THE ENDOCRINE SOCIETY

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THE ENDOCRINE SOCIETY STATEMENT ON THE USE OF A1C FOR DIABETES DIAGNOSIS AND RISK ESTIMATION

January, 2010—The recently published Clinical Practice Recommendations of the American Diabetes Association (ADA)[1] have taken a major new step in advocating the use of the A1C test for the diagnosis of diabetes, and for the identification of patients at risk for diabetes. The new recommendations indicate that patients with an A1C of 6.5% or higher can be identified as having diabetes without the need for a different confirmatory test, and patients with A1C 5.7%-6.4% can be considered as being at risk for the development of diabetes (a condition previously referred to as pre-diabetes). Before this statement, the only acceptable tests for the diagnosis of diabetes in non-pregnant adults were plasma glucose levels (≥126 mg/dL fasting, ≥200 mg/dL randomly obtained with symptoms of diabetes, and ≥200 mg/dL after an oral glucose tolerance test).

The use of A1C for screening and diagnosis of patients with diabetes offers some distinct advantages for patients and caregivers. It does not require sampling patients after an overnight fast or two hours after the administration of oral glucose. Although the ADA is recommending the use of this test *as an alternative to* the previously-used measures of fasting plasma glucose and two hour oral glucose tolerance test, it is likely that A1C will replace these other tests in most cases because of its ease of use. The rationale for the use of A1C for diagnostic purposes is largely based upon data showing that the microvascular complications of diabetes (retinopathy, nephropathy, and neuropathy) tend to occur or already have occurred in patients with A1C ≥6.5%. The population-based correlation of these complications with A1C is as good as other definitions of diabetes based upon fasting glucose or glucose tolerance test.

The Endocrine Society supports the ADA recommendations for use of A1C as an option to diagnose diabetes, because of its close correlation with microvascular complications, and its ease of use. However, it should be noted that there will be certain caveats to the use of this test that will have to be understood by clinicians and the population at large. Based upon review of national data sets, it appears that there is substantial non-overlap of patients who would be diagnosed by A1C or by glucose testing. Use of A1C ≥6.5% identifies substantially fewer individuals as having diabetes than do fasting plasma glucose and oral glucose tolerance tests. Examining national population data[2] may result in only 19.7 million U.S. adults identified as having diabetes, as opposed to 21.5 million by fasting plasma glucose and 26.5 million by glucose tolerance test. The more restrictive definition of diabetes fostered by A1C testing may have an impact on the number of patients who would be treated according to The Endocrine Society's Clinical Practice Guideline recommendations for cardiovascular risk management[3]. Currently, more aggressive treatment of dyslipidemia and hypertension is advocated for all patients with diabetes. There will be a significant number of patients who would have been

diagnosed with diabetes with plasma glucose criteria who would now not be diagnosed with diabetes using A1C. These individuals should probably still be regarded as being at high risk for cardiovascular disease, for which the more aggressive treatment goals for dyslipidemia and hypertension apply. The Endocrine Society recommends a more stringent CV risk management for metabolic syndrome patients and patients with an A1C>5.7%.

Clinicians should also be aware that there are a number of clinical conditions in which A1C and average blood glucose do not correlate well. These include iron deficiency and hemolytic anemia, various hemoglobinopathies, thalassemias, hereditary spherocytosis, malignancies, and severe chronic hepatic and renal disease. Patients with these conditions should not have A1C testing performed for diabetes screening or diagnosis. It is also not known which of the newer point-of-service tests for glycohemoglobin is sufficiently accurate to be used for diabetes diagnosis. As noted in the ADA's statement, only standardized, validated techniques for A1C testing should be used. The point-of-service tests will need to be validated individually. Also, there is some evidence from published studies in multiple geographic sites that the use of A1C for diagnosis of diabetes may result in significant differences in prevalence when compared across different ethnic groups and populations. In addition, A1C should not replace the use of fasting and all other glucose testing which are beneficial in the diagnosis of patients with Type 1 diabetes, in pediatrics, and in pregnancy.

The ADA also recommends that A1C be used to diagnose a separate category of individuals who are especially at risk for the development of diabetes, i.e. those with "pre-diabetes." The Endocrine Society supports this general concept as well. It is clear, however, that the proposed A1C definition is much more restrictive than the definitions based upon plasma glucose. Using the A1C criteria of 5.7% to 6.4%, the U. S. prevalence of "pre-diabetes" would be approximately 12% of the adult population, as opposed to 25% using current fasting plasma glucose criteria[2]. On the other hand, the use of A1C *or* impaired fasting glucose would increase the number of those with "pre-diabetes" to 33%. The individual and public health implications of this re-accounting of patients at risk for diabetes need to be examined and evaluated.

[1] *Diabetes Care,* January 2010, Vol. 33:Supplement 1; doi:10.2337

[2] Centers for Disease Control and Prevention, National Health and Nutrition Examination Survey; 2005-2006 (NHANES)

[3] Rosenzweig, J. et al. Primary Prevention of Cardiovascular Disease and Type 2 Diabetes in Patients at Metabolic Risk: An Endocrine Society Clinical Practice Guideline**.** J. Clin. Endocrinol. Metab. 2008; 93: 3671 - 3689.