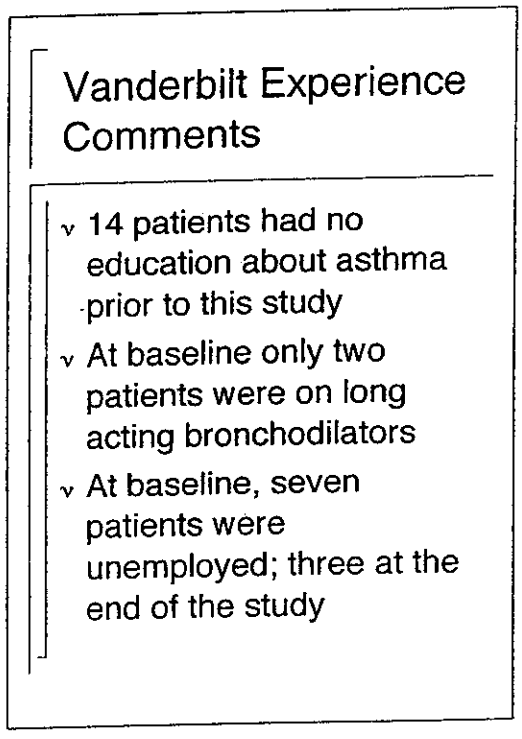
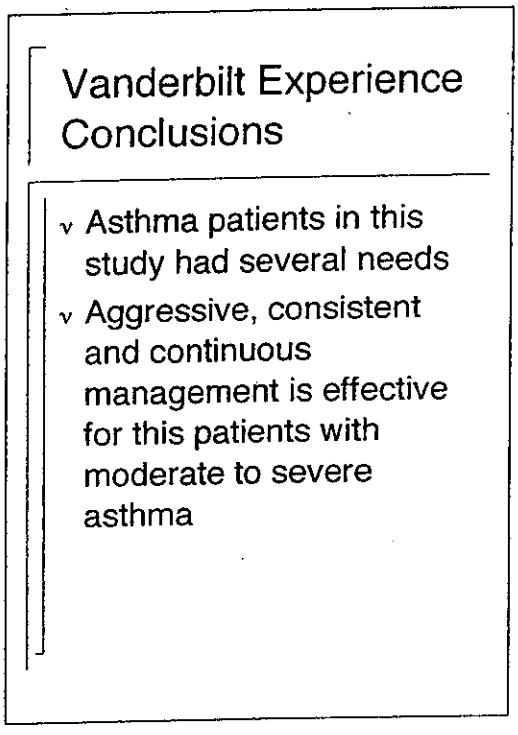


It was impressive to us that only one patient in the 15 had been educated about asthma!

Most of the patients were on short acting bronchodilators.

And, at the beginning of the study, seven of the patients were unemployed versus three at the end. This significant change needs to be calculated in future studies.

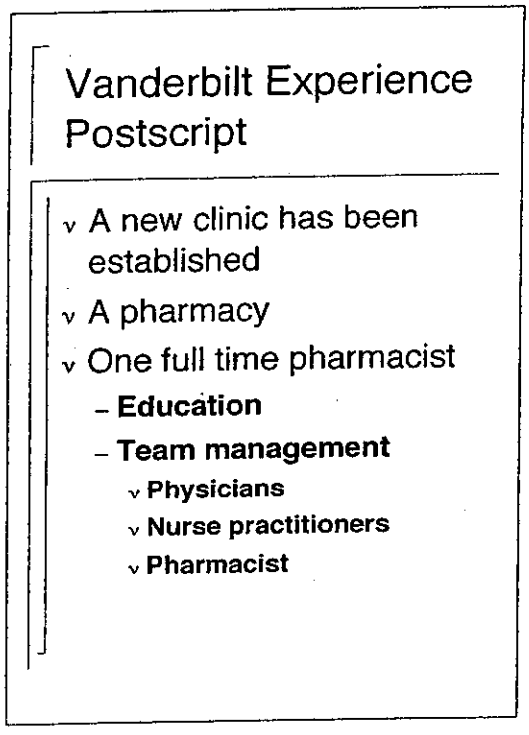


We found that asthma patients who frequently utilize our clinic, emergency room, and hospital for acute asthma events were not knowledgeable enough to take good care of themselves.

In addition, once they had aggressive, consistent and continuous management they improved.

It is hard to tell how long the effects of the intervention would last for these patients. In other studies, educational interventions last up to six months. It is highly possible that patients in programs such as these would need repeated assessments and support.

I would like to express my appreciation to Anita Evans, Pharm.D., who served as principle investigator for this study and completed her postgraduate residency at our institution, to John J. Murray, M.D., Ph.D., who assisted as a collaborating investigator and as our medical advisor, and Nancy Wells, R.N., D.N.Sc., who assisted us in the writing and analysis of our study.



There is good news that comes as a result of Dr. Evans' efforts. Since the study, an Asthma, Sinus, and Allergy Program has been opened near the Vanderbilt campus. It employees a full time pharmacist for dispensing of medications and devices. At this time, the clinic is evaluating four to seven new patients a day. We are very happy to say that the pharmacist is significantly involved in patient and staff education and service.

Thank you very much for your kind attention, and for your invitation to come and share experiences with one another.

DIABETES AND THE ELDERLY PATIENT
Special Considerations For Management and Monitoring

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OBJECTIVES:

Upon completion of this article the pharmacist should be able to:

* Understand basic differences in clinical presentation of diabetes in the elderly patient as opposed to the younger diabetic.

* Discuss general treatment considerations that are appropriate for elderly patients with diabetes.

* Select specific treatment modalities which are safe and effective in treating the elderly.

* Be knowledgeable of monitoring techniques which are easy for the elderly patient or caregiver to understand and utilize.

* Understand the pharmacists' important role in educating, advocating for and monitoring these patients to avoid short and long term complications.

Diabetes is a disease, the symptoms of which have been known to mankind since the time of the Ebers papyrus in 1500 B.C.

The American Diabetic Association estimates that there are over 14 million people with diabetes. Today with over 100 diabetic care products available to control and monitor blood sugar, diabetes is still the third leading cause of death in America. We know that less than 5% of diabetics are managed by physician specialists with specific knowledge of this disease state. Only one patient in ten receives the appropriate counseling in diabetes care and management. There is much work to be done by all health professionals if we are to curb the effects of this widespread disease.

The above statistics are magnified when we consider the fact that many if not most diabetics are not diagnosed. This is especially true in the geriatric population. Many of the complications of diabetes accumulate over years and begin to appear only in the latter years of life.

It is estimated that 10% of the population over 65 and 20% of the population over 80 years of age have diabetes. With the anticipated increase of this population age group, it has been suggested that in the next twenty years the prevalence of diabetes in those persons over 65 years of age may well be as high as 44%.

Diagnosis and management in this age group is further complicated by a host of age-related concomitant diseases and the numerous medications required to control these diseases.

It will be the purpose of this article to review diabetes in the elderly patient and provide basic information to assist you as a health care practitioner in the early detection and management of these patients in an effort to minimize the complications associated with this dread American public health condition.

THE DISEASE AND ITS CAUSE

There are two types of diabetes which are classified on the basis of their clinical presentation. (See Table 1) Type I diabetes (insulin-dependent diabetes mellitus) occurs in only 5% to 10% of the diabetic population. These patients have little or no pancreatic function, are prone to ketoacidosis and require exogenous insulin.

Diabetes in the elderly is typically Type II. This type accounts for more than 90% of the general diabetic population. Type II patients usually present with some pancreatic function and can be managed with diet, exercise or oral sulfonylureas. A substantial number of these patients will eventually require insulin or an insulin/drug combination to control the symptoms of their disease.

It must be emphasized that the precise pathophysiology of diabetes is not known. It is probably a heterogenous disease. There are at least three (3) basic defects which contribute to the pathogenesis of the disease. First, the early release of insulin is altered and the quantity of insulin released in response to glucose is decreased. Second, there is tissue resistance to insulin both in the peripheral tissues and the liver. A third defect in diabetes is an increased glucose output by the liver. We normally rely on the liver to produce glucose in the fasting state. In the diabetic patient, it produces glucose both in the fasting and nonfasting state.

It is important to have an understanding of the above pathogenesis of Type II diabetes, since virtually all treatment regimens are directed at one or more of these defects.

DIAGNOSIS IN THE ELDERLY

The diabetic who typically presents with the classic signs of polyphagia, polydipsia and polyuria, with a blood glucose of $\geq$ 200mg/dL is relatively easy to diagnose. Diabetes in the elderly, however, is often asymptomatic and the

classic signs are either hard to detect, or can attributed to other health problems or age-related physiological changes.

The sense of hunger and thirst are often altered in the elderly and the classic signs of polydipsia and polyphagia become less specific in the diagnostic effort. Urinary symptoms of the disease are often misinterpreted as a sign associated with another health condition, e.g. benign prostatic hypertrophy, urinary incontinence or urinary infection.

Subjective assessment of fatigue, weakness, loss of weight and alteration in eyesight are quite often attributed to simply old age. One should be alert when the above symptoms are intermittent in presentation. This is usually a key fact which is indicative of diabetes especially in the older patient. Quite often infection may be the first sign of diabetes in the elderly and extremely high blood sugars are only detected by blood chemistry done for an acute infection or a cardiac related disease complication. Frequent, accurate and simple blood glucose testing in the elderly patient is essential and is the only way to assure safe and effective detection and control of the older diabetic.

LONG-TERM COMPLICATIONS

Most adult diabetic patients, who fail to manage their disease, succumb to long term complications associated with hyperglycemic-induced changes to the nerves and blood vessels. Blood glucose greater than 150 mg/dL for extended periods of time creates numerous metabolic changes that can alter normal organ function and result in retinopathy, nephropathy and neuropathy. In addition, substantially high blood glucose concentration can be correlated with microvascular and macrovascular diseases which result in capillary thickening, increased blood viscosity, faulty lipid metabolism and abnormally high levels of glycosylated hemoglobin.

The elderly diabetic population has a 36% rate of cerebral vascular disease and a 26% rate of

peripheral vascular disease, as compared to 16% and 12% respectively in the age-comparable nondiabetic population. Diabetes is the sixth leading cause of death in persons greater than 65 years of age and these individuals most often die of cardiovascular complications associated with diabetes.

In 1983, the National Institute of Diabetes and Digestive and Kidney Diseases launched the Diabetes Control and Complication Trial (DCCT). The results, released in June, 1993, put to rest a controversy which had raged for 50 years; the results showed that tight control of blood glucose levels with intensive therapy in Type I diabetics will significantly improve the long-term outcome of changes associated with microvascular and macrovascular alteration. Retinopathy was decreased from 76% to 34%. There was a 35% decrease in microalbuminuria and a 56% decrease in clinically graded albuminuria. Neuropathy was decreased by 60%.

The interpretation and application of the results of this study in elderly patients must be cautiously applied. The elderly patient is exquisitely sensitive to hypoglycemic states and must be treated somewhat conservatively. A target range for blood glucose in the elderly diabetic would be 70 to 140 mg/dL. These patients can tolerate transient acute hyperglycemia much more easily than hypoglycemia.

Accurate and efficient blood glucose treatment and monitoring in the diabetic elderly patient can, however, significantly minimize, delay or prevent long-term complications.

THERAPEUTIC GOALS

The three major goals of therapy for the treatment of the elderly diabetic patient are listed in Table 2. Treatment regimens are employed to prevent the acute consequences of hyperglycemia. At glucose concentrations > 240mg/dL, white blood cells do not function effectively and increased glucose concentrations in body fluids and secretions

predispose patients to infections. Loss of weight, fatigue, water loss and dehydration are other acute consequences of hyperglycemia.

Secondly, we utilize regimens and monitoring techniques which avoid hypoglycemia in order to avoid life-threatening neurologic and cardiovascular consequences. Epinephrine, which is released as a body regulatory response to hypoglycemia, can have severe adverse effects which may include increased blood pressure, stroke or myocardial infarction. The brain, in order to function properly, must have a consistent and adequate supply of glucose. In a hypoglycemic state, it becomes severely lethargic and somewhat dysfunctional. Both of these responses can produce serious consequences in the seriously debilitated elderly individual.

A final goal for treatment of diabetes in the elderly patient should be to minimize, delay and avoid long-term complications associated with the disease. Although most patients with Type II diabetes already have long-term complications at diagnosis, primarily cardiovascular in nature, we must strive to treat and minimize the other risk factors such as hypertension, hyperlipidemia, obesity and smoking as well as conservatively control their blood glucose.

There is probably no more disheartening complication associated with diabetes than the diabetic foot ulcer. It is well established that early detection is the best cure for any pressure ulcer. Pharmacists can play a key role in teaching the patient techniques to increase their awareness of soreness or redness in the feet, usually a precursor to an ulcer. Use of soothing lotions can stimulate circulation and soften skin. Observations on the fit of shoes can be particularly helpful in avoiding the development of an ulcer. Common sense and early education in diabetic foot care can avoid traumatic and costly amputations as well as prevent life-threatening infections. Should an ulcer develop, aggressive and effective therapy, is essential. The pharmacist should assume the role of consultant in the selection and proper use of pharmacological

agents to promote healing of any ulcers which do develop.

TREATMENT OF ELDERLY DIABETIC

General Considerations

Table 3 lists the general modalities available for the treatment of diabetes.

In the elderly patient there are some physiologic and socioeconomic factors which may affect control and treatment.

Virtually all of the senses of vision, smell, taste and feel are altered with age. This age-related fact coupled with diminished cognitive function and concurrent diseases, such as rheumatoid arthritis, may significantly affect the use of complex treatment modalities and sophisticated monitoring tools. To be able to see small markings and simply grasp tiny syringes and devices can be quite a chore for an elderly diabetic. Simple and effective injection devices and pre-filled syringes become a necessity in some of the patients.

First line treatments such as diet are very difficult to employ in the elderly. Age related problems include poor dentition, difficulties in purchasing or preparing meals in a timely fashion, and severely altered senses of thirst and hunger, all of which can severely compromise the effective management of this disease by dietary control alone.

Other physiologic changes such as decreased renal and hepatic function can significantly affect renal thresholds for glucose as well as metabolism and excretion of insulin and other oral agents employed in treatment regimens.

Exercise is a very effective and commonly employed treatment approach employed in normal adult diabetic patients. Problems with chronic, progressive diseases, such as arthritis and osteoarthritis, severely limit the quality and

quantity of exercise regimens which will be effective in the control diabetes in the elderly patient.

Many of our elderly are on very small, fixed incomes and the quality of care that can be employed to manage their disease is limited. Purchase of food and diabetic supplies compete with each other. Patients employ cost saving shortcuts such as cutting glucose testing strips in half and otherwise modify what might be a safe and effective prescribed treatment approach.

Finally, polypharmacy is a common problem with the elderly. They take, on the average, six to ten medications, some of which can have profound impact on their diabetic disease, and they receive them from multiple local pharmacies and mail order operations. Appropriate management and certainly effective counseling become a challenge in these cases who have no consistent educator and advocate.

Diet

Diet plays a significant role in the therapy of the general diabetic patient population.

The American Diabetic Association's recommendations for a diabetic diet specifically address calories needed to maintain normal growth, to normalize glucose concentration and lipid levels and to prevent cardiovascular disease. To the Type II diabetic who is obese, this can mean severe caloric restrictions. The ADA diet also assumes regularly scheduled meals which coincide with peak actions of exogenously administered insulin.

Given the physiologic changes, socioeconomic differences and living habits of the elderly patient, dietary treatment must be selectively utilized, highly individualized, carefully counseled and closely monitored by a competent caregiver to be effective.

Exercise

The question of exercise in the management of the elderly diabetic patient is complex. In general, moderate regular exercise (combined with diet and/or oral agents) is highly recommended for individuals with Type II diabetes. Exercise is only encouraged in patients taking insulin (Type I) and only with special precaution. Exercise in insulin-dependent patients must be combined with appropriate increased food intake, altered or delayed administration times for insulin, decreased doses of insulin or a combination of the above. The complexity of these alterations frequently overwhelm the elderly patient.

The chronic and progressive diseases which commonly affect this age group, severely limit this treatment approach, but it should be considered.

Sulfonylureas

The use of the oral sulfonylureas is reserved for the treatment of patients with Type II diabetes whose disease cannot be controlled by diet and exercise alone. This is the typical elderly diabetic.

The sulfonylureas are the only oral hypoglycemic agents available in the United States. There is a good selection of agents which differ relative to efficacy, toxicity, metabolism, excretion and duration of action.

The sulfonylureas when used in appropriate doses are equally efficacious. These agents, however, are the number one cause of hypoglycemic reactions in the United States today. For this reason, especially in the elderly, we must begin sulfonylurea administration at very low doses (eg. 1.25 mg glyburide, 5 mg of glipizide, or 100mg of tolazamide) and thoroughly evaluate the patient on a weekly basis. The target blood glucose in the elderly diabetic is 70-140 mg/dL and one should avoid hypoglycemia in these patients at all costs.

Tolazamide and glipizide are the sulfonylureas most commonly used to treat Type II diabetes in the

elderly. Glyburide, also an effective agent, must be used with caution in the patient with decreased renal function. Tolbutamide is used less often due to its relatively short duration of action and need for multiple daily dosing.

When a patient fails to respond to maximum doses of one agent they may be switched to another which in select cases may prompt a therapeutic response. Combination of sulfonylureas is not recommended.

If an elderly patient fails to respond to oral hypoglycemics, we should first check compliance. This is a very common cause of failure in this group of patients. We must exert greater effort in patient education technique to avoid or minimize this problem.

Treatment failures should be further evaluated for underlying factors which could be causing increased blood glucose such as infection, stress or drugs. (Table 4).

Finally, implement an at home blood glucose monitoring effort that is affordable and effective for the patients. Frequent testing in a normalized environment has been shown effective in improving compliance and indeed modifying eating habits.

If, when appropriately used and monitored, the sulfonylureas fail, one should consider insulin or a combination of insulin and sulfonylureas.

Insulin Plus Sulfonylureas

A common practice over the past few years has been to combine insulin with the sulfonylureas. This practice is based on the theory that the combination can lower insulin requirements and enhance glucose control. An evening dose of an intermediate acting insulin can suppress hepatic glucose production and theoretically enhance the action of sulfonylureas throughout the next day. From a theoretical and pharmacological standpoint, this theory is sound, although resistance to the combined therapy is being observed after about six months in some patients.

Unfortunately, in the elderly patient, this combination is not practical in that it makes the regimen more complex and costly and places the patient at a somewhat higher risk of hypoglycemia.

Insulin

Insulin remains as a significant cornerstone in the treatment of Type II diabetes. Approximately one-third of these diabetics employ insulin to control their disease, one-third use diet and exercise and the rest use oral agents. It has been estimated that 80% of the insulin used in the United States is used by non-insulin dependent patients.

Insulin is a protein endocrine hormone secreted by the beta cells of the pancreas to regulate the metabolism and storage of glucose, fatty acids and amino acids. The healthy pancreas will secrete approximately one unit of insulin per hour and deliver a bolus of insulin in response to food ingestion.

In patients with diabetes, there is either an insulin insufficiency or there is a resistance to the action of insulin.

There are currently three forms of insulin available: standard, purified and human.

Since the discovery of insulin in 1922 by Banting and Best, virtually all patients with diabetes have received either beef or pork insulin. Improvement in manufacturing processes have continually increased the purity of these products, however, the problems of antibody formation and the emergence of resistance and allergy have remained as a significant complication.

The introduction of human insulin has truly revolutionized the treatment of diabetes. Human insulin produced by recombinant DNA technology has a structure which is identical to endogenous human insulin and is thus less immunogenic than its animal source counterparts. (Table 5)

Although processes of production differ slightly, it has been shown pharmacokinetically that there is

no significant difference in glucose lowering effect of single doses of any human insulin product, regardless of source.

It is estimated that human insulin now has 80% of the market and within a few years will be the only insulin available for treatment of the diabetic patients.

It is currently recommended that all newly diagnosed patients and patients with insulin allergy, lipoatrophy and certain types of insulin resistance be started on human insulin. It is suggested for pregnant women with diabetes to avoid production of antibodies which may cross the placenta and enter fetal circulation. It is also recommended in patients who are receiving intermittent insulin therapy, for example, the elderly surgical patient, in an effort to avoid the formation of antibodies which intermittent therapy is prone to induce.

The variety of insulin products available in the United States allows each diabetic patient to individualize their treatment regimen to suit their lifestyle.

Dosing schedules vary greatly for Type I and Type II diabetics and although there is no "standard" dose for any individual, it is recommended that initial doses of 0.5 to 0.8 units/kg daily in single or twice daily doses of NPH insulin be used and that bedtime NPH insulin be considered. In the elderly patient, a fasting blood glucose of greater than 180mg/dL is generally considered to be an indication for the use of insulin. One must, however, consider the risk versus benefit ratio of employing insulin therapy and consider its impact on life style and the quality of life before committing to a life long regimen which requires daily injections.

Some new concepts are emerging relative to the administration and absorption of the human insulins. To minimize variation of effect, it is currently recommended to rotate the site of injection, not among various sites, but within a

site. The abdomen is the preferred site, followed by the arm, thigh and hip. Subcutaneous absorption from the abdomen is not affected by exercise or other physical activity.

Insulin and combinations of insulin products (NPH and Regular) have provided greater flexibility in arriving at an injection whose profile will meet each individual patients' needs relative to their lifestyle, eating habits and individualized response to insulin.

The insulin market is changing rapidly. In the future, look for more pre-mixed insulins, new injection devices, improved monitoring instruments and perhaps even a nasally administered insulin.

DIABETIC GLUCOSE MONITORING

The key to successful insulin therapy is blood glucose monitoring. The goal in the elderly patient should be a blood glucose in the range of 70-140 mg/dL and to avoid hypoglycemic episodes at all cost.

There are some monitoring techniques which may not be useful in the elderly patient. Urine tests, for example, which are easy to perform and much less costly have been a standard in the general diabetic population for some time. In the elderly, however, there is little if any correlation between blood glucose and urine glucose levels. Reasons for this are that (1) elderly patients have higher renal glucose thresholds (2) many have conditions which cause urinary retention, e.g. benign prostatic hypertrophy; and (3) many have neurogenic bladders which cause them to retain urine and produce a mix of old and new urine in a single test specimen. The best we can hope for with urine tests in the elderly is to determine simply if sugar is present, we cannot accurately rely on this test to determine the amount.

The use of clinical signs and symptoms to monitor for glucose control is very difficult in the elderly. The signs of hypoglycemia are especially difficult to detect in the elderly with the many symptoms presenting from concurrent diseases.

The ideal way to monitor glucose in the elderly is with blood glucose meters at home. There are a number of such instruments to choose from ranging in price from $49 to $499. For the elderly patient, we should recommend an instrument which has a large visual readout, simple calibrations, a memory and one that is self-timing (no wipe) to minimize patient error in readings.

The glycated hemoglobin test is particularly useful in the elderly diabetic in that it reflects effective control of blood sugars over a period of time (3 months). Elevated glycosylated hemoglobins would indicate that on the average the patient's regimen, or the patient, is not maintaining control of their blood sugar. Normal values range from 4% to 7% of the total hemoglobin. In patients who have not adequately maintained blood glucose control the values may be as high as 14% to 17%.

COMPLICATIONS OF INSULIN THERAPY

Hypoglycemia is the most common and serious complication of insulin therapy. (Table 6) There are a number of reasons why hypoglycemia occurs in the elderly patient. Often they do not realize that they must match their food intake with the action of insulin. Exercise enhances the use of glucose and consequently the action of insulin. Increased activity of any kind can predispose the patient to hypoglycemia. Drugs and alcohol can cause hypoglycemia. Alcohol inhibits glucose production by the liver and drugs such as propranolol can block the effects of regulatory hormones such as epinephrine which is released by the body to counteract hypoglycemia and thus mask the early warning signs of this condition.

Virtually all of the signs of hypoglycemia are related to either increased levels of epinephrine or to insufficient glucose supply to the central nervous system. The signs include hunger, trembling, sweating, palpitations, anxiety, confusion, irritability, restless sleep and nightmares.

It is especially important in the elderly that we educate the patient on this potential complication and avoid what could be a life-threatening episode.

ROLE OF THE PHARMACIST

The primary role of the pharmacist is to supply diabetic and care products and to educate the patient. We must educate the patient as well as the caregiver. Educated patients appear to be motivated patients and the control of their disease becomes much more probable.

Pharmacists have a further role in the selection of products, management of costs associated with the disease, troubleshooting and solving practical problems associated with regimens and finally simplifying treatments. This last role can be most important in the older patient.

We can assure success of treatment regimens by simply advocating for the patient.

Less than 5% of patients with diabetes see a specialist in diabetic care. Only one patient in 10 has been adequately educated in diabetes self-management. The majority of individuals who use insulin make dosing errors. Less than one patient in 90 have a Glucagon Emergency Kit. The vast majority are not monitoring glucose at all and many of those who are self-monitoring are not doing it often enough. Diabetes remains the third leading cause of death due to disease, taking approximately 200,000 lives per year.

We still have some work to do!

References available upon request.

Table 2:

ELDERLY DIABETIC PATIENT
THERAPEUTIC TREATMENT GOALS

* Avoid acute consequences of hyperglycemia
* Avoid hypoglycemia
* Minimize/delay/avoid long-term complications
* Eliminate cardiovascular risk factors
* Educate patient on disease and management

Table 3:

ELDERLY DIABETIC PATIENT
SPECIFIC TREATMENT APPROACHES

* Diet
* Exercise
* Sulfonylureas
* Insulin
* Combination insulin and sulfonylureas