12</td>
<td>Fetal hemoglobin</td>
</tr>
<tr>
<td></td>
<td>B12 deficiency</td>
<td>Reticulocytosis</td>
<td>Hemoglobinopathies</td>
</tr>
<tr>
<td></td>
<td>Decreased erythropoiesis</td>
<td>Chronic liver disease</td>
<td>Methemoglobin</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Genetic determinants</td>
</tr>
<tr>
<td>Altered hemoglobin</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Glycation</td>
<td>Alcoholism</td>
<td>Ingestion of aspirin, vitamin C or vitamin E</td>
<td></td>
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<tr>
<td></td>
<td>Chronic renal failure</td>
<td>Hemoglobinopathies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decreased erythrocyte pH</td>
<td>Increased erythrocyte pH</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte destruction</td>
<td><strong>Increased erythrocyte lifespan:</strong></td>
<td><strong>Decreased erythrocyte lifespan:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Splenectomy</td>
<td>Chronic renal failure</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Hemoglobinopathies</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Splenomegaly</td>
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<tr>
<td></td>
<td></td>
<td>Rheumatoid arthritis</td>
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<tr>
<td></td>
<td></td>
<td>Antiretrovirals</td>
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<tr>
<td></td>
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<td>Ribavirin</td>
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<td></td>
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<td>Dapsone</td>
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<tr>
<td>Assays</td>
<td>Hyperbilirubinemia</td>
<td>Hypertriglyceridemia</td>
<td>Hemoglobinopathies</td>
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<td></td>
<td>Carbamylated hemoglobin</td>
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<tr>
<td></td>
<td>Alcoholism</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large doses of aspirin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic opiate use</td>
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</tr>
</tbody>
</table>
LACK OF STANDARDIZATION IN HEMOGLOBIN $A_1C$ ASSAYS

• NATIONAL GLYCOHEMOGLOBIN STANDARDIZATION PROGRAM (NGSP) to the rescue!

• DEVELOPED IN 1996 TO STANDARDIZE HEMOGLOBIN TEST RESULTS SO THAT CLINICAL LABORATORY RESULTS ARE COMPARABLE TO THOSE REPORTED IN DCCT.
Improvement in Standardization of Hemoglobin A₁c Assays 1993-2006
New Diagnostic Criteria for DM in Canada Now Includes HbA1c 2012

Table 2. Diagnostic criteria for diabetes (adapted from 17)

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FPG ≥7.0 mmol/L</strong></td>
</tr>
<tr>
<td>Fasting = no caloric intake for at least 8 hours</td>
</tr>
<tr>
<td><strong>or</strong></td>
</tr>
<tr>
<td><strong>Casual PG ≥11.1 mmol/L + symptoms of diabetes</strong></td>
</tr>
<tr>
<td>Casual = any time of the day, without regard to the interval since the last meal</td>
</tr>
<tr>
<td>Classic symptoms of diabetes = polyuria, polydipsia and unexplained weight loss</td>
</tr>
<tr>
<td><strong>or</strong></td>
</tr>
<tr>
<td><strong>2hPG in a 75-g OGGT ≥11.1 mmol/L</strong></td>
</tr>
<tr>
<td><strong>or</strong></td>
</tr>
<tr>
<td><strong>A1C ≥6.5%</strong></td>
</tr>
<tr>
<td>Using a standardized, validated assay, in the absence of conditions that affect the accuracy of the A1C</td>
</tr>
</tbody>
</table>
Key Latest Recommendations for Screening

- Web based risk calculator (CANRISK or FINDRISC) now recommended before formal testing for DM
- The risk is based on age, obesity, hyperglycemia in past history, hypertension, family history of diabetes, activity levels, and dietary factors.
- The first line test should be HbA1c (FPG and oGTT are acceptable alternatives)
- Testing should only be performed on those < 40 who are at high risk based on score
The Agreement (accepted by IFCC, EASD, IDF, ADA Sept 2007)

- HgA1c results and reporting should be standardized
- The IFCC reference method (mass spectrometry) should be the anchor for standardization
- HbA1c should be reported in IFCC units (mmol/mol) or NGSP units (%)
- eAG should also be reported
- All 3 units can be used (In Canada?)
The American Viewpoint

Use of the Estimated Average Glucose (eAG) in Patient Care
A Typical Patient Encounter

“So, Mrs. Smith, it looks like you do have diabetes. Your repeat fasting blood sugar was 10, and as you recall the first one was 10.5. Over 7 is diabetes. Also, your hemoglobin A1c was way too high at 8.6%. Normal is less than 6%. We need to get it below 7%.”
A Typical Patient Encounter

“What’s a hemoglobin A...whatever you said? I remember my hemoglobin was low when I was pregnant. What were those other numbers? What do you mean, 7%...of what?”
Uh...
The Clinical Dilemma

- HbA1c: useful for research, risk prediction, target of therapy
- Well standardized
- HOWEVER, difficult to explain to patients
- Concept of % is not intuitive
- Glucose more familiar to patients from self-monitoring or from laboratory glucose results
The Concept of Average Glucose

- We tell patients the HbA1c reflects their “average glucose over 2-3 months”

- But: do we know this for sure?
ADAG Study: Study Success

90% of values fell within +/- 15%

90% of cohort values fall in this range
ADAG Study: Other Factors Examined

- Does the HbA1c-Average Glucose relationship differ by:
  - Type 1 or type 2 diabetes: NO
  - Diabetes or no diabetes: NO
  - Amount of glucose variability: NO
  - Gender: NO
  - Age: NO
  - Ethnicity/Race: NO
  - Smoking: NO
ADAG Study Excluded Known Sources of “Inaccuracy” of HbA1c

- Hemoglobinopathy
- Anemia
- Pregnancy
- Hepatic or renal disease
- Etc.
ADAG Study: “Translation” of HbA1c into eAG

<table>
<thead>
<tr>
<th>HbA1c (%)</th>
<th>eAG (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>5.4</td>
</tr>
<tr>
<td>6</td>
<td>7.0</td>
</tr>
<tr>
<td>7</td>
<td>8.6</td>
</tr>
<tr>
<td>8</td>
<td>10.2</td>
</tr>
<tr>
<td>9</td>
<td>11.8</td>
</tr>
<tr>
<td>10</td>
<td>13.4</td>
</tr>
</tbody>
</table>
A Typical Patient Encounter using eAG

“So, Mrs. Smith, it looks like you do have diabetes. Your average blood sugar is around 11. When people don’t have diabetes, this number is below 7. We need to work with you to try to get this number, the average glucose, down below 8 over the next few months with some weight loss, exercise, and a medication. Let’s talk some more about what you can do...”
A Typical Patient Encounter

“Wow, I’m not happy to hear that…I know that diabetes can do some bad things. Tell me what I can do to get my average glucose down.”
What Can Clinical Chemists Do?

- Even with tools, most clinicians will not take the time to calculate conversions.
- Reporting both HbA1c (DCCT-aligned) AND eAG on lab reports will do the most to promote wide use of the term.
- Professional and patient education may drive demand.
- Conversion is a simple regression equation.
The American Position!

Average Glucose
Blood pressure
Cholesterol
to help make the “A” understandable!
The Canadian Position on HbA1c and eAG

No agreement at this time between CSCC and the CDA
Diabetes is the leading cause of end stage renal failure

Earliest change seen is increase in urine albumin excretion rate in the range of 30 - 300 mg albumin/d. Patient has overt proteinuria if >300 mg/d. Normal <30 mg/d

Once proteinuria develops renal failure may occur within 5 years.

It is now recommended that patients with DM be screened for albuminuria using albumin to creatinine ratio on an annual basis using random urine specimens. Normal: males <2.0 mg/mmol Cr, females <2.8 mg/mmol Cr
Measures to Prevent Progression of Diabetic Nephropathy

- Achieve glycemic control (HbA1c < 7%)
- Aggressively manage BP (Target <130/80) Multiple drugs may be required
- ACEI or Angiotensin II receptor blockers preferred
- Stop smoking
Guidelines for Patients with Diabetes

- Measure HbA1c 4X/yr
- Glucose meter readings before and after meal
- Measure BP at every office visit
- Measure lipid profile every year
- Determine and monitor BMI (wt (kg)/ht (m²))
- Lifestyle changes (exercise, diet, smoking)
- ASA low dose(?) and ACEI or ARB
- Examine feet at least annually
- Urine ACR (albumin creatinine ratio) annually
- Annual neurological exam, retinal exam
Summary of Therapeutic Goals for Diabetes Mellitus

- UKPDS trial clearly showed the importance of glycemic control and BP control in reducing secondary complications
- Glycemic control: HbA1c < 7%
- BP control: <130/80
- Lipid control: LDL Cholesterol <2.0 mmol/L, T Chol: HDL Chol < 4
Recent Interesting Controversies

- Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study BMJ 2008): Conclusions: In patients with newly diagnosed type 2 diabetes self monitoring of blood glucose concentration has no effect on glycemic control but is associated with higher scores on a depression scale.

- Effects of Intensive Glucose Lowering in Type 2 Diabetes (Accord Study NEJM 2008): Conclusion: As compared with standard therapy, the use of intensive therapy to target normal glycated hemoglobin levels for 3.5 years increased mortality and did not significantly reduce major cardiovascular events.