2005 Presidential Address: Diabetes: Past, Present, and Future

One of my favorite authors is the English writer Charles Dickens. His novels captured the human spirit, while detailing life in England in the 1800s. In 1843, he published a book entitled "A Christmas Carol." In it, Ebenezer Scrooge, a stingy man of business is visited by the ghost of his deceased partner, Jacob Marley. The purpose of the visit is to prepare Scrooge for the subsequent appearance of three spirits: the spirit of Christmas past, the spirit of Christmas present, and the spirit of Christmas yet to come. The first spirit provides Scrooge with a look back at his early days. The second spirit opens his eyes to the reality of the present. Finally, the third, and most ominous spirit, allows him a glimpse into his future.

It is my goal today to use this approach to examine the epidemic of diabetes in the U.S. I will first remind you of where we were a generation ago; I will then focus on the situation today, and finally I will attempt to look into the future. The first spirit to visit Scrooge was the ghost of Christmas past, so let us begin there.

In 1985, there were 6.4 million adults with diagnosed diabetes in the U.S. The cost of the disease that year (both direct and indirect) was 14 billion dollars. The National Institutes of Health (NIH) investment in diabetes research was only 189 million dollars. The American Diabetes Association (ADA) and the Juvenile Diabetes Research Foundation (JDRF), on the other hand, were collectively investing only 8.2 million dollars.

By 1990, there were 6.7 million adults with diagnosed diabetes, but only four states had a prevalence >6%. Treatment options were limited. Five insulin preparations were available, including the newly approved human insulin. For the treatment of type 2 diabetes, the only drugs available were the sulfonylureas. These drugs were known to stimulate insulin secretion from the pancreas but to fail as the disease progressed.

Home glucose monitoring was in its infancy, as was insulin pump technology. While the early devices were novel advances at the time, their value was not appreciated, and their use was limited.

The concept of pancreas replacement as a treatment for type 1 diabetes had emerged but met with little success. Only a few pancreas transplants were carried out each year. The surgery was risky, and the number of recipients who were insulin free for a year after the operation was limited.

The concept of islet transplantation had been proposed, but few attempts to actually transplant islets had taken place. Furthermore, for the transplants that did occur, there was virtually no success in terms of insulin independence, even for a brief period.

Many important questions remained unanswered. Little was known about the genetic basis of either type 1 or type 2 diabetes, and even less was known about the environmental triggers that initiate the disease. We knew that insulin interacted with receptors at the cell surface and that it augmented glucose uptake by fat and muscle and decreased glucose production by the liver, but we did not understand the signaling cascade that linked receptor binding to the physiologic response.

The importance of good blood glucose control in preventing the development of complications was assumed but not proven. Prevention strategies were nonexistent. Finally, the concept of the team approach to diabetes treatment, in which the role of various health care professionals is clear and patient education is emphasized, was just coming into focus. Obviously large gaps existed in our knowledge base.

The second spirit to visit Scrooge was the ghost of Christmas present, so in keeping with the story, let us next turn our attention to the current situation.

The latest data available from the Centers for Disease Control and Prevention indicate that there has been an alarming increase in diabetes all across this country. As of 2002, the prevalence in one state exceeded 10%. As of 2005, there were 14.6 million people with diagnosed diabetes in this country, over another 6 million with undiagnosed diabetes, and an estimated 41 million people with prediabetes.

The top panel of Fig. 1 shows that the number of people with diagnosed diabetes in the U.S. has increased in virtually every year since 1990. The bottom panel of Fig. 1 shows that by 2005, the incidence of diabetes had risen to 1.5 million new cases per year. The cost of the disease in 2002 was almost 132 billion dollars. The investment in research by the NIH, ADA, and JDRF combined was just under a billion dollars, an amount somewhat <1% of the cost of the disease. Let's pause for a moment and try to understand the reason for the recent increase in the incidence of diabetes.

It is most likely related to four factors. First, it is associated with the growth in our population and the change in its characteristics. Life expectancy is increasing, and since we know that the prevalence of diabetes increases with increasing age, it follows that the incidence of the disease will increase over time. In addition, minority populations are increasing disproportionately to the Caucasian majority. Since many minority groups have a greater chance of developing diabetes and have less access to care than Caucasians, the incidence of diabetes would again be expected to increase over time.

Second, there is now greater awareness of diabetes. This has led to increased detection and a decrease in the percent of individuals remaining undiagnosed.

Third, diagnostic criterion changed in 1997 when the cutoff for abnormal fasting plasma glucose was lowered from 140 to 126 mg/dl. This quickly added almost a million people to the diabetic population.

Without doubt, however, the most important contributor to the rise in the incidence of diabetes over the past 15 years has been the increase in obesity. We have now reached a point where almost one in three people is obese and as many as two of three are overweight. Since obesity is often associated with insulin resistance, it follows that as the prevalence of obesity increases, so too will the prevalence of diabetes.

It should be remembered, however, that the change in the number of people

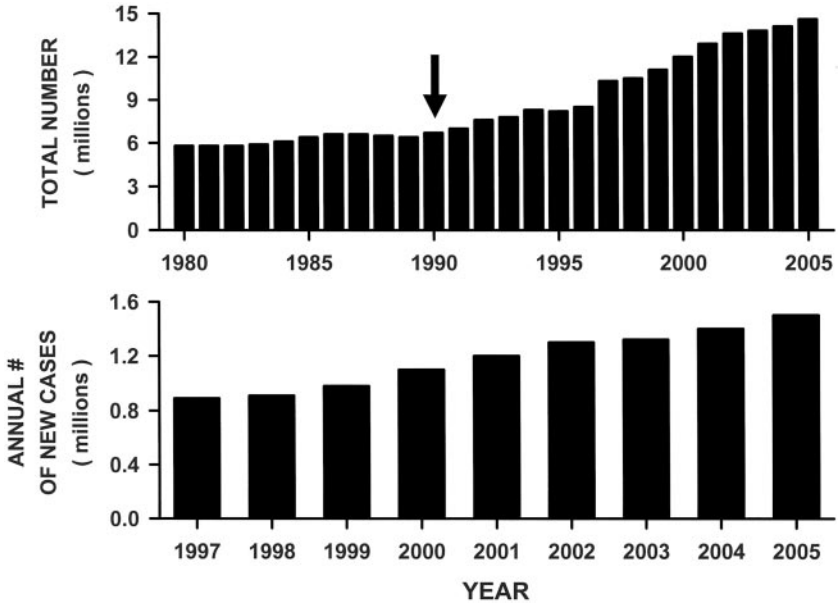

Figure 1—*Individuals with diagnosed diabetes. The arrow indicates the point of inflection.*

with diabetes reflects a balance between the incidence of the disease and the rate at which the disease is cured or patients die. Not only is the incidence of diabetes rising, but we have slowed the fractional loss of people with diabetes from the population.

New treatment options, including improved treatment of lipid abnormalities and elevated blood pressure, have slowed the development of macrovascular complications and the adverse outcomes with which they are associated.

We have thus lengthened the life of people with diabetes, and in doing so we have contributed to the increase in the number of individuals with the disease. To some extent, therefore, we are victims of our own success.

It is ironic that this increase in diabetes has occurred despite a period of unparalleled advances in our understanding of the disease and in the availability of options to treat it. We have begun to understand the genetic basis of the disease and the events that initiate it. We have also made great strides in clarifying the complexity of insulin signaling.

The results of the Diabetes Control and Complications Trial (DCCT) published in 1993 showed that glycemic control in people with type 1 diabetes is critical to the prevention of complications and established once and for all that the lower the blood glucose level, the better the intermediate and long-term outcomes. The U.K. Prospective Diabetes Study showed that blood glucose control was also important in preventing complications in people with type 2 diabetes. The results of the Finnish and U.S. diabetes prevention trials showed that the onset of type 2 diabetes could be slowed by drug treatment or lifestyle modification in high-risk individuals.

Finally, it is now clear that the team approach to care is essential to improved care. Research within the pharmaceutical sector has resulted in a number of new therapeutic options becoming available to physicians and their patients.

Let me elaborate on some of these advances. The DCCT exposed an unintended consequence of tight blood glucose control, that of increased hypoglycemia. This area remains one of great clinical importance and in part provided the impetus for the development of new insulin molecules.

Lispro and Aspart have a quick onset of action and a rapid off time, thus more effectively controlling meal time glucose. Glargine provides a sustained basal level of insulin, thereby improving fasting plasma glucose levels. These products allow for better simulation of endogenous insulin secretion, and as a result they improve glycemic control.

The treatment of patients with type 2 diabetes was also improved by the availability of new products. These include a biguanide thought to inhibit hepatic glucose production; the thiazolodendiones, which alter muscle and fat metabolism; the α-glucosidase inhibitors, which slow glucose absorption; the nonsulfonylurea secretagogues, which enhance insulin secretion; and agents that facilitate weight loss.

Insulin pumps are now smaller and more reliable. Glucose sensors that can be placed subcutaneously and can telemeter information to a monitoring device have been developed. This real-time tracking of glucose can help the physician and patient to better adjust therapy.

Likewise, significant advances have been made in the area of pancreas replacement. Pancreas transplantation is now safe. At some centers, as many as 70% of patients receiving transplants are insulin independent 5 years after surgery. In 2004, there were almost 1,500 pancreas transplants in the U.S.

In addition, islet transplantation has at last proven feasible. In 1999, a group in Edmonton published their exciting results showing that islets injected into the portal vein leading to the liver could cure diabetes. While we now know that only 60% of recipients remain insulin independent 3 years after the transplant, many appear to have an improved quality of life. In 2004, there were 118 islet transplants in the U.S.

Finally, the role of nonphysician health care professionals in the treatment of patients with diabetes has clearly emerged. Patient education has become of paramount importance. The number of certified diabetes education programs has increased dramatically, and there are now almost 15,000 certified diabetes educators throughout the country.

In summary, we have come a long way. New treatment options now allow for control of blood glucose with drug therapy for a longer period of time than ever before, new insulins allow for a reduction in the range of glycemic excursions in the insulin-requiring patient, and new drugs permit improved control of blood pressure and lipid levels in all patients.

We have not, however, developed a cure for the disease (with the exception of the 1,500 or so pancreas transplants done each year), nor have we put in place an effective prevention strategy. It is not surprising, therefore, that the prevalence of diabetes has reached epidemic proportions.

Given the tremendous increase in our knowledge, one must ask the question, has the quality of care of the individual with diabetes improved?

We know that the ADA and other groups have established clinical guidelines to assist health care professionals in

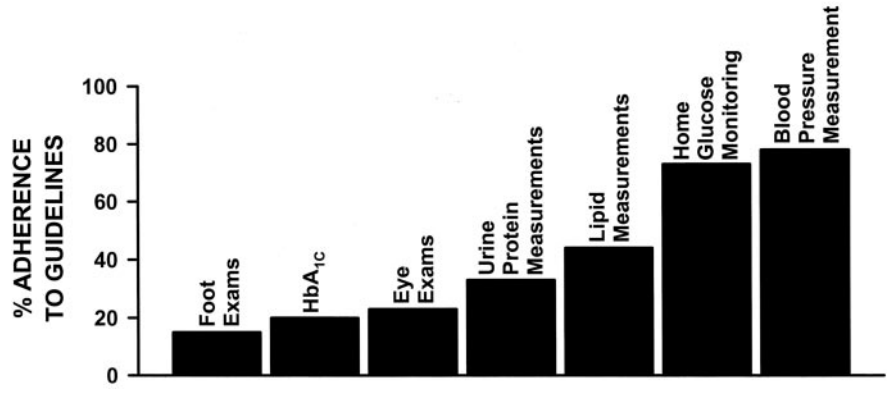

Figure 2—*Adherence to diabetes care guidelines by primary care physicians. From Kirkman et al. (4).*

treating their patients. One might expect that with those evidence-based guidelines in hand and an array of drugs and devices available to facilitate treatment that the quality of care would have improved dramatically, but in fact it hasn't.

If we compare data from the National Health and Nutrition Examination Survey (NHANES) of adults with previously diagnosed diabetes conducted in the late 1980s to NHANES data collected in 1999–2000, certain interesting facts emerge (1). The BMI has increased significantly, indicating that patients are now even more over weight. The disease is now diagnosed at an earlier age. Remarkably, there has been no improvement in the HbA_{1c} (A1C) level. On reflection, however, perhaps that should not be surprising.

First, achievement of an A1C <7% is associated with an increased risk of hypoglycemia; this limits therapy. Second, the drugs currently available to control blood sugar in patients with type 2 diabetes are only effective for a few years; thus, despite the possibility of combination therapy, in many cases the disease progresses until insulin is required. Third, less than half of patients with diabetes receive recommended care. Finally, patients are not adequately engaged in their own care.

In contrast to A1C, systolic blood pressure and cholesterol levels are now lower than they used to be. The latter findings are consistent with the availability of effective new medications to treat blood pressure and lipid levels and with the realization that it is important to move away from a glucocentric approach to the treatment of diabetes.

It turns out that the problem with quality of care in the U.S. is not specific to diabetes. In 2001, the Institute of Medicine published a report entitled "Crossing the Quality Chasm: A New Health System for the 21st Century," in which they referred to the gap between recommended care and actual care as a "chasm" (2).

According to an article published in the *New England Journal of Medicine* in 2003 (3), only half of patients receive recommended care. This is true regardless of the disease and whether the focus is on preventative, acute, or chronic care. In the case of diabetes, only 45% of patients receive recommended care. According to the American Medical Association, there are ~5,000 adult endocrinologists and ~1,000 pediatric endocrinologists in this country. It is thus obvious that the majority of individuals with diabetes are cared for by primary care physicians.

In 2002, Kirkman et al. (4) published an article that provided a snapshot of the adherence to diabetes care guidelines by primary care physicians (PCPs) in a rural county in Indiana. As can be seen in Fig. 2, adherence ranged from <20% to a maximum of 80% depending on the measure. The expectation that PCPs, who have a myriad of medical problems to deal with and only a few minutes to spend with each patient alone, can alter the course of this disease is simplistic. Attempts to improve the performance of physicians by providing them with more information have generally not been successful.

The fact is, however, that not all of the news is bad; perhaps we are finally beginning to see some light at the end of the tunnel.

In an article by Herman et al. (5) published last March in the *Annals of Internal Medicine*, a Markov simulation model was used to estimate the incidence of type 2 diabetes over time in treated and untreated individuals who were at risk for the disease. According to the model, it took 11.1 years longer for 50% of the individuals at risk to develop the disease if they modified their lifestyle by exercising for 30 min/day five times a week and reduced their body weight by ~5% (Fig. 3).

In addition, the model predicted that by the end of life, 60% of the at-risk individuals in the lifestyle intervention group would develop the disease, as opposed to 80% in the placebo group. This represents a 25% decrease in the incidence of diabetes.

This model, like most, has its limits, particularly as it relates to the cost-effectiveness of the intervention. The major value of the Herman article, however, and the data upon which it was based, lies

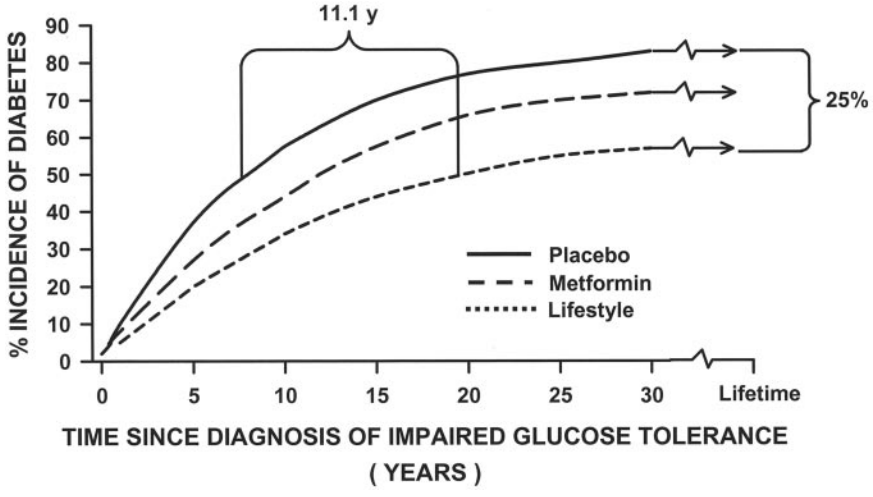

Figure 3—*Simulated cumulative incidence of diabetes among adults with impaired glucose tolerance. Redrawn from Herman et al. (5).*

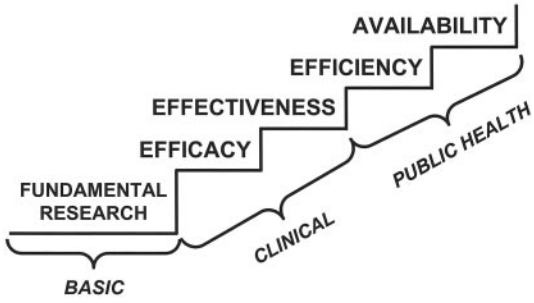

Figure 4—*Focus on outcomes research. Adapted from Detsky and Naglie (9).*

in the fact that it points us in a new direction—prevention.

Another success story involves the Madigan Army Medical Center (MAMC), a tertiary care academic medical center with ~250 staff and residents (2). There are 76,000 beneficiaries enrolled, including 3,000 with type 2 diabetes. MAMC launched an initiative to improve the quality of care for individuals with diabetes within its target population. The initiative focused on "preventive maintenance" and the use of information and communication technology to provide decision support for physicians and to actively engage patients. The centerpiece of the program was an electronic scorecard keyed to evidence-based Diabetes Quality Improvement Program measures and loaded automatically from the lab, the pharmacy, and other clinical data systems.

At the point of care, the clinician and patient reviewed the results from the scorecard together and used them to make collaborative decisions about the next steps in the care plan. As a result of this interactive approach and the monitoring of patient outcomes, emergency room visits and hospital admissions decreased by 40 and 9%, respectively. These results provide an example of how positive provider-patient interactions can improve outcomes. They also point us in a new direction, toward a chronic care model of disease treatment.

Finally, at long last, at the 2005 Scientific Sessions, two articles (6,7) reported improvements in the quality of care. One study showed that the incidence of end-stage renal disease in people with diabetes decreased by 30% in the 6 years ending in 2002. Another study reported a 35% reduction in diabetes-related potentially preventable hospitalizations from 1994 to 2002. Although improved quality of care is but one potential explanation for these changes, they represent a major advance and provide a hopeful sign for the future.

The final apparition to visit Scrooge was the spirit of Christmas yet to come. When it came, Scrooge bent down upon his knees, for in the very air through which the spirit moved, it seemed to scatter gloom and mystery.

Let us now look ahead. Given all that I've said, what are the predictions for a generation from now? According to Wild et al. (8), if current trends continue, by the year 2030 there will be ~23 million people in this country with diagnosed diabetes. Almost half of the states will have a prevalence >10%. The total number of people with the disease (both diagnosed and undiagnosed) will top 30 million. The U.S. will rank third in the world in the number of people with diabetes.

If one includes individuals with prediabetes, all told 100 million people will have impaired fasting, abnormal postprandial glucose, or both. Since data are rapidly accumulating to indicate that even mild hyperglycemia can lead to the development of complications and adverse events, this will create a health care challenge of immense proportion.

The cost of the disease will approach 250 billion dollars that year. If an amount equal to 1.0% of the cost were to be invested in research, it will require the NIH to spend over 2 billion dollars. Keeping the proportion of federal to private support at its current level, the ADA and the JDRF would be required to collectively raise 380 million dollars for diabetes research. If these predictions come to pass, the economic and personal burden of diabetes in this country will be overwhelming.

After being given a glimpse of his most unpleasant future by the spirit of Christmas yet to come, Scrooge says to the apparition, "Assure me that I may yet change the shadows you have shown me."

The question before us, therefore, is what can we do to avoid the outcome so clearly portrayed by Wild et al. (8)? I would suggest that there are four ways to approach the problem. First, we must continue to invest in research; second, we must adopt a chronic care model for the treatment of the disease; third, we must focus on the development of affordable and effective prevention strategies; and finally, we must find a way to control or prevent the associated metabolic disease, obesity.

We must continue to invest in basic as well as clinical and health services research. The potential of research to provide better approaches to care, improved opportunities for cure, and strategies for prevention is great. For example, in the treatment of people with type 1 diabetes there is the possibility of tissue-selective insulins, as well as new insulin delivery routes. Inhalation of insulin is now a recognized alternate to insulin injection. Oral insulin delivery is under active investigation and remains a long-term goal. There is no doubt that new drugs will also soon become available for the treatment of type 2 diabetes.

Glucagon-like peptide-1 analogs, one of which was very recently approved by the U.S. Food and Drug Administration, and dipeptidyl-peptidase-4 inhibitors, compounds that slow the destruction of endogenously released glucagon-like peptide-1, will become available. Drugs in this class have been reported to enhance insulin secretion, inhibit glucagon release, slow gastric emptying, reduce appetite, and perhaps even increase β-cell mass.

With the discovery that fat cells secrete a variety of signaling peptides that regulate liver, fat, and muscle metabolism, a myriad of new therapeutic options arise. Our improved understanding of appetite regulation has led to the discovery that inhibition of the cannabanoid I receptor by CB-1 antagonists can produce meaningful weight loss. Undoubtedly, other approaches to appetite control will be forthcoming.

Compounds that regulate glucose production or uptake by the liver will likely be developed, as will drugs focused on the prevention of complications. Additionally, it is also likely that new products within currently existing drug classes will become available.

There seems little doubt, in fact, that as the discovery process continues, approaches not even thought of today will emerge. With improved pump and glucose sensor technology, we will soon be able to close the glucose feedback loop, thereby creating an artificial pancreas. This could involve either an internal or

external pump. The challenge now is to install information into the pump so that it can accurately make decisions about insulin delivery rates without the intervention of the patient or physician.

In the area of whole pancreas transplantation, there may be an improved success rate. However, it is unlikely that there will be much quantitative progress given the limit in organ donors.

On the other hand, it is likely that major advances will be made in the area of islet biology and β-cell replacement. The Edmonton protocol made clear that problems associated with islet availability and immunosuppression limit the translation of islet transplantation into practice. Many approaches are being pursued to solve these problems. First, embryonic stem cells are being used to generate new β-cells. If successful, this could provide an unlimited supply of tissue. Second, researchers are studying ways to turn adult stem cells into new β-cells; this would also overcome the problem of supply and may have immunologic advantage. Gene transfer is being used to turn cells already existing in the body into those capable of sensing glucose, synthesizing insulin, and exporting it in a physiologically appropriate manner. Finally, studies are being carried out to explore the feasibility of xenotransplantation, i.e., the transplantation of islets from nonhuman species into humans using encapsulation technology. At present, it is unclear which, if any, of these approaches will lead to a cure, but the potential is there.

Last, but not least, research with a focus on health outcomes will improve our ability to deliver quality care. Detsky and Naglie (9) pointed out in 1990 that there are a series of steps that occur between an initial discovery and when most people benefit from that discovery (Fig. 4). An idea born out of basic research must first be tried in an ideal clinical setting to determine its efficacy. It must then be applied in the real world to test its effectiveness and then be viewed in terms of its efficiency. Is it affordable? Finally, are the systems in place to make it available to the population as a whole? Health services research is concerned with the last two steps. It is clear that such research is vital if we are to realize the full value of any of the aforementioned advances.

Translation of basic and clinical research findings into everyday practice is difficult but of utmost importance. It will only occur when we learn to deal more effectively with the economic and political barriers to care. In light of the magnitude of the diabetes problem and the incredible potential of research to make a difference, it is disturbing that the government is limiting its allocation to the NIH. There could not be a worse time to do so. Not only will such action slow the acquisition of new and important knowledge, but it will also decrease the likelihood that individuals graduating from college will choose research as a career. The latter will have a negative impact on our fight against diabetes for years to come. It is imperative that we do all we can to engage the administration in the war against this disease.

The second thing we must do if we are to avoid the fate described above is to change our approach to the treatment of the disease. It is now becoming clear that the acute care model is not effective in treating patients with diabetes.

Improved outcomes depend on good self-management, and it is now abundantly clear that the latter depends on positive patient-provider interactions. Health care providers can give helpful recommendations, advice, and counseling, but it is the patient that must decide which strategies to put into practice. Patients and their families, not health care professionals, are responsible for management of the disease. Thus, it makes sense to develop collaborative plans and management goals with patients rather than simply prescribing a regimen to which the patient must adhere.

This shift in focus from the provider to the patient being the most active decision maker is central to the emerging chronic care model of treatment. The chronic care model starts by focusing on what characterizes a productive interaction and then specifies what things need to be improved in order for that productive interaction to occur.

In productive interactions, patients are given enough time to explain what concerns them the most. There is an assessment not only of their clinical status, but also of their knowledge and understanding of their medical condition, their self-management skills, and their confidence about making changes.

Clinical management is evidence based. Treatment goals are set by a collaborative process and broken down into small achievable pieces. Potential barriers are overcome by problem solving, and a shared plan of action is developed. Finally, an explicit follow-up plan is formulated with direct contact between the health care team and the patient at agreed upon intervals. For this to happen, patients must be informed and the health care team must be prepared.

Patients who feel understood and supported by their providers are more likely to have a high level of self-confidence and to succeed in behavioral change. To facilitate the interaction of patient and provider, the practice team must be supported by the health care system in terms of patient information, decision support, people, and equipment. They must also be given the time required to deliver evidence-based clinical management and self-management support. Finally, this should all be done within the context of a supportive community.

While this approach to care is likely to bring enhanced success, it will require great effort to implement. Health care providers must accept that knowledge alone is not enough to produce behavior changes. The focus has to be on problem solving and coping strategies, not just on didactic education. Communities must buy in and develop support programs.

Glasgow et al. (10) suggested two key elements to the implementation of the chronic care model. First, the focus on population-based and public health approaches to chronic care must be increased in the undergraduate, graduate, and continuing education of health care professionals. Second, if successful outcomes are to be realized, financial incentives must be put in place to reward both the health care provider and the patient for good performance.

Interestingly, in April of 2004, family practitioners in the U.K. entered into a contract with the government that will provide bonus payments for high-quality care. Physicians can earn points for achievements in relation to a set of indicators that make up the quality and outcomes framework. Points are earned for process measures, intermediate outcome measures, organization indicators, and patient satisfaction. These points can then be redeemed for increased income. It will be extremely interesting to evaluate the impact of this plan on the quality of care as it relates to diabetes.

The third thing we must do to avoid the fate predicted by Wild et al. (8) is to focus on prevention and early treatment of the disease. It is becoming increasingly clear that hyperglycemia at levels below those used for the diagnosis of diabetes leads to the development of complications. This argues for glucose screening in

at-risk individuals. It is also becoming clear that early treatment of glycemia can have beneficial effects for many years to come, even if tight glucose control is only temporary.

As was reported in the *New England Journal of Medicine* in 2003 (11), patients in the DCCT study were followed for a decade after the trial ended. Despite the fact that the A1C values in the control and intervention groups in the post-trial period were at approximately the same level, the development of artherosclerosis was significantly lower in the once intensively treated group. The biochemical basis of this memory effect remains unclear, but it provides a powerful argument for early treatment.

Likewise, the previously mentioned results from the Diabetes Prevention Program, and other studies like it, established the clinical effectiveness of lifestyle intervention in slowing the onset of diabetes and in preventing the disease in as many as 20% of at-risk individuals. Such data provide a strong basis for an emphasis on early intensive treatment and prevention.

The problem is that understanding the basic science behind a prevention strategy and demonstrating its clinical efficacy in an ideal setting and even its effectiveness in the real world is not enough. A prevention strategy also needs to provide an efficient solution to the problem, one that has a reasonable net cost associated with it. That is to say, the cost of prevention over a prolonged period, plus the cost of treating people who would in fact never get the disease, must be balanced against the cost of treatment of individuals who would otherwise have the disease for a considerably shorter time. This balance in turn must be viewed in the context of the quality of life of the patient.

One then must face the complexity of reimbursement in this country, which also creates a significant barrier to care. For example, Medicare still does not reimburse for interventions to prevent diabetes. We must find cost-effective prevention strategies, we must have the political will to force their support, and we must then apply them nationwide.

The last thing we must do to slow the increase in diabetes is to deal with the problem of obesity. This condition threatens to undo decades of progress made against not only diabetes but also cardiovascular disease and cancer. Clearly, as the prevalence of obesity rises, so does the prevalence of diabetes. It stands to reason, therefore, that if we can decrease the prevalence of obesity, we will decrease the prevalence of diabetes.

Amazingly, as reported in two studies published in 1999 (12,13), only 42% of obese adults were advised to lose weight by their physician, and only 34% were advised to exercise. This is simply unacceptable. We must support research that focuses on the regulation of energy metabolism and appetite regulation, as well as feeding and exercise behaviors. We must work within our school systems to reintroduce physical education and to remove vending machines that dispense unhealthy food and beverages. We must raise the nation's awareness of healthy and unhealthy foods.

A prominent role for the ADA in response to the challenge of obesity is inescapable. It is with this in mind that the ADA has established a new organization focused on the science and medicine surrounding weight management and obesity prevention. In this way, we will play a leading role in the fight against a condition that affects >75% of people with diabetes in this country. Furthermore, by forming a separate organization to deal with obesity, we will be able to do so without compromising the focus of the ADA itself on type 1 and type 2 diabetes.

You are all here because you have some connection to diabetes. Each and every one of you needs to be engaged in the fight against this disease. Researchers need to continue the discovery process, create new knowledge and new opportunities for treatment, cure, and prevention.

Physicians and other health care professionals need to be early adopters of innovation, take advantage of new opportunities, and overcome the barriers to their implementation. As individuals, we need to become more engaged in the process of care and take increased responsibility for our own health management.

Scrooge was able to avoid the fate shown him by the spirit of Christmas yet to come. The question is, can we do the same?

I would like to finish by thanking those individuals with whom I discussed various aspects of this lecture. Their input was much appreciated. I would also like to thank my colleagues at Vanderbilt for their support and patience over the last 3 years. Likewise, I wish to express my gratitude to the members of my own lab, who have dealt with my frequent absences gracefully and who were of tremendous help in the technical preparation of this address. I would like to acknowledge the support of the ADA staff and the ADA executive committee, in particular my fellow principle officers Larry Ellingson and Cathy Tibbetts. I could not have had better teammates. Finally, I would also like to thank my family, all of whom are here today, for their enthusiastic support during what has been an inspiring journey.

I will close with a quote from the German poet, Goethe, which I think captures the spirit of my message: "Knowing is not enough; we must apply. Willing is not enough; we must do."

Thank you.

ALAN D. CHERRINGTON, PHD

From the Department of Molecular Physiology and Biophysics, Vanderbilt University Medical School, Nashville, Tennessee.

Address correspondence to Alan D. Cherrington, Vanderbilt University Medical School, Molecular Physiology and Biophysics Dept., 704 RRB, Nashville, TN 37232-0615. E-mail: alan.cherrington@vanderbilt.edu.

This address was delivered at the 66th Annual Meeting and Scientific Sessions of the American Diabetes Association, Washington, DC, 9–13 June 2006.

DOI: 10.2337/dc06-9915

References

1. Saydah SH, Fradkin H, Cowie CC: Poor control of risk factors for vascular disease among adults with previous diagnosed diabetes. *JAMA* 291:335–342, 2004
2. IOM Health Care Quality Initiative, Institute of Medicine of the National Academies: *1st Annual Crossing the Quality Chasm Summit: A Focus on Communities*. Adams K, Greiner AC, Corrigan JM, Eds. Washington, DC, National Academies Press, 2004
3. McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, Kerr EA: The quality of health care delivered to adults in the United States. *N Engl J Med* 348: 2635–2645, 2003
4. Kirkman MS, Williams SR, Caffrey HH, Marrero DG: Impact of a program to improve adherence to diabetes guidelines by primary care physicians. *Diabetes Care* 25: 1946–1951, 2002
5. Herman WH, Hoerger TJ, Brandle M, Hicks K, Sorensen S, Zhang P, Hamman RF, Ackermann RT, Engelgau MM, Ratner RE: The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med* 142:323–332, 2005
6. Imai K, Engelgau M, Zhang P: Trends in diabetes-related preventable hospitalizations in the United States, 1993–2002 (Ab-

stract). *Diabetes* 54 (Suppl. 1):A305, 2005
7. Burrows NR, Wang J, Geiss LS, Engelgau MM: Incidence of end-stage renal disease among persons with diabetes, United States, 1990–2002 (Abstract). *Diabetes* 54 (Suppl. 1):A201, 2005
8. Wild S, Roglic G, Green A, Sicree R, King H: Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care* 27:1047–1053, 2004
9. Detsky AS, Naglie IG: A clinician's guide to cost-effectiveness analysis. *Ann Intern Med* 113:147–154, 1990
10. Glasgow RE, Hiss RG, Anderson RM, Friedman NM, Hayward RA, Marrero DG, Taylor CB, Vinicor F: Report of the health care delivery work group: behavioral research related to the establishment of a chronic disease model for diabetes care. *Diabetes Care* 24:124–130, 2001
11. Nathan DM, Lachin J, Cleary P, Orchard T, Brillon DJ, Backlund J-Y, O'leary DH, Genuth G: Intensive diabetes therapy and carotid intima-media thickness in type 1 diabetes mellitus. *N Engl J Med* 348: 2294–2303, 2003
12. Galuska DA, Will JC, Serdula MK, Ford ES: Are health care professionals advising obese patients to lose weight? *JAMA* 282: 1576–1678, 1999
13. Wee CC, McCarthy EP, David RB, Phillips RS: Physician counseling about exercise. *JAMA* 282:1583–1588, 1999