# DIABETES UPDATE

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## Introduction And Overview

There are over eleven million diabetics in the United States. Approximaely 46%, or five million, of these are undiagnosed. Almost 50% of these, or 2.1 million, are over the age of 65 years. The prevalence of diabetes is 2% to 3% of the American population. Thirteen percent of the patients on a medical service in a hospital have diabetes, 7% of the patients on a surgical service also have diabetes. Diabetes is the third leading cause of renal failure, third leading cause of death, and the leading cause of blindness.

The podiatric physician often plays an important role in the diagnosis and management of the diabetic patient. Because these patients have an overwhelming number of foot problems, they may seek the care of a podiatrist early in the course of their disease.

Any one of the classic symptoms of diabetes, recent weight loss, polydypsia, polyuria, or polyphasia, may be encountered on routine history and physical examination. The criteria for diagnosing and labeling diabetes have recently changed. The podiatrist needs to be familiar with the two major types of diabetes, their diagnosis, management, relation to operative evaluation and stress, complications, and the effect of diabetes on wound healing.

## Definition And Classification

Diabetes is defined as an elevated plasma glucose due to insufficient insulin effect. There are two major clinical groups of people with diabetes: those who are near ideal body weight, and those who are overweight. Lean individuals are usually insulin-dependent due to a decrease in the pancreatic beta cell mass. This results in insufficient insulin production. Overweight individuals have an increase in the number of beta cells, and in total insulin in the pancreas early in the course of diabetes. However, this decreases with time. Obesity increases the body's demand for insulin production nearly four times the amount required for a lean person. This results in aging or "burnout" of the beta cells (1, 2).

The two major types of diabetes are classified as:

1. Type I diabetes (insulin dependent diabetes mellitus—IDDM). The literature often refers to this as ketosis-prone diabetes, or brittle diabetes.
2. Type II diabetes (non insulin dependent diabetes mellitus NIDDM). The differences are reviewed from the basis of etiology and pathology (3).

## Type I Diabetes

The incidence of this disease process is 10/100,000 children, increasing to 16/100,000 in adolescence. The prevalence is 1/500 to 1/1,000 young people. Etiology: there are probably a combination of three factors(4).

### *I. Genetics*

There is a strong HLA (human leukocyte antigen) association with IDDM. In one study, 98% of IDDM children were HLA DR 3 and/or DR4 positive (5). HLA DR2 is protective. The relative risks are:

DR 3 = 5 times risk
DR 4 = 7 times risk
DR3/DR4 = 14 times risk

### *Environmental trigger*

Rubella in utero unquestionally causes diabetes in 20%-30% of offspring. All children were DR3, DR4, or DR 7 positive (6). Other causative viruses are still speculative. The most likely explanation is that multiple viruses (mumps, rubella, and coxsackie B4) act as triggers to begin a self-perpetuating autoimmunity process resulting in cellular destruction.

### *Autoimmunity*

Anti-pancreatic beta cell antibodies (autoantibodies to the islet cells), or antibodies to insulin are found in 90% of new onset Type I individuals. Progressive loss of beta cell function has been demonstrated with a latency up to eight years before the onset of clinical diabetes (7).

### *II. Pathophysiology*

Insulin is our primary anabolic hormone involved in a number of metabolic processes. These include glucose homeostasis and lipoprotein balance. With food intake, the levels of insulin increase and help build the body. In the absence of food, or during times of stress, insulin plays a

critical anti-catabolic role. It limits the rate at which body constituents break down.

If the insulin blood level falls below the critical basal level necessary to serve this anticatabolic role, liver gluconeogenesis and ketogenesis become unregulated. This results in diabetic ketoacidosis (DKA). The normal daily insulin production by an ideal body weight (IBW) adult, is 33 units. The individual who is brittle and prone to ketosis will produce only 10% of this need, an average of 3 units per 24 hours (1). It is estimated that one-half to two-thirds of the daily insulin need is basal. This basal need has a diurnal rhythm with an increased need of insulin occurring from 5:00 a.m. to 10:00 a.m. (8). After eating, a further increase of insulin is needed to stimulate the metabolism of glucose for energy, and for the storage of nutrients as glycogen, fat, and muscle.

## Type II Diabetes

The prevalence increases lineally with the obesity of the population. People who weigh ten pounds less than ideal body weight (IBW), have a prevalence of diabetes of around 1%. In America where the average weight is 20 pounds above IBW, the prevalence of diabetes is near 3%. In cultures where people average 40 to 60 pounds above IBW the prevalence of diabetes can reach 40% (2, 9).

### *I. Etiology*

There is a stronger genetic association with Type II than with Type I diabetes. Over 50% of the patients have close family members with diabetes (10). The gene location(s) and mechanism are still not known. Increased work by the beta cells, because of the extra fat tissue, is a key etiological factor. The pancreas of the obese person must produce nearly four times the amount of insulin, compared with that of the lean person (114 units per day vs. 31 units per day) (1). It is likely that beta cells have a limited production capacity and limited reproductive capacity (11). Currently, the peak onset years are age 40 to age 60. Longer life increase the liklihood that an individual will contract Type II diabetes before death. However, prevention of obesity and extra work by the pancreas by diet and exercise should help decrease the prevalence of Type II diabetes.

### *II. Pathophysiology*

Overweight patients may require extra insulin for multiple reasons. The fat mass itself appears to require more insulin to keep it from breaking down (lipolysis). Fat tissue also appears to act like a "hog" and get "its share first". Type II patients usually can produce enough basal insulin to prevent excessive lipolysis and liver ketogenesis, but this is insufficient insulin in an inactive, overweight adult to block liver glucogenesis or adequately stimulate muscle glucose uptake. Increased levels of insulin result in more binding to the insulin receptor, internalization of the receptor plus insulin, a decrease in the number of insulin receptors (down regulation), and a decrease in insulin sensitivity (12). For most patients weight loss results in increased insulin sensitivity. If a weight loss program is successful through a prudent diet, patients need less insulin and can come closer to meeting the needs of the body with endogenous insulin. However, with time most Type II patients will be unable to keep their blood glucose level less than 150 mg/dl with diet only (10).

## Diagnosis, Screening And Monitoring

The criteria for diagnosing diabetes mellitus, as defined by the American Diabetes Association, has recently changed. The fasting blood sugar is again the key test; a fasting blood sugar greater than 140 mg/dl on two successive trials makes the diagnosis. One may also make a diagnosis using a two hour plasma glucose greater than 200 mg/dl, and one other value from a glucose tolerance greater than 200 mg/dl is required for diagnosis if the fasting glucose is less than 140mg/dl. Obviously, one may also make a diagnosis during acute, uncompensated symptoms of diabetes (3).

The diagnosis of abnormal glucose tolerance, or diabetes suspect, may be made using a two hour post-prandial glucose of 140-200 mg/dl and the half-hour, one-hour, or one-and-a-half hour glucose reading greater than 200 mg/dl. There are many patients now classified as "abnormal GTT" who were classified diabetic in the past and placed on medication (3). Many of these patients will be able to stop all medication without difficulty. The question remains whether those patients with a fasting glucose lower than 140 mg/dl need treatment other than diet.

Screening for diabetes and peripheral neuropathy is important for the podiatric physician. The early warning symptoms of diabetes: increased thrist, urination, and appetitite, are frequently not found in overweight individuals with Type II diabetes. Office screening for diabetes is now easy with the glucose oxidase strips. The Autolet, with a small needle called a Monolet, makes for relatively painless bloodletting. Within two minutes one can have a blood glucose reading in the office. Fasting blood sugar should be under 140 and no post prandial glucose should be over 200.

The main physical examination feature to help the physician suspect undiagnosed diabetes would be peripheral neuropathy. It was described in the late 1800s that the 128 tuning fork, sharply struck, was the best way to detect the neuroapthy of aging or diabetes (13). Every tuning fork is different and needs to be standardized for healthy 20 year olds and healthy 70 year olds. The tuning fork, after a maximum strike, is placed upon the patient. If a patient under 50 years of age feels the vibration of the tuning fork less than 20 seconds, or a patient over 50 years of age feels it less than 15 seconds, that makes a presumptive diagnosis of a peripheral neuropathy, and makes diabetes screening mandatory. The vibrothisiometer is an inexpensive instrument for quantifying the beginning and end of vibratory sensation. The vibrothisiometer is recommended if follow-up

examination for change in neuropathy is needed. Thermography may be a better measure for correlating pain and measurable abnormalities (14).

Monitoring of diabetes is performed short term by the patient and long term by the physician. Blood glucose levels are usually monitored by diabetic patients one to four times daily. This is done using glucose oxidase strips read visually (Chemstrip bG or Visidex), or similar strips which are read quite accurately by a small portable machine such as an Accuchek or Glucometer. The physician can assay long term glucose control over three to four months by use of the irreversible binding of glucose to lysine molecules on the hemoglobin molecule, the glycosylation reaction. For example, a normal range for the hemoglobin A1C (Hb/A1C) is 3.4-6.1. If the average blood glucose for two months is 100 mg/dl, the results on this assay would be approximately 6.0%. If the glucose average was 140 mg/dl for two months, the assay would return with a value of approximately 7.0%. For a glucose average of 220, the assay would be 9.0%, etc. Since red cells live approximately 120 days, measurement every three to four months is a reasonable frequency (15). The goal for most patients is 7.5% or less; 150 mg/dl or less as an average. This can usually be attained without hypoglycemia. The Hb A1C is low in hemoglobinopathies and in conditions where there is a shortened red cell half-life (16).

## Assessing Pre-Operative Diabetes Control

In the known diabetic a few simple questions will help ascertain the patient's knowledge of diabetes, level of skills, and control. The patient should be able to tell you the current medication and the finger-stick glucose levels done at various times during the day for the last two weeks. The physician's appointment secretary could inform all patients with diabetes that the doctor would like to see this log of medications and glucose levels before scheduling surgery. In the future, it is likely that a glycohemoglobin, giving the average glucose readings for the last three months, may become a required test before elective surgery on a person with diabetes. It is recommended that most patients obtain this test two to four times yearly, with an average glucose at least under 200 mg/dl before elective surgery. (Hb A1C less than 9.0).

## Beta Cell Reserve And Insulin Need

Difficulty in clinical management of the individual with diabetes can be anticipated if two questions are asked:

> How much beta cell reserve does this patient have?
>
> How much is the usual daily insulin need, and is that going to change greatly in the hospital?

Figure 1 reviews what was discussed earlier as to the pathyphysiology of Type I and Type II diabetes. Indicators of a low beta reserve are: the duration of diabetes, a history of wide swings of glucose, and thinness. A long-standing Type II diabetic on oral agent treatment needs to anticipate using insulin, at least temporarily, with the stress of surgery. A person with a prior history of diabetic ketoacidosis is much more likely to have problems with a "Hold insulin the day of surgery" order than an overweight person in good control on a low dosage of insulin.

Figure 2 summarizes the relative impact of obesity and various stresses on insulin need. The stress of the hospital and change in diet is likely to result in a 30% to 100% change in insulin requirements. Lack of exercise and a better diet may offset each other, resulting in no change in insulin need in the uncomplicated patient with elective surgery. Nevertheless, infection, steroids, and hyperalimentation might result in a 300% increase in insulin need.

## Chronic Complication Status

### *Microvascular Disease*

The duration of diabetes and average glucose readings during that time correlates with the development of *microvascular* complications (17). An easy way to think of diabetes management is to assume that from 1922 to 1982 most individuals with diabetes were maintaining an average blood sugar of 250-350 mg/dl. The use of urine testing, one insulin shot daily, or oral hypoglycemic agents, and a visit to the doctor once every two to three months resulted in fairly uniformly poor control of glucose. Type II patients had major complications about 15 years after diagnosis.

Type I patients had major complications about 20 years after diagnosis. A patient who has had laser therapy to the eyes, has a serum creatinine of 1.5 with 1 + proteinuria, and vibratory sensation less than ten seconds with a well-struck 128 oscillation tuning fork will have a severe healing problem. The podiatric physician already knows this patient will be recognized by the characteristic loss of hair and shininess to the skin of the foot with hammer toe deformity, and interosseous atrophy. The sample patient described would also be likely to have some paresthesias with numbness and tingling of the feet. The patient might have a tendency toward gastroparesis and nausea. (17).

### *Macrovascular Disease*

Macrovascular disease is also accelerated in diabetes. Careful palpation of pulses and, if diminished, a Doppler examination should be in the preoperative assessment of a person with known diabetes (18).

The presence of peripheral neuropathy or retinopathy also raises the strong possibility of *autonomic* neuropathy (19, 20). The patient with long-standing diabetes and foot problems frequently has a rather non-specific fatigue that is multi-factorial in etiology. Coronary artery disease with painless angina or silent myocardial infarction must always be the first consideration, with careful internal medicine or cardiac review.

The supine and standing blood pressures immediately,

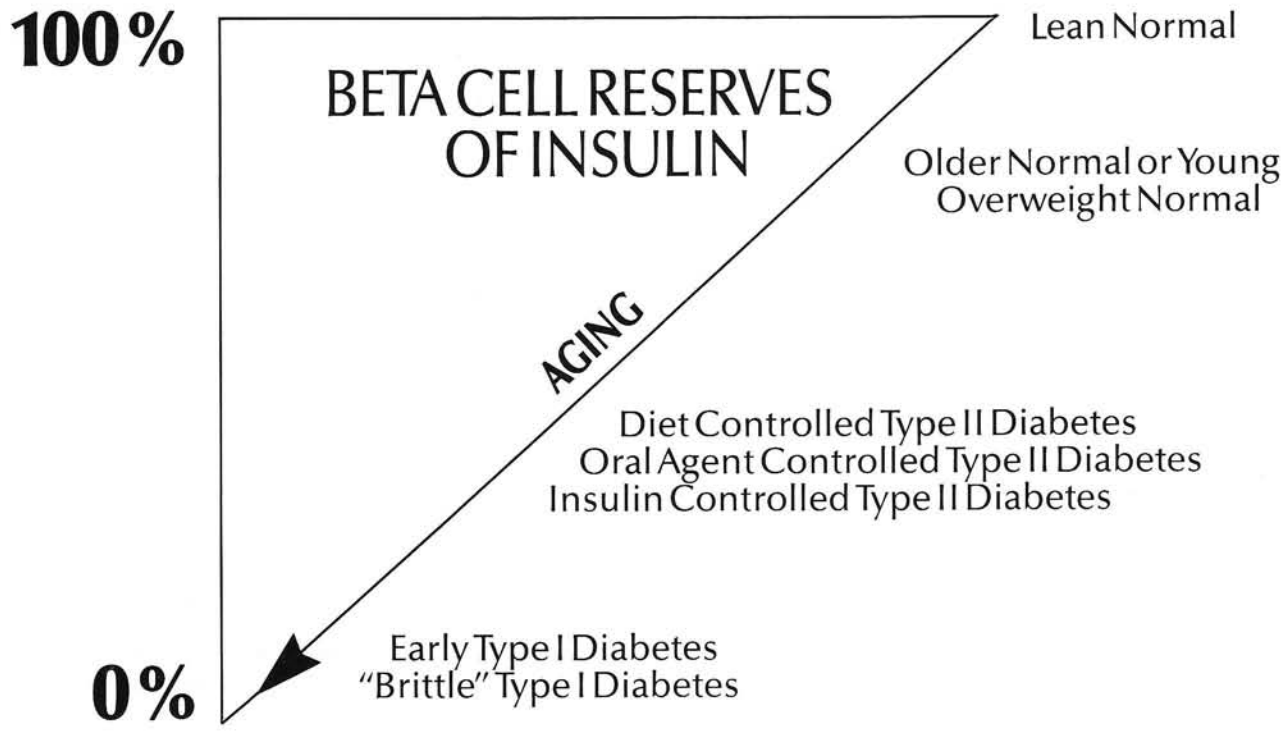
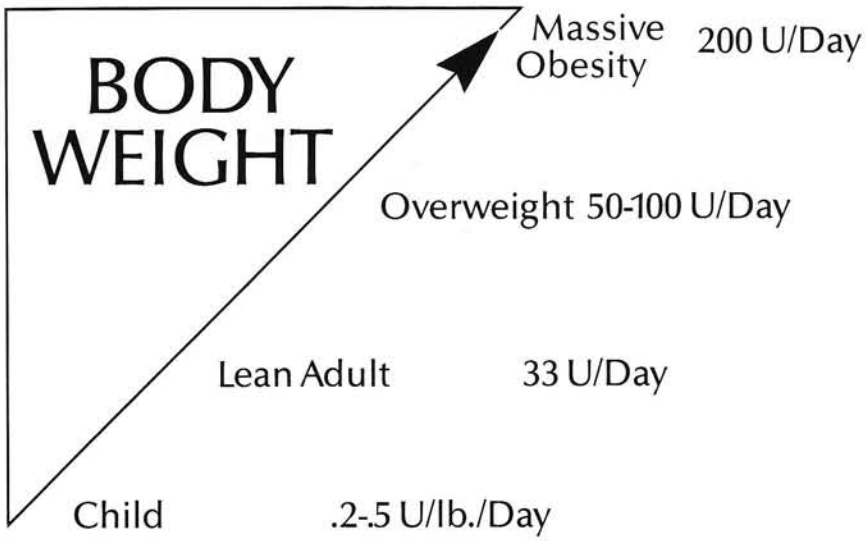



**Fig. 1.** Beta cell: Reserves of Insulin for stress. Beta cells probably have limited reproductive and insulin production capabilities which steadily decrease with aging. Obese person uses up reserves to handle extra weight in 20 to 40 year age period. Most evidence shows that as severity of diabetes increases, insulin production decreases. There results a continum of loss of beta cell reserves with most brittle diabetic patients having least insulin production capacity left.

# BODY NEED FOR INSULIN




**RESISTANCE FACTORS**

| | |
|---|---|
| Major Surgery | 3.0 |
| Pregnancy | 2.5 |
| Large Broken Bone | 2.0 |
| Diet ↑ | 1.5 — 3.0 |
| Infection | 1.5 |
| Life Stress | 1.3 |
| Winter | 1.1 |
| Exercise | .9 |
| Diet ↓ | .3 — .8 |

**Fig. 2.** Body need for insulin. As weight increases, insulin need increases from few units daily, for child, to over 200 units daily for massively obese person. Variety of other factors, labeled "resistance factors" change need for insulin. If this factor is multiplied by number of units of insulin per day individual needed before, the result estimate is the number of units of insulin per day needed under current hospital "stress". Large change in insulin need effected by diet occurs primarily in Type II individuals. Smaller change in insulin effected by diet in Type I patients.

thirty seconds, and a full minute after standing, are necessary to detect postural hypotension (21). This will be even more important postoperatively as people with diabetic autonomic neuropathy frequently have severe postural hypotension after diuresis and bed rest. The delay of 30 to 60 seconds before the blood pressure sometimes falls is particularly bothersome. The patient may stand beside the bed, feel good, and take five steps across the room before feeling dizziness and falling. Careful palpation of the heart rate during slow, deep breathing, usually elicits a slowing of the heart rate. This lack of beat-to-beat variation in diabetic cardiac autonomic neuropathy is well-described with EKG programs to calculate the R-to-R variation (22).

The presence of significant autonomic neuropathy places the patient in a higher risk category with 50% of patients dead within five years (23). The podiatric physician takes this longevity estimate into consideration in the magnitude of surgery recommended. The combination of peripheral neuropathy, edema of the lower extremity, and trauma or irritation from shoes or injury makes diabetic patients particularly prone to a superficial blister-bullous diabetacorum. Fractures, bandages, whirlpools, and new shoes are all frequently rewarded with a sudden, painless, blister which will continue to enlarge unless drained.

The fluid is sterile. A small puncture should be made to drain the fluid so that it will not continue to dissect into healthy skin. The blister skin can be left as a protective coating. Bed rest, clearing of the edema, and leaving the blister open to air usually result in quick healing.

## The Effect Of Diabetes On Wound Healing

Insulin independently may be important in wound healing. Insulin and the insulin receptor are proteins related in a family to epidermoid growth factor, nerve growth factor, somatomedin II, and angiogenesin. Insulin cross-reacts with the receptors for those hormones, and those hormones cross-react with the insulin receptor. It is probable, in the future, that insulin like proteins will be used in wounds to stimulate wound healing (24, 25). The roles of insulin, glucose, and potassium have been studied extensively post myocardial infarction. The latest reviews continue to show probable small benefit to limiting infarct size and assisting in healing (26). How hard to push insulin in a patient with a lesion which is difficult to heal is still being debated. However, no one would debate shifting from an oral agent to insulin in a patient who persistently shows a glucose over 140 mg/dl with a slow-healing wound. The insulin might directly promote healing and, by definition of diabetes, a glucose above 140 mg/dl fasting is abnormal.

Diet control of diabetes should be carefully scrutinized in any postoperative patient with a diminished muscle mass. An elevated blood sugar is frequently at the expense of muscle. Bed rest results in loss of muscle mass. Hyperalimentation with insulin may benefit wound healing in malnourished patients. Careful observance that the patient receives sufficient calories is essential. Human insulin carries very little allergic risk. When in doubt, in the healing phase, increase calories and use low-dose insulin as a continuous IV infusion, or NPH before breakfast and supper.

Hyperglycemia can block the defense system of the body (27). Somewhere above 250 to 300 mg/dl, leukocyte function deteriorates and the risk of infection is clearly enhanced. In elective surgery the glucose should be less than 200 mg/dl. If it is greater than 300 mg/dl, strong consideration should be given to delay or cancellation of any surgery.

The more chronic complications of diabetes are present, the slower the diabetic patient will heal. Severe infections may take ten days instead of three to start to clear. Good granulation tissue may not be seen for two to three weeks. Exercise increases oxygen demand which is usually decreased due to A-V shunting (28). The neuropathic foot is also easily traumatized without awareness (28). Since decreased oxygenation is a common factor of the micro and macrovascular disease a great deal of patience, bedrest, and tender loving care is needed in the conservative management of the lower extremity of the long-standing diabetic.

## Summary

For 60 years after the discovery of insulin, diabetes management frequently resulted in average glucose readings around 300 mg/dl. This resulted fairly relentlessly in chronic complications 10 to 20 years after diagnosis. In the early 1980s it became clear that we were in a new era. Two relatively simple technological breakthroughs occurred: relatively painless blood-letting, and the glycohemoglobin assay. These permitted improvements in physiological understanding about diabetes to actually reach the patient in the form of improved diabetes control. The patient could take control by adjusting of diet, exercise, and medication in response to home blood glucose testing. Then, both the patient and the physician's teaching could be evaluated by looking at the glycohemoglobin or average glucose record every three months.

The podiatric physician will be caring for more individuals with diabetes who are better educated for preventive health care, and who will live longer with their aging and more slowly progressive chronic diabetic complications. There is also an opportunity to quickly screen for hyperglycemia and peripheral neuropathy in the aging nondiabetic population.

Routinely test and evalute the diabetic patient for glucose control, blood pressure, diet, and emotional stability, and update the neurological and vascular pathology to fully understand the scope of the disease. This will insure proper assessment and more effective consultation with other physicians actively involved in the co-management of the patient with diabetes.

## References

1. Genuth SM: Plasma insulin and glucose profiles in normal, obese, and diabetic persons. *Ann Intern Med*

79:812-822, 1973.

2. West KM: *Epidemiology of Diabetes and Its Vascular Lesions.* New York, Elsevier North-Holland, 1978.
3. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Appendix II. *Diabetes* 28:64-92, 1979.
4. Cahill GF Jr, McDevitt HO: Insulin-dependent diabetes mellitus: The initial lesson. *New Engl J Med* 304:1454-1465, 1981.
5. Wolf E, Spencer KM, Cudworth AG: The genetic susceptibility of type I (insulin dependent) diabetes: Analysis of the HLA-DR association. *Diabetologia* 24:224-230, 1983.
6. Rubinstein P, Fedun WB, Witt ME, Cooper LZ, Ginsberg-Fellner F: The HLA system in congenital rubella patients with and without diabetes. *Diabetes* 31:1088-1091, 1982.
7. Srikanta S, Ganda OP, Eisenbarth GS, Soeldner JS: Islet-cell antibodies and beta-cell function in monozygotic triplets and twins initially discordant for type I diabetes mellitus. *New Engl J Med* 308:322-325, 1983.
8. Schmidt MI, Hadji-Georgopoulos A, Rendell M, Margolis S, Kowarski A: The dawn phenomenon, an early morning glucose rise: Implications for diabetic intraday blood glucose variation. *Diabetes Care* 4:579-584, 1981.
9. Rushforth ND, Bennet PH, Steinberg AG, Burch TA, Miller M: Diabetes in the Pima Indians—evidence of bimodality in glucose tolerance distributions. *Diabetes* 20:756-763, 1971.
10. Zimmet P: Type 2 (non-insulin-dependent) diabetes—An epidemiological overview. *Diabetologia* 22:399-411, 1982.
11. Logothetopoulos J: Islet cell regeneration and neogenesis. In Freinkel N, Steiner DF (eds): *Handbook of Physiology, Endocrinology I.* Baltimore, Waverly Press Inc, 1972, pp 67-76.
12. Walford S, Gale EAM, Allison SP, Tattersal RB: Self-monitoring of blood glucose. *Improvement of diabetic control. Lancet*, Vol. ---: 732-735, 1979.
13. Fox JC Jr, Klemperer WW: Vibratory sensibility: A study of its thresholds in nervous disorders. *Archives Neurology Psychiatry* 48:622, 1942.
14. Guy RJC, Clark CA, Malcolm PN, Watkins PJ: Evaluation of thermal and vibration sensation in diabetic neuropathy. *Diabetologia* 28:131-137, 1985.
15. Jackson RL, Hess R, England JD: Hemoglobin A1C values in children with overt diabetes maintained in varying degrees of control. *Diabetes Care* 2:391-395, 1979.
16. Kennedy L, Baynes JW: Non-enzymatic glucosylation and the chronic complications of diabetes: an overview. *Diabetologia* 26:93-98, 1984.
17. Pirart J: Diabetes mellitus and its degenerative complications: A prospective study of 4,400 patients observed between 1947 and 1973. *Diabetes Care* 1:168-263, 1978.
18. Kannel WB, McGhee DL: Diabetes and cardiovascular risk factors: the Framingham study. *Circulation* 59:8-13, 1979.
19. Sundkvist G: Autonomic nervous function in asymptomatic diabetic patients with signs of peripheral neuropathy. *Diabetes Care* 4:529-534, 1981.
20. Smith SE, Smith SA, Brown PM: Cardiac autonomic dysfunction in patients with diabetic retinopathy. *Diabetologia* 21:525-528, 1981.
21. Brown MJ, Asbury AK: Diabetic neuropathy. *Ann Neurol* 15:2-12, 1984.
22. Shapiro LM: Echocardiographic features of impaired ventricular function in diabetes mellitus. *Br Heart J* 47:439, 1982.
23. Ewing DJ, Campbell IW, Clarke MB, Clarke BV, Edinburgh MB: Assessment of cardiovascular effects in diabetic autonomic neuropathy and prognostic implications. *Ann Intern Med* 92:308-311, 1980.
24. Woolfson AMJ, Heatley RV, Allison SP: Insulin to inhibit protein catabolism after injury. *New Engl J Med* 18:14-17, 1979.
25. Rubinstein A, Pierce CE, Bloomgarden Z: Rapid healing of diabetic foot ulcers with continuous subcutaneous insulin infusion. *Am J Med* 75:161, 1983.
26. Whitlow PL, Rogers WJ, Smith LR, McDaniel HG, Papapietro SE, Mantle JA, Logic JR, Russell RO, Rackley CE: Enhancement of left ventricular function by glucose-insulin-potassium infusion in acute myocardial infarction. *Am J Cardiol* 49:811-920, 1982.
27. Bagdale JD, Stewart M Walters E: Impaired granulocyte adherence: A reversible defect in host defense in patients with poorly controlled diabetes. *Diabetes* 27:677, 1978.
28. Boulton AJM, Scarpello JHB, Ward JD: Venous oxygenation in the diabetic neuropathic foot: evidence of arteriovenous shunting? *Diabetologia* 22:6-8, 1982.