Role of A1C in Diagnosing Diabetes

Expert committee convened in 2008 to consider the current and future means of diagnosing diabetes in nonpregnant individuals. ***The intent of the report is to serve as a stimulus to the international community and professional organizations to consider the use of the A1C assay for the diagnosis of diabetes.***

In 1979, the National Diabetes Data Group provided the diagnostic criteria that would serve as the blueprint for nearly two decades. They relied on distribution of glucose levels, rather than on the relationship of glucose levels with complications, to diagnose diabetes despite emerging evidence that the microvascular complications of diabetes were associated with a higher range of fasting and (OGTT glucose values. The diagnostic glucose values chosen were based on their association with decompensation to "overt" or symptomatic diabetes.

In 1997 the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus reexamined the basis for diagnosing diabetes. This committee made two seminal contributions: First, they refocused attention on the relationship between glucose levels and the presence of long-term complications as the basis for the diagnosis of diabetes. Second, they summarized the data negating the wide-spread hypothesis that the 2 HPG was the gold-standard test for diagnosing diabetes.

The 1997 report also recommended that the FPG level, rather than the 2 HPG, be the preferred test to diagnose diabetes because it was more convenient for patients and lest costly and time consuming and the repeat-test reproducibility was superior.
The committee additionally introduced the term "impaired fasting glucose" (IFG) to differentiate the metabolic state between a normal state and diabetes when the FPG test was used.

A 2003 follow-up report from the expert committee refined the fasting glucose value range for IFG from greater than 110 but less than 126 mg/dl to greater than 100 but less than 126 mg/dl to make it more comparable with the IGT value.

The A1C captures the degree of glucose exposure over time and which is related more intimately to the risk of complications than single or episodic measure of glucose levels, may serve as a better biochemical marker of diabetes and should be considered a diagnostic tool. The committee report recommended against using A1C values for diagnosis in part because of the lack of assay standardization.

In summary, the large volume of data from diverse populations has not established an A1C level associated with an increase in the prevalence of moderate retinopathy and provides strong justification for assigning an A1C cut point of more or less 6.5% for the diagnosis of diabetes. This cut point should not be construed as an absolute dividing line between normal glycemia and diabetes: however, the A1C level of 6.5% is sufficiently

sensitive and specific to identify individuals who are at risk for developing retinopathy and who should be diagnosed as diabetic.

Advantages of A1C testing compared with FPG or 2 HPG for the diagnosis of diabetes

- Standardized and aligned to the DCCT/UKPDS; measurement of glucose is less well standardized
- Better index of overall glycemic exposure and risk for long-term complications
- Substantially less biologic variability
- Substantially less preanalytic instability
- No need for fasting or times samples
- Relatively unaffected by acute (e.g. stress or illness related) perturbations in glucose levels
- Currently used to guide management and adjust therapy

Role of the A1C assay in the diagnosis of diabetes –
Recommendations of the International Expert Committee

For the diagnosis of diabetes:

- The A1C assay is an accurate, precise measure of chronic glycemic levels and correlates well with the risk of diabetes complications
- The A1C assay has several advantages over laboratory measures of glucose.
- Diabetes should be diagnosed when A1C is $\geq$ 6.5%. Diagnosis should be confirmed with a repeat A1C test. Confirmation is not required in symptomatic subjects with plasma glucose levels > 200 mg/dl (>11.1 mmol/l).
- If A1C testing is not possible, previously recommended diagnostic methods (e.g., FPG or 2HPG, with confirmation) are acceptable.
- If A1C testing is indicated in children in whom diabetes is suspected but the classic symptoms and a casual plasma glucose > 200mg/dl (> 11.1 mmol/l are not found.

For the identification of those at high risk for diabetes:

- The risk for diabetes based on levels of glycemia is a continuum; therefore, there is no lower glycemic threshold at which risk clearly begins.
- The categorical clinical states pre-diabetes, IFG, and IGT fail to capture the continuum of risk and will be phased out of use as A1C measurements replace glucose measurements.
- As for the diagnosis of diabetes, the A1C assay has several advantages over laboratory measures of glucose in identifying individuals at high risk for developing diabetes.
- Those with A1C levels below the threshold for diabetes but $\geq$ 6.0% should receive demonstrably effective preventive interventions. Those with A1C below this range may still be at risk and, depending on the presence of other diabetes risk factors, may also benefit from prevention efforts.

- The A1C level at which population-based prevention services begin should be based on the nature of the intervention, the resources available, and the size of the affected population.

International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes. Diabetes Care, July 2009 32: 1327-1334.

Commentary from www.medscape.com:

First major proposed change in diagnosing diabetes in 30 years.

A1C values vary less than the FPG values and the assay for A1C has technical advantages compared with the glucose assay. A1C gives a picture of the average blood glucose level over the preceding 2 to 3 months.

A disadvantage is the cost as the test is more expensive. However, cost analyses have not been done and costs are not the same as charges to the patient. Limitations noted in countries with high populations with severe chronic anemia, hemolytic anemia etc. as these conditions – very low hemoglobin levels cause the A1C to be inaccurate.

What is next?
The ADA is not issuing a position statement at this time. The committee's findings will be referred to practice groups for review of the implications and for recommendations.