

Overcoming Patient Barriers to Initiating Insulin Therapy in Type 2 Diabetes Mellitus

DAVID G. MARRERO, PhD

J.O. Ritchey Professor of Medicine

Division of Endocrinology & Metabolism

Indiana University School of Medicine

Indianapolis, Indiana

Data from clinical trials underscore the fact that loss of β -cell function and insulin hyposecretion are progressive in type 2 diabetes. To achieve adequate glycemic control, most patients will eventually require insulin. Addition of insulin to sulfonylurea therapy, when maximal sulfonylurea does not adequately maintain fasting plasma glucose levels at <108 mg/dL, has been found to be more effective than initiating insulin therapy after oral agents have failed to maintain glycemic control. Nonetheless, both patients and providers are reluctant to begin insulin therapy. Research has shown that providers often delay modification of the diabetes treatment regimen because they believe their patients would be concerned about starting insulin therapy. In addition, they are concerned about patient nonadherence to nonpharmacologic and pharmacologic therapy. There are multiple reasons for patient nonadherence to insulin therapy; however, patients must be made to understand, early in the course of the disease, the progressive nature of type 2 diabetes and that exogenous insulin is an additional therapeutic option to help them achieve and maintain adequate glycemic control. (*Clinical Cornerstone*. 2007;8[2]:33–43) Copyright © 2007 Excerpta Medica, Inc.

Type 2 diabetes is characterized by defects in both insulin sensitivity and insulin secretion due to a progressive loss of β -cell function. In the United Kingdom Prospective Diabetes Study (UKPDS),¹ insulin secretion was 50% of normal at enrollment, suggesting that even at the time of diagnosis, β -cell function had already declined substantially in patients with type 2 diabetes. At the 6-year follow-up, β -cell function had decreased further, to only 25% of normal.^{1,2} In a substudy of the UKPDS,³ more than half of the patients receiving sulfonylurea therapy eventually required insulin during the 6-year study period. These data underscore the fact that loss of β -cell function and insulin hyposecretion are progressive in type 2 diabetes and that most patients will eventually require insulin to achieve adequate glycemic control.

THE ROLE OF INSULIN IN THE TREATMENT OF TYPE 2 DIABETES

For several years, the treatment paradigm for type 2 diabetes has been to initiate insulin therapy when sulfonylurea therapy fails. However, Wright et al³ found that

KEY POINT

Loss of β -cell function and insulin hyposecretion are progressive in type 2 diabetes and most patients will eventually require insulin to achieve adequate glycemic control.

early addition of insulin to sulfonylurea therapy, that is, when maximal sulfonylurea therapy does not adequately maintain fasting plasma glucose (FPG) levels below target, is a more effective strategy. In this study, patients received insulin therapy if maximal doses of sulfonylurea did not maintain FPG levels <108 mg/dL. The combination of insulin and sulfonylurea maintained glycosylated hemoglobin (A1C) at lower levels than did insulin alone and resulted in a higher proportion of patients who achieved the target A1C of $<7\%$. Early addition of

insulin to sulfonylurea therapy was shown to effectively maintain glycemic control for 6 years without increasing the risk of hypoglycemia or weight gain. The doses of insulin used with combination therapy were significantly less than those used with insulin monotherapy. In addition, the incidence of major hypoglycemia was lower in the combination-therapy group than among patients using insulin alone. Thus, initiation of insulin therapy when oral antidiabetic agents do not adequately achieve A1C targets is a more effective approach than beginning insulin therapy only after oral agents fail. Moreover, continuation of oral agents after addition of insulin may help reduce insulin dose requirements and the risk of hypoglycemia.

KEY POINT

Early addition of insulin to sulfonylurea therapy was shown to effectively maintain glycemic control for 6 years without increasing the risk of hypoglycemia or weight gain.

Insulin therapy has also been shown to improve insulin sensitivity and, in some cases, to reverse insulin resistance.^{4–7} In recent years, the availability of insulin formulations with more favorable pharmacokinetic profiles has reduced concerns about hypoglycemia and weight gain. In addition, the introduction of new patient-friendly technologies, such as the needle-free insulin injector and inhaled insulin, has facilitated the use of insulin in patients with type 2 diabetes.

RESISTANCE TO INITIATING INSULIN THERAPY

Despite ample clinical evidence of the efficacy and safety of early insulin therapy in type 2 diabetes, there is still significant reluctance on the part of both providers and patients to begin insulin therapy. Brown et al⁸ reported that providers wait an average of 27 to 35 months before initiating a change in antidiabetic monotherapy (eg, switching to another agent or adding another agent). From diagnosis, therefore, the average patient accumulates nearly 5 years of glycemic burden (A1C >8.0%) before insulin therapy is started.⁸ More alarming is the

observation that providers modify therapy only after A1C levels are in the range of 8.8% to 9.1% (Figure),⁸ well beyond the glycemic targets defined by the American Diabetes Association (7.0%)⁹ and the American Association of Clinical Endocrinologists (6.5%).¹⁰

These findings are supported by results from the Diabetes Attitudes, Wishes, and Needs (DAWN) study,^{11,12} a global diabetes study involving face-to-face or telephone interviews with >5000 patients and ~3800 health care providers from 13 countries, including the United States. The DAWN study assessed provider attitudes regarding initiation of oral antidiabetic therapy and insulin therapy. Among general physicians in the United States, 68% prefer to delay insulin until it is absolutely necessary, while 23% prefer to delay oral antidiabetic therapy until it is absolutely necessary.^{11,12}

Interestingly, results of the study suggest that health care providers are reluctant to start insulin because of patient concerns about therapy. In fact, ~65% of providers reported that their patients would be very concerned about starting insulin therapy.^{11,12} In addition, one third of providers reported that their patients would consider insulin therapy to be an indication that they did not follow their providers' health care recommendations properly.^{11,12} Responses from interviews with patients in the DAWN study are consistent with these assumptions. More than half of the patients interviewed reported that they were very worried about starting insulin therapy.^{11,12}

Use of insulin as a last-resort treatment has very real consequences. Insulin use actually declined from 24% in the Third National Health and Nutrition Examination Survey (NHANES III) to 16% in NHANES 1999–2000, while the use of oral antidiabetic monotherapy increased, despite ample evidence that oral monotherapy is not effective in the long term. This may explain why glycemic control rates decreased from 44.5% to 35.8% during the same period.¹³ The overall data suggest a marked underutilization of insulin in patients who have not achieved glycemic control with oral agents.

Patient nonadherence to insulin therapy may also be a real concern for physicians. In a 2000 Behavioral Risk Factor Surveillance System study involving 153,805 patients,¹⁴ the majority of American adults did not control their weight, eat adequate amounts of fruits and vegetables, or exercise frequently. A study by Chapman et al¹⁵ showed that adherence to oral antihypertensive and lipid-lowering therapy was <50% in as few as 3 months after

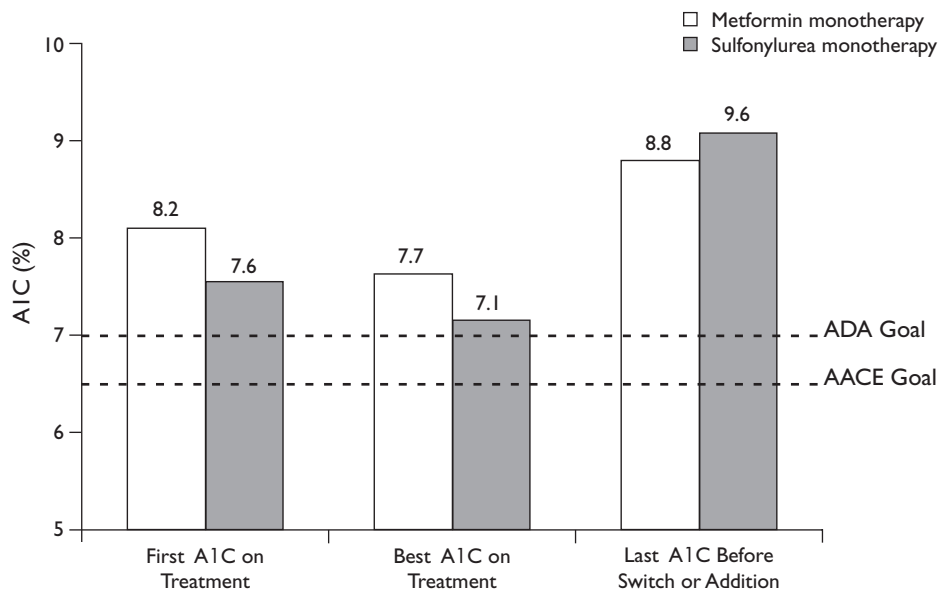


Figure. Therapy often is not modified (ie, switched to another agent or an additional agent added) until glycosylated hemoglobin (A1C) levels are well above the goals set by the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE).⁸

initiation of therapy and only 36% after 6 months.¹⁵ The problems of adherence are compounded when injected medications and complex dosing regimens are involved. In a study by Cramer,¹⁶ adherence to insulin therapy among patients with type 2 diabetes was only 62% to 64%. Nonadherence to lifestyle modification recommendations and pharmacologic therapy is of particular relevance in type 2 diabetes and may explain why glycemic control is difficult to achieve, even when effective medications are prescribed. Health care providers need to devise ways to improve adherence to prescribed antidiabetic therapies.

In a recent survey study of ~12,000 patients with type 2 diabetes,¹⁷ the major reasons for nonadherence cited by patients were lack of access to the drug (ie, inability to fill the prescription and copayment and reimbursement issues), the perception that the drugs are not effective, and side effects. Typically, a patient with type 2 diabetes takes an average of 6 medications. Some of the negative patient attitude toward insulin may be due to a reluctance to add yet another medication to their daily regimen. These data underscore the importance of rigorous patient education, specifically on what oral antidiabetic drugs and insulin are designed to do, the importance of taking the drugs regularly and as prescribed, and expected side effects.

PATIENT-REPORTED BARRIERS TO INITIATING INSULIN THERAPY

As discussed, more than half of the patients interviewed in the DAWN study reported that they were very worried about starting insulin therapy.^{11,12} This attitude was consistent across the 13 countries studied. Patients cited several reasons for their reluctance to start insulin therapy—from a genuine fear of needles, hypoglycemia, and weight gain, to personal feelings of guilt or failure, among others.^{18–20} All of these barriers may be addressed with appropriate education and counseling (Table).^{18–20}

KEY POINT

Patients cited several reasons for their reluctance to start insulin therapy—from a genuine fear of needles, hypoglycemia, and weight gain, to personal feelings of guilt or failure.

Fear of Needles or Injection

Fear of needles or injection is one of the most common reasons for patient resistance to starting insulin therapy.¹⁸

TABLE. ADDRESSING PATIENT CONCERNS ABOUT STARTING INSULIN THERAPY.¹⁸⁻²⁰

Patient Concern	Counseling Points
Fear of injections, needles	Ultrafine needles are nearly painless Pen injectors are available Inhaled insulin is an option
Adverse consequences (eg, amputation, blindness)	Insulin can help achieve and maintain glycemic control to avoid adverse consequences
Hypoglycemia	Incidence of serious hypoglycemia is <2.5% Long-acting insulins are associated with less hypoglycemia Following regimen as prescribed reduces incidence of hypoglycemia
Weight gain	Addition of metformin to insulin therapy can attenuate weight gain Once-daily formulations are associated with less weight gain than split-dose regimens Dietary and exercise regimens need to be continued
Efficacy	Insulin works well; hypoglycemia is evidence of efficacy in reducing blood glucose levels
Personal failure	Type 2 diabetes is a progressive disease in which insulin secretion becomes inadequate The longer one lives with type 2 diabetes, the more likely the need for exogenous insulin
Complex therapy regimen	Insulin therapy can be tailored to suit patient needs Long-acting insulin can be administered at bedtime to minimize impact on activities of daily living

Patients may genuinely fear the pain associated with needle sticks, or they may be concerned about the social stigma associated with syringe use. The way in which a health care provider frames the subject may also increase feelings of fear (eg, “I’m going to put you on the needle.”). Recent advances in injection technology have made administration of insulin considerably easier, nearly painless, and psychologically more acceptable. Patients should be reassured that the ultrafine needles currently used with insulin are smaller, thinner, and coated so as to lessen pain on injection. Insulin pens have been shown to reduce the fear associated with needles. The needles in insulin pens are hidden from view and, as a result, may be more acceptable to patients. There also may be less stigma associated with an insulin pen than with a needle and syringe. Technological advances such as needle-free jet injectors have eliminated the needle altogether in some devices.

Health care providers need to frame the prospect of starting insulin therapy in an appropriate way. A matter-of-fact approach that clearly illustrates how insulin is injected and reassures the patient that the process is nearly painless may be useful. Dummy insulin pens can be used to ease patients into the idea of self-injection. A personal or recorded testimonial from a diabetic patient

experienced in insulin administration can also help allay the fear of self-injection.

The recently approved inhaled insulin, which delivers insulin to the lungs by oral inhalation, is another approach to insulin therapy that eliminates needles altogether.²¹ This formulation is administered via an oral inhaler similar to an asthma inhaler. The insulin inhalation powder and the specially designed inhaler are portable, easy to maintain, and do not require refrigeration. Inhalation does not require any special breathing techniques and can be learned easily. Inhaled insulin has been shown to provide glycemic control comparable to that provided by regular subcutaneous insulin, and it can be used as monotherapy or in combination with oral antidiabetic agents in patients with type 2 diabetes.

An insulin pump is another option for patients with a serious fear of needles. These devices deliver a continuous measured dose of insulin through a catheter that is inserted into the skin; however, use of the pump may be cumbersome.

Fear of Consequences of Insulin Therapy

Patients often associate insulin therapy with adverse consequences, such as amputation and renal failure, and they may not realize that these consequences are a result

of uncontrolled diabetes and not insulin therapy.¹⁸ However, the frequent psychological association of insulin with increased morbidity may have some basis in reality. Physicians are often reluctant to initiate insulin therapy unless it is absolutely necessary, namely, when all other options have failed. Thus, patients who are treated with insulin may be at a later stage in the disease, when complications such as neuropathy and nephropathy have already progressed. But the negative attitude toward insulin therapy reflects a general lack of understanding of the progressive nature of diabetes. Patients must be made to understand that type 2 diabetes is a progressive disease characterized by a gradual loss of insulin secretion and an increased need for exogenous insulin. Patients should be informed that, because of the nature of the disease, it is likely they will eventually require insulin.

KEY POINT

Physicians are often reluctant to initiate insulin unless all other options have failed. Thus, patients who are treated with insulin may be at a later stage in the disease, when complications have already progressed.

Fear of Side Effects

For patients as well as health care providers, the possibility of hypoglycemia is a major barrier to initiating insulin therapy. However, the rate of serious hypoglycemia (episodes requiring the help of another person or medical intervention) in patients with type 2 diabetes is <2.5%.¹ Nonetheless, it continues to be a concern. Patients should be made to understand how insulin works, as well as the signs of hypoglycemia and how best to avoid it. Clinicians should also discuss the difference in the risk of hypoglycemia with once-daily insulin formulations compared with insulins that are taken more frequently. In the Treat-to-Target Trial,²² long-acting insulin glargine administered once daily was more effective in reducing documented nocturnal hypoglycemia and other categories of symptomatic hypoglycemia compared with intermediate-acting neutral protamine Hagedorn (NPH)

insulin. Other studies have confirmed the lower incidence of nocturnal hypoglycemia with insulin glargine compared with NPH insulin.^{23,24} Similarly, in a study comparing twice-daily biphasic insulin aspart 70/30 with insulin glargine, patients with type 2 diabetes receiving insulin aspart had a 3-fold higher incidence of hypoglycemia.²⁵ The availability of newer insulin formulations with improved 24-hour time-action profiles may help reduce concerns about hypoglycemia in patients with type 2 diabetes.

Insulin-related weight gain is of concern to both patients and health care providers. Because patients with type 2 diabetes are often obese, even a small amount of weight gain may have a significant impact on glycemic control. Health care providers may be reluctant to initiate insulin for fear of weight gain, particularly when patients have not been able to adhere to dietary or exercise regimens. In addition, greater weight gain is usually observed with split-dose insulin regimens.^{25,26} The combination of metformin and insulin, however, has been found to attenuate weight gain associated with insulin therapy.^{26,27} In a randomized controlled trial of 96 patients, those receiving bedtime insulin plus metformin experienced no change in weight, whereas those receiving bedtime insulin plus glyburide, metformin plus glyburide, or an additional dose of insulin in the morning experienced significant weight gain.²⁶ In a second trial, the addition of metformin to insulin improved glycemic control, lowered insulin requirements by ~30%, and attenuated the weight gain associated with insulin therapy alone.²⁷

Fear of Worsening Disease

Patients may be concerned about the reasons for starting insulin therapy. They may believe that insulin is being initiated because the disease has worsened.¹⁹ This perception is reinforced when health care providers present insulin as a threat, a punishment for failure to manage the disease, or a treatment of last resort. Patient education about the progressive nature of type 2 diabetes and the eventual loss of endogenous insulin secretion is essential. Insulin should be presented, early in the course of the disease, as a way to achieve and maintain glycemic control.

Doubts About the Efficacy of Insulin

Many patients with type 2 diabetes do not view insulin as an effective therapy, despite ample evidence that early addition of insulin to oral antidiabetic therapy can safely

KEY POINT

Patient education about the progressive nature of type 2 diabetes and the eventual loss of insulin secretion is essential. Insulin should be presented, early in the course of the disease, as a way to achieve and maintain glycemic control.

maintain A1C levels near target levels in the first 6 years after diagnosis.³ In the international DAWN study,¹² only 23% of patients with diabetes who were not on insulin therapy believed that insulin would help them manage their diabetes better. Interestingly, the belief in the efficacy of insulin was particularly low in the United States—only in India was it lower. Patients with more advanced disease or other disease-related problems (eg, worse control, more complications, more disease-related distress, and poorer treatment adherence) tended to have more confidence in the efficacy of insulin therapy.

To assuage doubts about the efficacy of insulin therapy, health care providers need to educate patients on the natural progression of type 2 diabetes, the gradual and inevitable decline in insulin secretion, and the eventual need for exogenous insulin. A brief description of how insulin works and how it reduces blood glucose levels may be helpful. Providers also need to educate patients on the signs of hypoglycemia and how to prevent it. They may present hypoglycemia as evidence that insulin therapy sometimes works “too well.”

Insulin Perceived as Personal Failure

In the DAWN study,^{11,12} nearly half of the patients interviewed believed that starting insulin therapy meant that they had not followed the health and lifestyle recommendations of their health care providers. Patients tend to view insulin therapy as a punishment for their failure to manage their disease through lifestyle modifications (eg, diet and exercise) and/or oral antidiabetic therapy. Self-blame for having to start insulin therapy tended to be higher among older patients and those with a longer duration of disease. Much of this phenomenon can be traced to how health care providers approach the subject of insulin therapy. As discussed, many providers prefer

to delay insulin therapy until it is absolutely necessary; unfortunately, the discussion around initiating insulin therapy is often framed based on this conviction (eg, “If you don’t follow these diet and exercise recommendations, I will have to put you on insulin.”). When insulin is presented as a threat, a punishment, or the treatment of last resort, it is viewed negatively. Insulin can instead be presented as another therapeutic option that the patient should consider before starting any pharmacologic treatment. The subject of insulin therapy should be discussed early in the treatment course, and the possibility of using insulin in combination with oral antidiabetic agents as first therapy should be considered.

Insulin as a Complex Therapy

In a survey of insulin-naïve patients, almost half believed that insulin therapy would restrict their lives and that they were not capable of managing the demands of the regimen.¹⁹ Insulin therapy can be overwhelming for patients when they are faced with the prospect of determining dosages, handling syringes and vials, administering the medication at specific times, and monitoring blood glucose levels. However, insulin-naïve patients perceive the treatment burden of insulin therapy to be much greater than patients who have insulin experience.²⁸ To help allay concerns about the treatment burden of insulin, health care providers can partner insulin-naïve patients with insulin-experienced patients. Having a peer discuss his or her experience with insulin can be reassuring and may help quell fears about the complexity of insulin therapy.

CONCLUSIONS

Early initiation of insulin as add-on therapy to oral antidiabetic agents has been shown to maintain glycemic control for 6 years. Nonetheless, patients and health care providers have concerns about initiating insulin therapy. Patients may have concerns about daily injections, side effects such as hypoglycemia and weight gain, and the complexity of insulin therapy. These fears may be alleviated by presenting insulin as a more flexible option that allows patients to schedule therapy to suit their lifestyles. New regimens such as once-daily bedtime insulin interfere only minimally with activities of daily living and are associated with a lower incidence of hypoglycemia. The addition of metformin to insulin therapy attenuates the weight gain associated with insulin alone. Advances in

insulin delivery technology such as insulin pens and inhaled insulin formulations have also made dosing easier and obviate the need for handling needles and vials. Health care providers need to assess their patients' needs and tailor insulin therapy to ensure an optimal dosing regimen, minimize treatment burden, and maximize patient satisfaction and adherence.

Patients may also have concerns about why insulin therapy is being started, feelings of guilt about failing to follow lifestyle recommendations, and doubts about the efficacy of insulin. To address these concerns, health care providers need to educate patients on the progressive nature of diabetes, the eventual decline in insulin secretion and therefore the need for exogenous insulin, and how insulin works in the body to reduce blood glucose levels. The subject of insulin should be presented early in the course of the disease as an effective therapeutic option for achieving and maintaining glycemic control.

ACKNOWLEDGMENT

The author wishes to thank Viji Anantharaman for her medical writing and research assistance in the preparation of this manuscript.

REFERENCES

1. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998;352:837–853.
2. UK Prospective Diabetes Study (UKPDS) 16. Overview of 6 years' therapy of type II diabetes: A progressive disease [published correction appears in *Diabetes*. 1996;45:1655]. *Diabetes*. 1995;44:1249–1258.
3. Wright A, Burden AC, Paisey RB, et al. Sulfonylurea inadequacy: Efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the U.K. Prospective Diabetes Study (UKPDS 57) [published correction appears in *Diabetes Care*. 2002;25:1268]. *Diabetes Care*. 2002;25:330–336.
4. Riddle MC. The underuse of insulin therapy in North America. *Diabetes Metab Res Rev*. 2002;18(Suppl 3):S42–S49.
5. Scarlett JA, Gray RS, Griffin J, et al. Insulin treatment reverses the insulin resistance of type II diabetes mellitus. *Diabetes Care*. 1982;5:353–363.
6. Andrews WJ, Vasquez B, Nagulesparan M, et al. Insulin therapy in obese, non-insulin-dependent diabetes induces improvements in insulin action and secretion that are maintained for two weeks after insulin withdrawal. *Diabetes*. 1984;33:634–642.
7. Garvey WT, Olefsky JM, Griffin J, et al. The effect of insulin treatment on insulin secretion and insulin action in type II diabetes mellitus. *Diabetes*. 1985;34:222–234.
8. Brown JB, Nichols GA, Perry A. The burden of treatment failure in type 2 diabetes. *Diabetes Care*. 2004;27:1535–1540.
9. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care*. 2005;28(Suppl 1):S4–S36.
10. American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus: The AACE System of Intensive Diabetes Self-Management—2002 Update. *Endocr Pract*. 2002;8(Suppl 1):43–56.
11. Peyrot M, Rubin RR, Lauritzen T, et al. Resistance to insulin therapy among patients and providers. Results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. *Diabetes Care*. 2005;28:2673–2679.
12. Diabetes Attitudes, Wishes, and Needs (DAWN) Study. Barriers to treatment. Available at: <http://www.dawnstudy.com>. Accessed January 30, 2007.
13. Koro CE, Bowlin SJ, Bourgeois N, Fedder DO. Glycemic control from 1988 to 2000 among U.S. adults diagnosed with type 2 diabetes. A preliminary report. *Diabetes Care*. 2004;27:17–20.
14. Reeves MJ, Rafferty AP. Healthy lifestyle characteristics among adults in the United States, 2000. *Arch Intern Med*. 2005;165:854–857.
15. Chapman RH, Benner JS, Petrilla AA, et al. Predictors of adherence with antihypertensive and lipid-lowering therapy. *Arch Intern Med*. 2005;165:1147–1152.
16. Cramer JA. A systematic review of adherence with medications for diabetes. *Diabetes Care*. 2004;27:1218–1224.
17. Marrero DG, Monahan PO, Lane KA, Hayes RP. Validation of a scale to measure patient-perceived barriers to medication use. 2006 International Society for Quality of Life Research meeting abstracts. [www.isoqol.org/2006mtgabstracts]. *The QLR Journal*. 2006:A-34–A-35. Abstract #1223.
18. Polonosky WH, Jackson RA. What's so tough about taking insulin? Addressing the problem of psychological insulin resistance in type 2 diabetes. *Clin Diabetes*. 2004;22:147–150.
19. Polonosky WH, Fisher L, Guzman S, et al. Psychological insulin resistance in patients with type 2 diabetes. The scope of the problem. *Diabetes Care*. 2005;28:2543–2545.
20. Funnell MM, Kruger DF, Spencer M. Self-management support for insulin therapy in type 2 diabetes. *Diabetes Educator*. 2004;30:274–280.
21. Exubera® (insulin human [rDNA origin]). Inhalation Powder. Available at: <http://www.exubera.com>. Accessed March 14, 2007.
22. Riddle MC, Rosenstock J, Gerich J, et al. The Treat-to-Target Trial. Randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. *Diabetes Care*. 2003;26:3080–3086.
23. Yki-Jarvinen H, Dressler A, Ziemien M. Less nocturnal hypoglycemia and better post-dinner glucose control with bedtime insulin glargine compared with bedtime NPH insulin during insulin combination therapy in type 2 diabetes. *Diabetes Care*. 2000;23:1130–1136.
24. Janka HU, Plewe G, Riddle MC, et al. Comparison of basal insulin added to oral agents versus twice-daily pre-

- mixed insulin as initial insulin therapy for type 2 diabetes. *Diabetes Care*. 2005;28:254–259.
25. Raskin P, Allen E, Hollander P, et al. Initiating insulin therapy in type 2 diabetes. *Diabetes Care*. 2005;28:260–265.
 26. Yki-Jarvinen H, Ryysy L, Nikkila K, et al. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus. A randomized, controlled trial. *Ann Intern Med*. 1999;130:389–396.
 27. Aviles-Santes L, Sinding J, Raskin P. Effects of metformin in patients with poorly controlled, insulin-treated type 2 diabetes mellitus. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med*. 1999;131:182–188.
 28. Vijan S, Hayward RA, Ronish DL, Hofer TP. The burden of diabetes therapy: Implications for the design of effective patient-centered treatment regimens. *J Gen Intern Med*. 2005;20:479–482.

Address correspondence to: David G. Marrero, PhD, J.O. Ritchey Professor of Medicine, Division of Endocrinology & Metabolism, Indiana University School of Medicine, 250 N. University Blvd., Suite 122, Indianapolis, IN 46202.
E-mail: dgmarrer@iupui.edu

Dialogue Box

EDITORIAL BOARD

Please elaborate on the role diabetes educators play in your program.

MARRERO

Being well aware that self-management is crucial to the success of treatment for patients with diabetes, we have put together a very extensive diabetes education program that employs certified diabetes educators. These educators are nurses, exercise physiologists, dietitians, and even psychologists who have received certification from the American Association of Diabetes Educators. As part of our standing protocol, all new patients are provided with access to a variety of programs featuring diabetes education. Most are group programs, but one-on-one programs are available as well. Depending on the situations presented by patients, as well as those that come to light during the clinical consultation, we may then tailor more specific and focused educational interventions for individual patients as well.

EDITORIAL BOARD

How do you deal with the mountain of paperwork and correspondence required when you prescribe insulin and the equipment and testing materials that accompany it?

MARRERO

We've taken an automated approach. We have a series of standing orders that are put into place when the patient presents. A lot of the paperwork is thus done by nurses and nurse practitioners once the decision to initiate insulin is made. Automating the required letters and correspondence eliminates the need for the doctor to dictate and write them for each individual patient—the doctor simply fills out a form and adds the patient's name.

EDITORIAL BOARD

For patients with type 2 diabetes started on basal insulin therapy, how often do you have them check their fasting glucose after their insulin dose stabilizes?

MARRERO

Once a week, once every 2 weeks would be fine at that point. You really don't need to monitor it more aggressively. However, more frequent checks would be needed in patients who decide to step up their physical activity or who change their diets—anything that might change their insulin requirement.

EDITORIAL BOARD

Requiring less frequent testing would reduce an important barrier to initiating insulin therapy.

MARRERO

It does. How often one needs to test is really dependent on 2 factors: the stability of the dose required to achieve glycemic goals, and whether the patient is *hypoglycemic-aware* or not. For the *hypoglycemic-unaware*, they need to test more frequently to keep out of trouble. For those who are aware and fairly comfortable with self-management concepts, I tell them they can adjust their testing schedule to better accommodate their lifestyle.

EDITORIAL BOARD

How do you identify the patient who is hypoglycemic-aware?

MARRERO

You basically have to interview them and question them about whether they have glycopenic symptoms that they are aware of. Simply ask the patient, "Do you know when you're getting low and, if so, can you describe your symptoms?" If they can't describe anything that makes sense to you (eg, sweating and palpitations, anxiety, numb lips, disorientation, confusion) and they say they go from no warning symptoms to complete confusion, in my book you have somebody who likely is hypoglycemic-unaware. These are the patients we enroll in the Dan Cox program. This program has a straightforward curriculum that teaches patients to become more attentive and aware of the things that are indicating that, in fact, "your glucose is getting low."

Dialogue Box

EDITORIAL BOARD

Do you ever allow patients to use short-acting insulin without having them check their glucose?

MARRERO

It depends. There are a lot of factors to consider. It would depend a little bit on the patient and the patient's ability to self-regulate at a fine-tune level. For some patients, that would not be a good strategy, and having them test their glucose would be safer. The other consideration is their insulin regimen. Are they manipulating the dose of the short-acting insulin specific to carbohydrate load? If they are not adept at carbohydrate counting, we tend to have them do more postprandial checking, just to make sure they didn't get themselves into trouble.

EDITORIAL BOARD

Are there data looking at the efficacy of preprandial versus postprandial insulin treatment?

MARRERO

That's a tough question. If you really are trying to push that patient from a glycosylated hemoglobin (A1C) of 7% down to 6%, you really need to start chasing postprandial values. We can all get patients down to where they have pretty good fasting glucose values and reasonably good glycemic control with insulin titration through their day, resulting in an A1C of 7% to 7.3%. However, for those in whom you really want to push it, or in whom you think there's an indication that they should have stricter control, you need to start looking at their postprandial glucose excursions. In such patients, we may have to move to a different insulin regimen or, in fact, in some of those, if they're insulin-dependent, move them on to an insulin pump. Once we embark down the path of an exquisitely titrated level of control, the incidence of hypoglycemia becomes an issue. You really need to make sure that the dose adjustment and their carbohydrate load are in harmony.

EDITORIAL BOARD

Some states, such as California, have statutes that require reporting to the Department of Motor Vehi-

cles any person who has a propensity to a lapse of consciousness, such as alcoholics and insulin-dependent diabetics. Is this a concern when initiating basal insulin?

MARRERO

You know, it's a really important and tricky issue. There's conflicting evidence to suggest that insulin-using patients are more likely to have traffic accidents, depending on whose data you look at. There are data from Canada looking at drivers in the trucking association that showed that people who were insulin-dependent had fewer accidents than people with type 2 diabetes. There are data in the United States that suggest the opposite is true, that people who are more insulin-dependent tend to have a slightly higher accident rate than people who are not. I think the jury's out on that, but I'm very cautious about making the suggestion that we should legislate against people with diabetes who are using insulin, in terms of driving privileges, in the absence of conclusive or compelling evidence of a lapse of consciousness.

EDITORIAL BOARD

Are there steps you take to ensure that this doesn't become an issue?

MARRERO

Yes, we're very aggressive in our education programs here in Indiana about teaching people the rules of driving, including when to test their glucose before getting behind the wheel. For people who are hypoglycemic-unaware, these are the ones you have to say "you need to make it a habit to test your glucose before you drive." For others, the times they really need to test are after dose adjustments or reductions in dietary intake.

EDITORIAL BOARD

Many physicians argue that before β -cells are exhausted, using insulin as a threat represents the most time-efficient argument for fostering lifestyle changes and getting patients to lose weight. Since

Dialogue Box

adding insulin invariably leads to weight gain, starting insulin early seems almost like throwing in the towel. What do you think of this posture?

MARRERO

I have mixed feelings about it. I understand the logic of it. However, the physiology and natural history of type 2 diabetes suggests that a significant percentage of patients will have to start insulin regardless of what they do and despite all the oral agents they are prescribed. If you use insulin as a dangling threat and overemphasize its negative side, then what you set up is a really bad psychodynamic for those patients. I'm a believer, more and more, that we should regard insulin as an equal partner in the armamentarium we have for treating type 2 diabetes. I'm a believer that we need to present our patients with all the options we have and the trade-offs entailed with each of them. When we've done that in studies, we've actually been surprised at how many patients are willing to pull the trigger on insulin a lot sooner than we traditionally would have thought.

EDITORIAL BOARD

The lack of adherence of patients to interventions regarding lifestyles and the taking of medications would be an argument not to prescribe an agent like

insulin, which requires the patient to be even more compliant and regimented with regard to lifestyle.

MARRERO

I've been doing some research on medication adherence and I'm starting to learn some things that are very interesting to me. Number one, I'm learning that all of our type 2 diabetes patients are on a polypharmacy—taking 3, 4, and 5 drugs as a rule. And they tend to be selectively nonadherent, stopping one drug but not all. As I've delved into what the selectivity is based on, it's a couple of things. One factor is based on the perception of "I don't see what this drug is doing for me." The second factor is cost. Insulin is much cheaper than a lot of these medications and thus less likely to be dropped. Low-income patients, particularly those with a competing economic demand in the form of tobacco use or alcohol, are much more likely to drop more costly drugs that they don't perceive as providing immediate benefit. So they take their pain medications, they take their antidepressants sometimes, they take their oral hypoglycemic agents, and they take their insulin because these are all drugs that, if you stop them, you become symptomatic. Lipid-lowering drugs and blood pressure drugs are much more likely to be traded off for cigarettes.