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# Type 2 Diabetes Digest®

CLINICAL MANAGEMENT STRATEGIES

In this interview, Nancy Bohannon, MD, provides suggestions for identifying patients with type 2 diabetes early in the course of the disease, setting therapeutic goals for these patients, and achieving these goals in the clinical practice setting. Dr Bohannon is in private practice of internal medicine and endocrinology in San Francisco.

## Targeting Pre- and Postprandial Glucose Levels in Clinical Practice

*An interview with Nancy Bohannon, MD*

Nancy Bohannon, MD

### What are the goals for pre- and postprandial glucose levels for patients with type 2 diabetes?

The American Diabetes Association (ADA) goal for preprandial blood glucose is 90 to 130 mg/dL (Table, page 3). But, frankly, I think that's still too high. If blood glucose is 130 mg/dL before a meal, it will be much too high after the meal. The American Association of Clinical Endocrinologists (AACE) preprandial glucose goal is <110 mg/dL, and that is a better goal. Most endocrinologists really are aiming for preprandial glucose levels <100 mg/dL for our patients with type 2 diabetes.

The ADA, AACE, and the International Diabetes Federation (IDF) goals are all for people with diabetes in general, and that may be why the preprandial levels they recommend are somewhat higher than ideal for type 2 diabetes. In patients with type 1 diabetes, it may be hard to get their glucose <100 mg/dL before every meal without risking too much hypoglycemia. In patients with type 2 diabetes, even those on insulin, there is less risk of hypoglycemia. So I think we really should be striving for





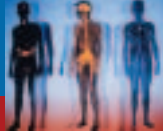
preprandial glucose levels <100 mg/dL for our patients with type 2 diabetes.

Two hours after a meal, blood glucose levels are typically <100 mg/dL in people without diabetes. According to the AACE, the postprandial goal for patients with diabetes is <140 mg/dL, and I believe the IDF says it should be <130 mg/dL. We should certainly be aiming for <120 mg/dL if we can achieve it without undue risk of hypoglycemia and maybe accepting <140 mg/dL if we can't do better. The ADA doesn't have a 2-hour postprandial goal. Instead, it has a peak postprandial blood glucose goal of <180 mg/dL. But many endocrinologists feel that's much too high.

### Speaking about preprandial and postprandial glucose levels, in the clinical situation is it necessary to determine what's the primary problem in an individual patient? And does that affect the choice of therapy?

By the time most Americans are diagnosed with diabetes, they are very far along in the natural history of the disease. Generally they have had diabetes for several years, and they already have a high fasting blood glucose (FBG) level, usually ≥126 mg/dL. Often the first abnormality to appear is postprandial hyperglycemia. So to make a diagnosis earlier, doctors should not be relying on FBG levels for screening.

I recommend that they go through their appointment book and identify



patients who are at high risk for developing type 2 diabetes. This includes people who have had gestational diabetes, those with a strong family history of diabetes, and those who are obese, sedentary, or have hypertension, low high-density lipoprotein (HDL) levels, or high triglycerides. The doctor can then have the receptionist call the people who are at high risk and ask them to have a big, starchy meal just before they come in. The doctor's staff can just do a fingerstick blood test in the office, which costs less than a dollar. If the person's blood glucose level is >200 mg/dL right after a meal, or >140 mg/dL after 2 hours, a more formal test should probably be done to determine whether that person has diabetes. That test should be a 2-hour oral glucose tolerance test (OGTT), not an FBG test, because many of these people have diabetes even though their FBG appears to be normal.

So if you try to confirm a diagnosis by doing an FBG test, you may get a normal value even though that person does in fact have diabetes. According to the ADA, 2 hours after a 75-g OGTT, normal blood glucose is <140 mg/dL, impaired glucose tolerance is 140 to 199 mg/dL, and diabetes is ≥200 mg/dL.

We should be trying to make the diagnosis of type 2 diabetes earlier. Screening in the postprandial state rather than in the fasting state makes that possible. The earlier we make the diagnosis, the easier it is to get blood glucose under ideal control and the more likely it is that we'll be able to change the natural history of the disease.

Hyperglycemia itself causes glucotoxicity, impaired insulin secretion, and more beta cell failure, so treating high blood glucose levels early, even if only postprandial levels are elevated, is likely to slow the progression of the disease. Epidemiologically, it has been shown that cardiovascular morbidity and mortality are more closely associated with postprandial hyperglycemia than with fasting hyperglycemia. This is why people who have impaired glucose tolerance but don't yet have diabetes still have greatly increased cardiovascular morbidity and mortality. If we can identi-

**Table—Target glycemic values for patients with diabetes**

| | ADA | AACE |
|---|---|---|
| **Preprandial plasma glucose** | 90-130 mg/dL | <110 mg/dL |
| **Postprandial plasma glucose** | <180 mg/dL* | <140 mg/dL |
| **A1C** | <7.0% | <6.5% |

*Peak postprandial plasma glucose.
ADA = American Diabetes Association; AACE = American Association of Clinical Endocrinologists; A1C = hemoglobin $A_{1c}$.



fy them earlier, before they progress to the point of having high FBG levels, and normalize their postprandial blood glucose levels, we'll probably be able to change the natural history of the disease and decrease cardiovascular morbidity and mortality.

## What would you use to treat high postprandial levels?

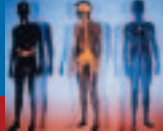
The sulfonylureas definitely improve postprandial blood glucose. Using glimepiride, for example, we can get a 40% reduction in the postprandial blood glucose in people who already have diabetes. Because the sulfonylureas and the meglitinides improve insulin secretion, however, there's always that small risk of hypoglycemia. For this reason, the only sulfonylurea I use is glimepiride, which has the least risk of hypoglycemia of all the sulfonylureas.

Metformin will improve postprandial blood glucose levels to some degree and also insulin sensitivity, although it's not as effective at lowering postprandial blood glucose as a sulfonylurea or a meglitinide. Thiazolidinediones will also help a little bit. The alpha-glucosidase inhibitors are excellent at lowering postprandial blood glucose and, with monotherapy, there is no risk of hypoglycemia. Unfortunately, most American doctors don't use these agents because it takes time to do the titration properly. When properly titrated, the alpha-glucosidase inhibitors are fairly well tolerated. But a proper titration may take up to 6 months. If you titrate too fast, they can have unacceptable gastrointestinal side effects. But for someone who has only postprandial hyperglycemia, it may be worth taking the time to titrate slowly.

Any of these choices would be appropriate for early treatment. The important thing is to do something. Diet and exercise are the backbone of therapy. It is unlikely, however, that diet and exercise will be sufficient to achieve and maintain control of the diabetes for very long. Some pharmacologic assistance is usually needed, and for many people, the first choice is an insulin sensitizer, either metformin or a thiazolidinedione. An insulin sensitizer will help to decrease the amount of work the pancreas has to do. Metformin along with diet and exercise will also help with weight loss. The thiazolidinediones, on the other hand, tend to promote weight gain, so for most people, they are not the first choice when it comes to adding a pharmacologic agent to diet and exercise. Another option is glimepiride, a sulfonylurea that has not been associated with weight gain and, in fact, has been associated with modest weight loss.

## When 1 drug doesn't provide adequate control, what is the usual next step?

Type 2 diabetes is not just a chronic disease, but a chronic, progressive disease (Figure). Even if the patient



does follow diet and exercise advice, the natural history of the disease is for the hyperglycemia to tend to get worse with time, and we need to keep adding other therapies to maintain control. Rather than blaming the patient for failing to follow lifestyle recommendations, doctors should make sure that the patient is properly educated about diet and exercise and then intervene with whatever pharmacologic assistance is needed to actually normalize the blood glucose.

If patients start with metformin, a sulfonylurea is frequently added. As the blood glucose increases because of the natural history of the disease, a third oral agent or a basal insulin may be needed. We're waiting far too long before progressing with therapy.

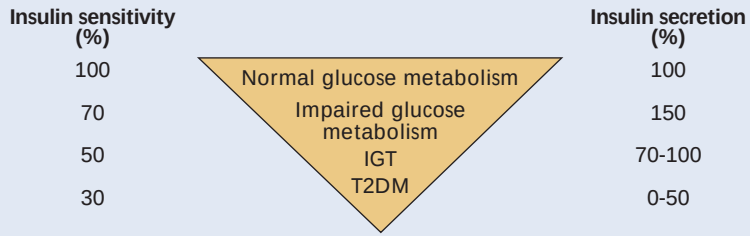
When we have made a new diagnosis of diabetes, we should be aiming for A1Cs in the 5% range. The median A1C level among nondiabetics is 5.0%. We're so used to seeing high A1Cs in people with uncontrolled diabetes that we tend to forget what our goal is.

In my opinion, our goal should be to keep A1Cs in our patients with type 2 diabetes as close to normal—a median of 5.0%—as we can achieve without undue risk of side effects. The time that you're most likely to be successful is early in the course of the disease. It doesn't make any sense to me to let people have their A1Cs go up to 6.5% or 7.0% on diet alone before adding on an oral agent. Once the A1Cs are over 6.0%, it's time to get more aggressive. For patients with type 2 diabetes, the risk of hypoglycemia with small (0.5-1 mg) doses of glimepiride is relatively small, so we ought to be able to get closer and closer to that 5.0% goal without undue risk.

## Do you usually start insulin therapy with a basal or a bolus insulin, or both?

With type 2 diabetes, the simplest way to initiate insulin is to use a basal insulin because 1 shot a day will supply up to 50% of the patient's total

**Figure—Progression of type 2 diabetes**




IGT = impaired glucose tolerance; T2DM = type 2 diabetes mellitus.
Modified from Laasko M. *Int J Clin Pract*. 2001;121:8-12.



daily insulin needs. It is important to understand though that you don't stop the oral agents when you add the basal insulin.

Adding a basal insulin will help the pancreas by supplying some of the background insulin that is necessary for metabolism to take place 24 hours a day. But basal insulin is not an insulin sensitizer, and giving insulin does not suddenly make an insulin-resistant person insulin-sensitive. So patients need to continue their insulin sensitizers. Nor does basal insulin supply the insulin needs associated with a meal. They still need their own pancreas to supply the insulin needed to cover the meal. That's why they also need an insulin secretagogue; these agents stimulate the pancreas to secrete insulin appropriately in response to the meal. The alpha-glucosidase inhibitors help to decrease the postprandial blood glucose excursions associated with meals and so they should be continued too.

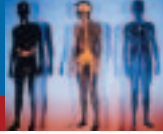
In other words, continue all the patient's oral agents. Even if the patient's blood glucose is much too high, it doesn't necessarily mean that the oral agents are no longer working. It could mean that the pancreas is being overwhelmed by glucose toxicity. Often it is not a matter of oral agent failure but rather beta cell paralysis. By this I mean that when the blood glucose gets above the glucose toxicity threshold, it impairs the ability of the beta cells to secrete insulin, and so it seems that the oral agents are not working. If you give enough basal insulin to lower the fasting and premeal blood glucose levels to a normal range, the beta cells may very well be able to respond by secreting insulin appropriately again under the influence of the oral agents.

Doctors are waiting much too long to start insulin. If patients are taking 2 or more oral agents and they have 2 A1C levels 3 months apart that are >6.5%, it's time to start basal insulin. If you wait until later in the course of the disease, the high blood glucose levels will contribute to the further demise of the beta cells.

## At some point do you add a rapid-acting insulin analog in addition to basal insulin in patients with type 2 diabetes?

Certainly. Because of the natural history of type 2 diabetes, you eventually may have to treat it like type 1 diabetes. Patients lose so much of their beta cell function that they need virtually complete insulin replacement. But the earlier you start treating the diabetes aggressively and the earlier you start insulin when ideal control is not being maintained with oral agents, the later that will be.

When a patient is on a basal insulin, an insulin sensitizer, and an insulin secretagogue with FBGs <100 mg/dL but high postprandial blood glucose levels or A1Cs, I would consider adding a fast-acting insulin analog. But first, if the blood



glucose is typically too high only after 1 meal a day, I would refer the patient to a dietitian to see if changing the composition of that meal or taking a long walk after the meal will get that blood glucose down.

If the blood glucose is still too high after just 1 meal a day, I'd continue the basal insulin and add 1 shot of a fast-acting analog before that meal. But once patients need 2 or more shots of fast-acting insulin to control postprandial blood glucose, I usually stop their insulin secretagogues and use fast-acting insulin before meals and a basal insulin once a day. For basal insulin my choice is insulin glargine, the only one that I consider to be a true basal insulin. I continue the insulin sensitizer if it is not contraindicated and is well tolerated.

## How do you encourage patients to take an active role in their care?

The stage is set with the first visit, and you have to give them goals. Diabetes, like hypertension and hyperlipidemia, is a goal-oriented disease. These diseases cannot be considered adequately treated until we have reached the goal or as near the goal as we can safely achieve. My goals for a person with type 2 diabetes are as follows:

- A1C as close to 5.0% as possible, as long as we're not causing undue hypoglycemia or other problems.
- FBG and all premeal blood glucose levels: <100 mg/dL.
- 2-hour postprandial blood glucose: <130 mg/dL.
- Blood pressure: ≤125/75 mm Hg.
- Low-density lipoprotein cholesterol: <70 mg/dL. That is my personal goal. I will probably accept <100 mg/dL if that's the best we can do without using 3 drugs.
- HDL: >50 mg/dL if achievable. New drugs in development may make this possible.
- Triglycerides: <100 mg/dL. We might have to accept <150 mg/dL, but our real goal is <100 mg/dL.
- Walking: at least a half an hour of nonstop walking every day or, even better, a total of 10 000 steps per day.

I write these goals down in the chart and give the patient a copy the first time they come in, and at each visit we go over their goals to see whether they have achieved them. Usually if you start treatment early in the disease, you can achieve them.

I have actually had patients tell me that it's time to start insulin. They know that they're not reaching their goals and they know what the next step is. That's a totally different approach from wagging your finger at them and saying, "If you don't follow your diet, we're going to put you on the needle."

People who have been threatened with insulin for years obviously are not going to want to take it. Whereas when they know that the natural history of the disease is to progress and they have certain goals, then they will accept it.



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