Hemoglobin A1c: What is it, and why does it matter?

"Most commonly people are told that having an A1c of 5.6 – 5.8% should be considered normal, but these levels already put you in the second highest category for brain shrinkage! I believe that, based on this information, we should strive to keep our A1c at 5.2 or even lower," writes Dr. David Perlmutter.

Guidance statement of the American College of Physicians, March 2018: *"Clinicians should aim to achieve an HbA1c level between 7% and 8% in most patients with type 2 diabetes."*

"For my patients…a truly normal HbA1c ranges from 4.2 percent to 4.6 percent. Mine is consistently 4.5 percent." Dr. Richard K. Bernstein, Dr. Bernstein's Diabetes Solution.

How do we reconcile these contradictory statements? Why do the latest medical guidelines call for an easing of hemoglobin A1C goals, when respected clinicians argue for aggressive blood sugar lowering?

First of all, what is hemoglobin A1c? In contrast to glucose, which measures blood sugar at a given point in time, hemoglobinA1c (often abbreviated HbA1c) measures average glucose over an interval of 3 to 4 months.

The HbA1c test takes advantage of a harmful consequence of blood sugar on the body's proteins: they literally "cook" in a low-temperature version of caramelization—the kitchen science process by which proteins in foods brown with exposure to sugary marinades when put to the flame. This process of "glycation" is one of the key processes of aging—it subjects all our organs to degenerative stress.

When our blood tests reveal a high, or even borderline HbA1c, it's just the tip of the iceberg. Our blood is conveniently accessible via vein puncture, but less apparent are the consequences to all the cells in our bodies—be they constituting heart, brain, muscles, eyes, internal organs. All are susceptible to slow, progressive glycation.

When it comes to our skin, the results of glycation are more overt: The appearance of damaged, wrinkly skin.

Red blood cells have a lifespan of 120 days, so if you get an HbA1c test in October after embarking on a strict low-carb diet after Labor Day, your results might be skewed by all the piña coladas, tiramisu, and pizza you consumed in August while on summer vacation.

Since it's an average, what the HbA1c can't tell you is how much your blood sugars

fluctuate. A person with erratic blood sugar with high peaks and valleys might have the same HgbA1c as someone whose numbers don't vary much from day to day.

To assess how much your blood sugars jump around, you need to do fingerstick glucoses, or else undergo a relatively new test, the GlycoMark. The GlycoMark is particularly useful to help find out if diabetic patients taking medication are ranging too high and/or too low.

Another test that sheds light on the HbA1c results is the C-peptide. If a person's HbA1c is drifting upwards, the most common cause is insulin resistance resulting in too much insulin; on the other hand, some patients lose blood sugar control when the pancreas ceases to produce enough insulin. The C-peptide test, which tracks insulin production, can be used as the tie-breaker to determine the cause of rising glucoses.

Since the HbA1c reflects an average of blood sugars over the last few months, it's not necessary to fast before it; if, at the last minute, you want to atone for your prior dietary profligacy, just a week or so of clean eating prior to your test won't hide the effects of your previous months' indiscretions.

Guidelines vary, but an HbA1c from 5.0-5.6 to 5.8% is considered normal; 5.6 to 5.8-6.2 to 6.4% is borderline; and 6.2 to 6.4% and above is diabetic. For example, to achieve an HbA1c of 5.4% you'd have to notch an *average* blood sugar of 115; if found to be 6.4% it means your glucoses average a too-high 151. (See conversion table here). The agreed-upon cut-off for suspicion of diabetes is a 90-minute post-meal glucose of 140 or higher.

Many of my patients complain that their doctors don't bother warning them about an HgbA1c of 5.9 or 6.1 because they're older. That's because MDs are resigned to deteriorating blood sugar control as people age because it's so prevalent. But it's not good, nor is it inevitable—and it should be addressed, because it's a harbinger of cardiometabolic syndrome, the leading pathway to strokes and heart attacks, as well as a myriad of degenerative conditions like Alzheimer's, osteoarthritis and osteoporosis. Even cancer risk has been linked to elevated HgbA1c absent a diagnosis of overt diabetes.

Is the HbA1c foolproof? Does it always provide a clear delineation of your blood sugar control?

Not always. First, there's wobble—normal lab error. Surveys show that there can be as much as a 0.5% variation from lab to lab, which might mean the difference between optimal control and borderline diabetes.

But even if the tests are accurate, a salient fact is that HbA1c is predicated on a normal lifespan of red blood cells and a normal pattern of hemoglobin. Any condition which alters that, or produces anemia, can change the exposure window of hemoglobin to blood sugar.

This means that heavy menstrual bleeding, severe liver or kidney disease, iron or B12 deficiency or sickle cell anemia, even relatively common Thalassemia or sickle traits among persons of Asian, Mediterranean or African background, can distort test results.

For example, iron deficiency, common in young women, can lead to a false positive elevation of HbA1c. Conversely, recent blood loss from surgery, heavy menstrual cycles, other types of anemia may cause your A1C to be falsely low.

To complicate matters, there appear to be genetic differences in HbA1c's relationship to blood glucose; these "unknown confounders," sometimes corresponding to race or ethnicity, explain why certain individuals are naturally prone to high or low HbA1c.

So, what are we to make of the conflicting advice about HbA1c? How low should we go? The answer: *It depends on how you get there.*

The recent American College of Physicians guidelines arguing for more lenient HbA1c goals were based on studies that showed that intensive blood sugar control in diabetics—with insulin and oral medications—generated more problems than benefits. Insulin and many oral diabetes drugs cause patients to gain weight and put them at risk for hypoglycemia, a potential trigger of accidents and falls. While the HbA1c improves, unforeseen medication side effects negate the potential longevity gains anticipated with glucose lowering.

What Perlmutter and Bernstein are talking about are radical HbA1c reductions achieved via lifestyle, mostly by stringent low-carb dieting and vigorous exercise. In Bernstein's paradigm for Type 1 diabetics, very close blood-sugar monitoring with frequent injections of low-dose, short-acting insulin are intended to minimize the adverse cumulative effects of excess insulin.

Neither program is for the faint-hearted, and they require a high degree of discipline to achieve. Most doctors are resigned to their patients' non-compliance, and therefore the ACP guidelines are content to settle for mediocrity for the sake of safety.

But I say, *go for the gold* when it comes to HbA1c! While I think that targeting a sub 5.0 HbA1c is a little unrealistic (it may require unfaltering adherence to a ketogenic diet), shooting for 5.0 to 5.4% should help you minimize the harmful effects of glycation without becoming too obsessive.

Of interest is the impact on HbA1c of the nutraceutical berberine—a constituent of goldenseal and Oregon grape root. In a small pilot study, a group of patients with Type 2 diabetes were given berberine (500 mg three times daily) or the medication metformin for 3 months. The hypoglycemic effect of berberine was similar to that of metformin: Significant decreases in hemoglobin A1c (from 9.5% to 7.5%). My favorite berberine product is CM Core from Ortho Molecular.

Hear my recent Clinical Focus podcast on the subject of hemoglobin A1c by clicking here.