Clinical Review

Current Concepts in Diabetes Mellitus

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Family physicians play a significant role in the management of patients with diabetes. The classification of diabetes has been revised, requiring higher plasma glucose levels for diagnosis. Insulins have been purified, with contamination by proinsulin-like substances now routinely being less than 50 parts per million. As a result of increasing evidence that improved metabolic control is associated with a lower incidence of complications, especially for microvascular complications in patients with insulin-dependent diabetes, a variety of strategies have been developed to improve control. Early experience with frequent injections of insulins and constant infusion systems (pumps) has been favorable, though achievement of lower blood glucose levels is not without risk. Good control in pregnancy is especially critical. Glycosylated hemoglobin has proven to be a useful addition to assessing control. To achieve optimal therapeutic results, diabetes should be viewed as a chronic biomedical disease with major behavioral components.

Research and treatment in the field of diabetes mellitus is in an exciting stage of advancement. Better understanding of the disease, manifested by a new classification system and treatment strategies, especially newer ideas about control, provides hope for better outcomes for patients with diabetes. Many, if not most, of the developments fall within the purview of the family physician to translate into the care of his or her patients.

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According to the National Ambulatory Medical Care Survey (NAMCS) for 1977, visits to general and family physicians accounted for 53.4 percent of the estimated 11 million office-based visits for which diabetes was the principal or first-listed diagnosis.[1] These numbers highlight both the great number of visits for diabetics and the significant role of family physicians in their management.

The third leading cause of death in the United States, diabetes and its complications account for 300,000 lives per year. Diabetes is now the leading cause of new cases of blindness, causing 12 percent of all cases of blindness in the United States.[2] It is estimated that diabetes affects 2.4 percent of the total population and results in a direct and indirect outlay of approximately $9.7 billion per

year.[3] In a recently completed study in Washington State, 772 insulin-dependent diabetics continually eligible for Medicaid during 1979 had a total cost of care per patient per year of $2,567. Interestingly, office-based care by the patient's physician accounted for only 6.1 percent of this amount (F. Connell, MD, personal communication, June 1982). In the Equitable Insurance study, people with onset of diabetes under the age of 15 years had a mortality rate over 11 times higher than age-matched controls, while those with onset of diabetes at the age of 60 years had 2.3 times the mortality rate of their controls.[4] The extent of the problem, the seriousness of its effects, and the family physician's major role in managing diabetes make current knowledge of the management of diabetes compelling. The focus of this review will be predominantly clinical, with a major emphasis on management of the ambulatory patient.

Classification

A new classification of diabetes, now generally accepted by most workers in the field, was developed by an international team and published in 1979.[5] The new classification was necessary for several reasons. It was apparent, for example, that patients formerly considered to have borderline diabetes often did not progress to overt diabetes. Under the new classification 1 to 5 percent of patients per year with impaired glucose tolerance progress to diabetes; many with impaired glucose tolerance, in fact, revert to normal glucose tolerance. Furthermore, microvascular complications, that is, retinopathy and nephropathy, do not tend to develop in this group, although arteriosclerotic disease does.

As more work is done, it becomes clearer that type I and type II diabetes are different entities. In type I diabetes, evidence for autoimmune abnormalities has emerged. Diabetes has been associated with certain alleles of the human leukocyte antigen system, and some work suggests strong environmental precipitants, particularly viral infections.[6,7] For instance, in genetically disposed individuals, an environmental insult such as a virus might trigger an autoimmune reaction that would have an adverse effect on the patient's beta cells. Thus, genetic factors may predispose to diabetes by making the person more susceptible to whatever environmental event might precipitate the disease. Studies on etiology suggest that insulin-dependent diabetes mellitus (IDDM) is not a discrete entity but is probably a heterogenous disorder.

Non-insulin-dependent diabetes mellitus (NIDDM) may also represent a spectrum of syndromes, although perhaps less so than IDDM. Genetic factors are clearly operating in NIDDM as well. There is definitely a higher incidence of NIDDM in family members of patients who have this disease than there is of IDDM in relatives of patients with IDDM.[8] In addition, studies of twins have demonstrated nearly complete concordance of diabetes in identical twins and suggest that genetic factors may well play a predominant role in the etiology of NIDDM.[9] Obesity seems to be a major factor, too; the main effect of obesity is to cause increased resistance to insulin action on most tissues, including adipose tissue, liver, and muscle. It therefore appears that obesity has a role in the onset of NIDDM.

Table 1, abstracted from the National Diabetes Data Group's paper,[5] summarizes some of the more important aspects of their work. The classification should not be considered unchangeable, however.

Diagnosing diabetes in older patients is a particular problem. There is no unanimity of opinion concerning the interpretation of glucose tolerance in aging people, but a fasting plasma glucose value above 140 mg/100 mL probably constitutes a valid means of diagnosing diabetes through the ninth decade.[10]

Biopsychosocial Aspects of Diabetes

The Institute of Medicine's report on health and behavior[11] noted that the main concerns which have emerged in the biobehavioral areas are coping emotionally with the disorder of diabetes, effectively using health services, adhering to treatment, and dealing with the physiological-behavioral interactions. They saw diabetes as a prototype chronic disorder having clear biological origins but also having major behavioral components that, if ignored, would risk treatment failure. Hauser and Pollets[12] reviewed psychological aspects from four perspectives. First, they found no conclusive evidence that psychic stress is etiologic

Table 1. Diagnostic Criteria, All Venous Plasma Glucose

Classification		Venous Plasma Fasting Value		OGTT* Value ½ h, 1 h, 1½ h	OGTT Value 2 h	OGTT Value 3 h
Diabetes mellitus in nonpregnant adults		Classic symptoms				
	Or	≥ 140 mg/100 mL on more than one occasion				
	Or	≤ 140 mg/100 mL	*and*	≥200 mg/100 mL *and*	>200 mg/100 mL	
Impaired glucose tolerance (IGT) in nonpregnant adults		<140 mg/100 mL	*and*	≥200 mg/100 mL	140-200 mg/100 mL	
Normal glucose levels in nonpregnant adults		<115 mg/100 mL		<200 mg/100 mL	<140 mg/100 mL	
Diabetes mellitus in children		Classic symptoms				
	Or	≥140 mg/100 mL	*and*	≥200 mg/100 mL *and*	≥200 mg/100 mL	
Impaired glucose tolerance (IGT) in children		<140 mg/100 mL	*and*		>140 mg/100 mL	
Normal glucose levels in children		<130 mg/100 mL			<140 mg/100 mL	
Gestational diabetes, with values exceeding any two of the following after 100 g glucose load		105 mg/100 mL		190 mg/100 mL	165 mg/ mL	145 mg/100 mL

From National Diabetes Data Group[5]
*OGTT—Oral glucose tolerance test

in the onset of diabetes. Second, although psychological and related factors need to be considered in understanding fluctuations in control in the course of the disease, the key variables and personality factors that influence the fluctuations remain unclear. Third, most work has focused on adjustment of the patient with diabetes; low self-esteem is often a major problem, as are difficulties with ego development. Fourth, family studies are relatively less common. It is clear that diabetes will influence behavior patterns in every patient to some degree and that behavior will influence manifestations and control of diabetes; however, family-oriented studies are of particular interest to family physicians, for without family approval, almost any treatment plan will fail.[13]

In a group of latency-aged children (aged 6 to 15 years) studied in a diabetic clinic, psychosocial adjustment problems occurred frequently, were associated with poor biochemical control, and required a family-centered approach to management.[14] Better adjustment was associated with higher parental and child self-esteem and optimal family functioning. The adolescent diabetic patient is a particular problem.[15] Tattersall and Lowe[16] have outlined how diabetes interferes with the aims and problems of "normal" adolescence. They stress a combination of expenditure of time and appropriate amounts of sympathy and toughness and continuity of care by the same physician.

Diabetic adolescents may adapt well to intensified control regimens,[17] and initial studies of young adult patients on intensive control including pumps suggest good adaptation[18] as well.

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Importance of Control

Though agreement is not universal, there is increasing consensus that better control does lessen the incidence of complications, specifically microvascular complications.[19] Current evidence favors the concept that complications are secondary to the metabolic disorder per se.[20,21] A 20-year prospective study[4] of 10,538 diabetics who applied for insurance coverage showed that mortality in cases with poor control was 2.5 times that of cases with good control. Currently, a carefully planned national multicenter prospective study (The Diabetes Control and Complications Trial) is being carried out to examine the relationship between control and complications. Given that improved control is desirable, the questions for the practicing physician remains, how much control, at what price, and for which patients?

Virtually all those involved in research and in the treatment of diabetes feel that at the very least most patients should aim for as much control as possible without sustaining undue risk or hypoglycemic reactions, even though normalization might not be reached. Reasonable goals for children would include control of symptoms, maintenance of normal growth and development, maintenance of normal blood lipid levels, and minimization of urinary glucose loss.[22]

Goals for young adult, middle-aged, and older patients are in a state of flux, as are definitions of poor or good control. Even if an effort to achieve euglycemia by fasting, preprandially and postprandially and throughout the day, is warranted, it is difficult and often impossible to achieve with present-day conventional therapy.[23] Recently the ability to attain such goals was explored by studying a consortium of privately practicing family physicians in Washington, Alaska, Montana, and Idaho.[24] Although most physicians had goals of under 150 mg/100 mL for fasting blood sugar, actual levels achieved were much higher, generally closer to 200 mg/100 mL or above. To give an idea of what kind of control is being advocated by some, acceptable fasting glucose levels of 60 mg/100 mL to 130 mg/100 mL were presented at the 28th Postgraduate Course of the American Diabetes Association.[25] It is apparent that these levels, if possible to achieve, would extract a high patient cost in terms of time, family effort, money, psychological effects, and risk of hypoglycemia. The newer strategies of managment, however, do focus on means of achieving better control.

Self-Monitoring of Blood Glucose

Clearly the majority of diabetic patients continues to perform at least some urine testing. Increasing evidence raises questions about the ability of urine testing to yield useful information.[26] Morris et al[27] compared plasma glucose with second-voided urine glucose of adult diabetics in an ambulatory setting. When plasma glucose levels were stratified, correlations were poor, with a high probability of underestimating plasma glucose levels when dealing with any semiquantitative urine reading of under 3+ to 4+.

As a result, home blood glucose monitoring is increasingly recommended for patients with IDDM.[28,29] A variety of methods are available to measure blood glucose rapidly: Dextrostix (Ames) and Chemstrip bG (Bio-Dynamics) are reagent strips in which color is compared visually with a color chart. A variety of battery-powered reflectance meters is also available, the most commonly used ones probably being the Dextrometer and Glucometer, both made by Ames. These are preferred by many patients because they give a digital readout of an exact number, but they are expensive and not necessarily more accurate.

Modified home monitoring is at the very least attempted with nearly all patients on insulin or oral agents, and it is particularly emphasized for insulin-dependent diabetics and for non-insulin-dependent diabetics on insulin.

The advantages of home blood glucose monitoring include assessment of the pattern of glycemia during ordinary daily activities, improvement of monitoring and management during intercurrent illnesses, reduction of hospitalization frequency, and enhancement of patient understanding of the diabetes.[30] The patient becomes much more a partner and more clearly emerges as a person responsible for the care of his or her own disease. The patient feels in control, and uncertainty and guesswork are greatly decreased. There is improved recognition of hypoglycemia. The cost is reasonable, and many, though not all, patients are willing to comply. Automatic finger-sticking devices, such as the Autolet, make the procedure much less uncomfortable and are an essential aid.

Those who have written about home monitoring have found that control has been greatly improved in most of their patients and that normal blood sugar levels can be achieved for prolonged periods.[31] Some very helpful algorithms have been published to help patients adjust their insulin dose when they are doing home monitoring.[32]

Glycosylated Hemoglobin

The measurement of glycosylated hemoglobin is being used more frequently as a way of monitoring metabolic control. This type of monitoring is based on the concept that the level of glycosylated hemoglobin is representative of the mean blood glucose concentration during the preceding several weeks. Glucose and other sugars become more or less continually attached to hemoglobin and its minor fractions during the approximately 120-day life span of the red blood cell. The higher and more sustained the levels of blood glucose, the higher the levels of glycosylated hemoglobin. There is a strong correlation between glycosylated hemoglobin levels and levels of blood sugar over a period of several weeks.[33] Widely used column chromatographic methods assay total HbA_1, which is composed of fractions HbA_{1a}, HbA_{1b}, labile HbA_{1c}, and stable HbA_{1c}. HbA_{1a} and HbA_{1b} are relatively constant and do not fluctuate with changes in blood glucose. By simple mass action labile HbA_{1c} levels vary directly with blood glucose levels at the time of sampling, while stable HbA_{1c} provides the most specific measure of long-term glucose control (James Detter, MD, personal communication, December 1982). The test is subject to many vagaries, and physicians should work with their local laboratory to understand the test as done in their particular location.

Diabetes and Pregnancy

It is generally agreed that diabetes in pregnancy should be closely controlled. Early Scandinavian studies[34] found a decrease in complications, such as toxemia, intrauterine death, and hydramnios, and generally improved fetal survival with better treatment of diabetes during pregnancy. Metabolic factors as such contribute to the complications of pregnancy. Metabolic normalization, along with better overall obstetrical care, has reduced perinatal mortality in insulin-dependent diabetic pregnancies from about 18 percent in the 1950s and 1960s to 6.5 percent during the 1976 to 1979 period.[35]

Good metabolic control in early pregnancy seems to be especially important. Miller et al[36] point out that fetal malformations may occur before eight weeks of gestation, when pregnant diabetic women are not receiving close medical attention. They found that increased levels of hemoglobin A_{1c} were associated with an increased incidence of major congenital abnormalities in the infants, primarily congenital heart defects and malformation of the brain. A separate major prospective national clinical trial is underway to determine whether good metabolic control before conception and in the early weeks of pregnancy might improve the outcome of diabetic pregnancies and decrease the incidence of major congenital abnormalities. The evidence seems strong enough to recommend that insulin-dependent diabetic patients who are planning to become pregnant should be managed especially carefully. Once pregnant, extremely close control, including home monitoring, is indicated.

Because prematurity is associated with an increased risk of hyaline membrane disease, the lecithin-sphingomyelin (L/S) ratio should be used to assess maturity of the fetal lungs. An overall goal is for spontaneous labor at terms and vaginal delivery when possible.[37] Even with careful diabetes management, fetal monitoring, and a comprehensive team approach, however, cesarean section rate may approach 50 percent in some centers.[38] For purposes of both diagnosis and treatment, it should be remembered that because of the fetus, blood sugar in the fasting state is lower in pregnancy. The postprandial levels are higher related to a given fasting level in the pregnant than in the nonpregnant state. In terms of preventing pregnancy, there is some evidence that intrauterine devices are not so effective in diabetic as in nondiabetic women.[39]

Diet

Dietary fiber may play some role in carbohydrate tolerance. A high-carbohydrate diet containing leguminous fiber has been shown to improve all aspects of diabetes control, including glucose values, triglycerides, and the high-density lipopro-

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tein–low-density lipoprotein cholesterol ratio.[40] Fiber may slow the absorption of carbohydrate, allowing the islets more time to deliver insulin and peripheral tissues more time to transport the glucose.

It is generally agreed that a lowered fat content for diabetic patients is indicated, since a high-fat diet may contribute to an increased incidence of arteriolosclerosis. In general, a decreased intake of fats, especially cholesterol and saturated fats, to 30 to 35 percent of calories is appropriate. Carbohydrate intake can fall within 45 to 60 percent of calories, with much of this as unrefined carbohydrate.[41,42] If the patient is obese and is not dependent on insulin, weight loss is the primary consideration. Weight loss is generally accompanied by marked improvement in fasting and postprandial hyperglycemia. For children, a diet the child will follow that will grant optimal nutritional status is the main consideration. There is a trend toward less rigidity in the diet because adherence may be poor. Physicians are more likely to let patients with IDDM choose an appropriate number of calories for themselves. Weight will often be well controlled if the patients avoid binges and fastings. For patients with NIDDM, caloric restriction is indicated, but there can be great flexibility in distribution of carbohydrates. Sodium intake should be moderated in all patients. The timing of meals should be reasonably consistent and synchronized appropriately with insulin action.[41]

Oral Hypoglycemic Agents

The University Group Diabetes Program (UGDP)[43] looked at the effect of oral agents and insulin on vascular complications, and their program report suggested that the combination of diet and tolbutamide is no more effective than diet alone in prolonging life. They also suggested tolbutamide and diet may be less effective than diet alone or diet and insulin, at least with respect to cardiovascular mortality.

Subsequent studies have raised strong objections to this evidence on a variety of grounds.[44,45] Many clinicians have continued to use the oral agents in selected situations. Whitehouse and Kahkonen's recommendations seem appropriate[46]: The recommendation for initial treatment of NIDDM is the use of diet alone, NIDDM patients should be considered candidates for oral agents only if dietary therapy is unsuccessful, oral agents should probably be used with caution in people with heart, liver, or kidney disease, and oral agents are probably best reserved for the diabetic patient aged over 50 years and otherwise healthy. If adequate control cannot be achieved with oral agents, then insulin should be used. Obviously, however, individualization is necessary. Some physicians prefer to treat obese patients who do not lose weight with oral agents rather than insulin because of the possibility of weight gain with overinsulinization. Most physicians have patients who would not use anything else, sometimes in spite of having had some complications while being treated with oral agents. A second generation of oral agents in use in Europe for several years includes glibenclamide (glyburide), glipizide, and glibornuride, which are more potent than the first-generation agents on a milligram for milligram basis. It has not been shown, however, that the second-generation agents can produce better diabetes control.

Insulins

Insulins have been considerably purified over the past few years. From the early 1970s until about 1980, the commonly used insulins made by Squibb and Lilly had a proinsulin-type substance content of less than 10,000 parts per million (ppm). Currently if one prescribes insulin without specifying a purified product, the patient would get an insulin with 20 ppm proinsulin-like substance that is 70 percent pork and 30 percent beef (Lilly Iletin I) or an insulin with about 25 ppm of proinsulin-like substance that is all beef (Squibb). These products cost about $7/10 cc. Lilly's Illetin II is 100 percent pork and has less than 10 ppm contaminants, and Squibb purified pork insulin is similar. Novo and Nordisk products are also within this range of purity. Some clinicians feel it is theoretically desirable to start new diabetics on the all-pork products, which are closer to human insulin and probably cost about $.10 to $.12 more per dose. Otherwise, the highly purified forms are not necessary unless there is a complication of therapy. Human insulin will be available soon. It is not clear whether there will be significant advantages. It certainly represents one of the first clinical applications of genetic engineering techniques and

it should provide a reliable source of supply.

Intensified Management Regimens

As already mentioned, close control and self-monitoring of blood glucose (SMBG) are highly desirable. It is clear that in IDDM multiple daily injections tend to improve diabetic control.[47] A great deal of current research centers around the difference between multiple subcutaneous injections and continuous subcutaneous insulin infusion (CSII) with pumps. The management of virtually all patients with IDDM should include consideration of one of these intensive treatment programs[48] if there seems to be appropriate patient motivation.

The achievement of meticulous control is not without risks. Short-term risks include possible worsening of retinopathy of patients previously in poor control and hypoglycemic encephalopathy.[49] In either regimen optimal glucose control cannot be maintained over long periods without constant SMBG, as insulin requirements vary often in the same person.[50] Skyler[51] summarizes studies comparing CSII and intensified conventional therapy, noting that if appropriately used with SMBG, both offer the possibility of achieving excellent glycemic control, especially when opposed to one to two daily injections with only monitoring of urines. He also calls attention to the care that must be taken to avoid nocturnal hypoglycemia. There is a subtle physiologic glucose nadir that occurs around 3 to 4 AM, even in nondiabetics, and there is the "dawn phenomenon," which may result in disproportionately high levels of glycemia before breakfast. He recommends that the treatment program not be altered on the basis of prebreakfast values without first being sure the patient does not have 3 to 4 AM hypoglycemia. Unger[49] suggests that by permitting mild fasting hyperglycemia of up to 130 mg/100 mL and viewing a 7 AM level below 80 mg/100 mL as a possible sign of predawn hypoglycemia, one should be able to reduce the nocturnal risk.

Continuous subcutaneous insulin infusion is in increasingly common use. A number of beneficial effects result from continuous infusion of insulin that do not seem to occur with periodic insulin injections. The advantage seems to come from the ongoing delivery of insulin between meals and at night in amounts that simulate basal rates of insulin secretion. A reduction in postprandial hyperglycemia may result partly from the maintenance of basal insulinization,[52] which allows more flexibility in being able to delay meals. There is also less risk of hypoglycemia during exercise because there is not a large depot of insulin that can be mobilized. Other metabolic effects occur as well. Improved glucose regulation has resulted in some reduction in plasma total cholesterol, triglyceride, and very low density and low-density lipoprotein-cholesterol levels with a rise in high-density lipoprotein-cholesterol levels.[53] These results have implications for long-term development of arteriosclerosis complications.

Pumps have been used in younger patients. In one study of a series of patients aged 13 to 29 years, increased somatomedin levels were seen, suggesting that improved insulin delivery or metabolic control might be useful in enhancing growth in diabetic children.[54] A number of centers are using the pumps, which essentially have passed the experimental stage. A large multispecialty clinic in Seattle has published results with 100 patients on pumps,[55] a clinical faculty member of the Department of Family Medicine at the University of Washington in full-time private practice has over 20 patients on pumps in his practice, and an internist in a nearby community has several times that number. It is reasonable to expect interested family physicians to become much more closely involved with intensive management of patients with IDDM.

As of November 1982, 35 deaths had been reported in pump users in the United States.[56] One death was attributed to device malfunction, one to endocarditis secondary to an abscess at the catheter insertion. Seven patients were found dead, and three died suddenly. Six deaths were related to ketoacidosis, and 14 to myocardial infarction, cerebrovascular disease, and renal failure. The observed number of deaths was not greater than expected from age-specific death rates for type I diabetes.

Diabetic Ketoacidosis

Low-dose insulin regimens are generally used for the treatment of diabetic ketoacidosis in patients at the University of Washington. Common arguments in favor of low-dose insulin therapy include a more gradual rate of fall in glucose levels, a lower incidence of late hypoglycemia, less danger

of hypokalemia, and a lower incidence of cerebral edema. Arguments against the low-dose regimen include the narrow margin of safety, the possibility of insulin resistance, and presence of insulin antibodies.[57] Kreisberg[58] notes that most patients with diabetic ketoacidosis will respond to low doses of hourly intravenous or intramuscular regular insulin and that low doses of insulin are as effective as high doses and have fewer associated complications of hypoglycemia and hypokalemia. Basically, the low-dose regimen consists of 5 to 10 units of regular insulin per hour or 0.01 U/kg/hr given intravenously. Many will give a loading dose of 10 units intravenously first. If low-dose insulin is not effective, the insulin dose should be increased as indicated to attain effective treatment. It does seem that even though low-dose insulin therapy is widely used, it has not necessarily lowered mortality.[59]

Potentially many other metabolic abnormalities, in addition to the hyperglycemia and the accelerated ketogenesis with metabolic acidosis, are present, including total body potassium deficiency, phosphate depletion, increased serum lactate, and hypertriglyceridemia.[60] The average fluid deficit is 4 to 5 L. Therapy can be started with 0.5 N saline, unless the patient has postural hypotension, in which case normal saline would be used. Glucose infusion can be started when the plasma glucose is about 250 mg/100 mL, as persistent ketoacidosis may require ongoing insulin infusion even when blood glucose is normalized. It is important to remember that ketoacidosis usually has a precipitating cause, particularly when it occurs in NIDDM. Of 92 cases reported from the Mayo Clinic over a 52-year period, only 42 percent occurred in patients with IDDM diabetes. Of those 92 patients, seven deaths occurred in the first 24 hours, only one of which was due to ketoacidosis alone, and an additional six patients died within 48 hours. The major cause of death was myocardial infarction.[61]

The syndrome of hyperosmolar nonketotic coma is manifested by severe hyperglycemia, no ketoacidosis, dehydration, and a wide variety of neurologic findings including a depressed sensorium. The syndrome is associated with a variety of drugs and medical problems, especially in elderly cardiac patients. They have extreme volume depletions, but with adequate treatment, including fluids, insulin, and sometimes potassium, most will recover.[62] A major event leading to its onset is decreased fluid intake, for example, in a patient who is restrained or mentally impaired.

Other Complications

Hypertension is a problem of particular concern, and the prevalence of hypertension may be increased in diabetics. There are a variety of forms of hypertension in diabetics, and management should be adjusted to the type of hypertension. A definitive study of the treatment of hypertension in diabetic patients similar to the Veterans Administration study has not been done, but there is evidence that many complications progress faster with elevated blood pressure, and aggressive treatment is indicated.[63] Williamson and Kilo note that age-related intimal sclerosis of the arteries and thickening of the basement membrane of capillaries in nondiabetics are qualitatively indistinguishable from the same lesion in diabetics, and vascular disease in diabetics and nondiabetics alike is accelerated by even a slight elevation of blood pressure.[64] The Framingham Study suggests that a diabetic patient's hypertension is associated with an increased risk of vascular disease. The incidence in diabetics is increased beyond that associated with any specific risk factor.[65] Since there is good evidence that control of even mild hypertension is beneficial in nondiabetics, it seems likely that hypertensive diabetics would benefit at least as much from antihypertension therapy.

Diabetic retinopathy is another area in which advances have been made. The natural history of retinopathy in patients with IDDM was outlined by Palmberg et al.[66] Retinopathy was not present at diagnosis. After a time lag the prevalence rose in a sigmoidal fashion reaching 50 percent at just over seven years and approaching 90 percent at 17 to 50 years. Before retinopathy can be visualized with the ophthalmoscope, changes can be seen with fluorescein angiography, which may show venous dilation and a more distinctly outlined capillary network in the macular area accompanied by localized extravascular leakage.[67] One of the earliest changes is the breakdown of the blood-retinal barrier, which progresses more slowly in patients under good metabolic control.[68] Long-term control has been noted to arrest some of the features of microangiopathy,[69] although others

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have noted established changes do not improve and may even worsen in patients with very poor previous control.[51] Visual loss can develop as a result either of intraretinal hemorrhage or exudation in the macular region. Careful examination of the fundus is therefore indicated at regular intervals. If neovascularization is suspected, fluorescein angiography or stereophotography is indicated. According to a collaborative eye study, laser therapy is effective in reducing the risk of development of visual loss and in inhibiting the progression of retinopathy, though there are some risks such as loss of visual acuity and peripheral visual fields.[70] Vitrectomy may be effective in certain patients when vitreous hemorrhage has occurred.[71] Practically speaking, many ophthalmologists note that the main problem is the failure of early detection of eye pathology.

Patients with end-stage renal disease can be considered candidates for transplantation.[72] Diabetic neuropathy is difficult to treat aside from improving control. In patients with impotence due to diabetic neuropathy, the implantation of a silicone penile prosthesis may be beneficial.[73] Peripheral vascular disease is also difficult to treat. Cigarette smoking should certainly be stopped in the patient with this problem. Bypass grafting is being used more commonly.

Recent Developments

Modifications of pancreatic transplant techniques are being developed, and in a recent report of six patients who were already immunosuppressed because of kidney transplantations, some promising results were reported.[74] Various investigators are working on artificial pancreases, which are essentially closed-looped systems that could continually monitor glucose and deliver appropriate doses of insulin. A variety of basic immunologic investigations are being carried out with the hope that vaccination against the disease may become possible and feasible.[75]

In summary, diabetes is a highly exciting, fast moving field. Increased use of home blood glucose monitoring, as well as an increased role for new insulin regimens or insulin infusion systems, and advances in the etiology of diabetes can be anticipated. In the management of the diabetic patient and his or her family, the family physician has a major role to play in the revolution in diabetes care.

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