Classification and Diagnosis of Diabetes Mellitus and Other Categories of Glucose Intolerance

NATIONAL DIABETES DATA GROUP

SUMMARY

A classification of diabetes and other categories of glucose intolerance, based on contemporary knowledge of this heterogeneous syndrome, was developed by an international workgroup sponsored by the National Diabetes Data Group of the NIH. This classification, and revised criteria for the diagnosis of diabetes, were reviewed by the professional members of the American Diabetes Association, and similar versions were circulated by the British Diabetic Association, the Australian Diabetes Society, and the European Association for the Study of Diabetes. The ADA has endorsed the proposals of the international workgroup, and the Expert Committee on Diabetes of the World Health Organization has accepted its substantive recommendations. It is proposed that this classification be used as a uniform framework in which to conduct clinical and epidemiologic research so that more meaningful and comparative data will be obtained on the scope and impact of the various forms of diabetes and other classes of glucose intolerance.

Medical treatment of diabetes is not considered in this paper, and the classification is not an attempt to define guidelines for therapy of patients.

The salient changes proposed in the classification are that 1. The insulin-dependent, ketosis-prone type of diabetes, which is associated with increased or decreased frequency of certain histocompatibility antigens (HLA) on chromosome 6 and with islet cell antibodies, be considered a distinct subclass of diabetes [insulin-dependent diabetes mellitus (IDDM)]. This type of diabetes has been inappropriately termed juvenile diabetes. Since it can occur at any age, it is recommended that diagnosis based on age of onset be eliminated.

2. The noninsulin-dependent, nonketosis-prone types of diabetes, which are not secondary to other diseases or conditions, be considered a second distinct subclass of diabetes [noninsulin-dependent diabetes mellitus (NIDDM)]. This subclass has been divided according to whether or not obesity is present (obese NIDDM and nonobese NIDDM, respectively), and patients in this subclass can be further characterized by the type of treatment they receive (insulin, oral hypoglycemic agents, diet) or by other characteristics of interest to the researcher. It is believed that heterogeneity within this subclass, and also within IDDM, will be demonstrated by further research.

3. The types of diabetes caused by other conditions or found in increased frequency with other conditions (implying an etiologic relationship) be considered a third subclass of diabetes mellitus—diabetes associated with certain conditions and syndromes. This subclass has been divided according to the known or suspected etiologic relationships.

4. The class gestational diabetes be restricted to women in whom glucose intolerance develops or is discovered during pregnancy.

5. Individuals with plasma glucose (PG) levels intermediate between those considered normal and those considered diabetic [see (8)] be termed to have impaired glucose tolerance. It is proposed that the terms chemical, latent, borderline, subclinical, and asymptomatic diabetes, which have been applied to persons in this class, be abandoned, since use of the term diabetes invokes social, psychologic, and economic sanctions that are unjustified in light of the lack of severity of their glucose intolerance.

6. Individuals with normal glucose tolerance, who have experienced transient hyperglycemia either spontaneously or in response to identifiable stimuli,

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be classed as previous abnormality of glucose tolerance; and that the terms latent diabetes and prediabetes be abandoned, since these individuals are not diabetic and for reasons stated in (5) above.

7. Individuals who are at substantially higher risk than the general population to develop diabetes be classed as potential abnormality of glucose tolerance; and that the terms potential diabetes and prediabetes be abandoned, since these individuals are not diabetic and for reasons stated in (5) above.

8. The diagnosis of diabetes in nonpregnant adults be restricted to (a) those with the classic symptoms of diabetes and unequivocal hyperglycemia; (b) those with fasting venous PG concentrations greater than or equal to 140 mg/dl on more than one occasion; and (c) those who, if fasting plasma glucose (FPG) is less than 140 mg/dl, exhibit sustained elevated venous PG values during the oral glucose tolerance test (OGTT) (greater than or equal to 200 mg/dl, both at 2 h after ingestion of the glucose dose and also at some other time point between time 0 and 2 h). With these proposed diagnostic levels, it is felt that adjustment in the criteria for age of the subject is not necessary.

9. The diagnosis of diabetes can be made in children who exhibit the classic symptoms of diabetes (polyuria, polydipsia, glycosuria) and have a random PG value in excess of 200 mg/dl. In these subjects, the OGTT is not required for diagnostic purposes. Furthermore, in asymptomatic and aglycosuric children, routine glucose tolerance testing is not indicated for the detection or diagnosis of diabetes. When there are clear reasons for administration of the OGTT, diabetes should be diagnosed only when the fasting PG is greater than 140 mg/dl, the 2-h value is greater than or equal to 200 mg/dl, *and* a value between time 0 and 2 h is also greater than or equal to 200 mg/dl. Impaired glucose tolerance is present in children with a fasting PG value of less than 140 mg/dl and a 2-h PG value in excess of 140 mg/dl, *even if* the 2-h value and some other value between time 0 and 2 h exceeds 200 mg/dl.

10. The OGTT be standardized to a 75-g-carbohydrate dose for nonpregnant adults (1.75 g/kg ideal body weight for children, not to exceed 75 g).

Although new criteria for the diagnosis of gestational diabetes have recently been proposed, the members of the workgroup felt that these have not been widely tested. Consequently, no new recommendations are made in this paper for diabetes developing in pregnancy, and the 1964 criteria of O'Sullivan and Mahan are reiterated as the guidelines most commonly accepted in North America. **DIABETES *28*:1039–1057, December 1979.**

During the last decade, the growth of knowledge regarding the etiology and pathogenesis of diabetes has led many individuals and groups in the diabetes community to express the need for a revision of the nomenclature, diagnostic criteria, and classification of diabetes mellitus, seeking an international consensus if possible. This need has arisen from the lack of uniformity or consistency in the past in defining diabetes and other stages of glucose intolerance, leading to data from different research centers that are difficult to compare and, consequently, are limited in utility. In addition, while evidence has accumulated to indicate diabetes is a heterogeneous disease, there has been no general agreement on the classification of the syndrome, based on either etiology or clinical manifestations. These factors have made it difficult to assess the impact of diabetes and its complications and to determine the epidemiology of the different types of the disease. As a consequence, it was deemed essential to develop an appropriate, uniform terminology and a functional, working classification of diabetes that reflects the current knowledge about the disease. To accomplish this task, an international workgroup was convened on April 27–28, 1978, under the sponsorship of the National Diabetes Data Group of the National Institutes of Health (Table 1). The draft document developed by this workgroup was circulated widely in the diabetes community, including all professional members of the American Diabetes Association, and this paper incorporates many of the comments and suggestions made.

The aims for the classification numbered three—(1) to serve as a uniform basis on which to plan and conduct clinical research in diabetes, including its causes, treatment, development of complications, and prevention; (2) to serve as a framework for the collection of epidemiologic data on the etiology, natural history, and impact of diabetes and its complications in diverse populations throughout the world; (3) to aid the clinician in categorizing patients who have various degrees of glucose intolerance or who possess characteristics that place them at increased risk of developing diabetes.

The terminology and classification system had to fulfill the following requirements: (1) the classes should be defined so as to be mutually exclusive, that is, an individual at any given time in his life can be placed in only one class, although with prospective follow-up he may change characteristics and need to be reclassified subsequently; (2) the classification should require only simple clinical measurements or descriptive observations that are readily obtainable and have biologic significance; (3) the classes should be as precise and well defined as current knowledge of the etiopathology of diabetes allows, so that each class contains a population as homogeneous as possible; (4) the terminology should be precise and well defined and should describe the phenotypic expression of the abnormality as much as possible; (5) the classification should be adaptable and able to incorporate new research findings on the etiopathology of diabetes.

THE CLASSIFICATION

Table 2 is a presentation of the factors associated with each class and the clinical and diagnostic criteria or other descriptors by which each class (and subclass) is defined. The classification includes three clinical classes: diabetes mellitus [characterized by either fasting hyperglycemia or levels of plasma glucose (PG) during an oral glucose tolerance test (OGTT) above defined limits]; impaired glucose tolerance (PG levels during an OGTT that lie above normal but below those defined as diabetes); and gestational diabetes. In addition, the classification includes stages that may be part of the natural history of diabetes in which there are no abnormalities of carbohydrate metabolism, namely, previous abnormality of glucose tolerance and potential abnormality of glucose tolerance.

This classification is based on contemporary knowledge

TABLE 1
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International workgroup to develop a nomenclature and classification system for diabetes mellitus

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of diabetes and also represents compromises of different points of view. As knowledge of diabetes develops with future research advances, Table 2 will need to be amended and revised. For example, it is anticipated that genetic markers for diabetes will be discovered and further heterogeneity in both etiology and pathogenesis will be demonstrated, which will allow separation of diabetes into even more types than those shown in Table 2.

DIABETES MELLITUS

It has been clearly established in recent years that diabetes mellitus is a genetically and clinically heterogeneous group of disorders that share glucose intolerance in common.

The evidence in favor of this heterogeneity is overwhelming:[1,2] (1) there are more than 30 distinct, mostly rare, disorders in which glucose intolerance is a feature; (2) ethnic variability in prevalence and clinical features; (3) genetic heterogeneity in diabetic animal models; (4) clinical variability between thin, ketosis-prone, insulin-dependent diabetes and obese, nonketotic, insulin-resistant diabetes; (5) genetic and immunologic studies that show "juvenile" and "adult-onset" diabetes to be distinct entities; and (6) demonstration that a type of mild diabetes in young people, which is inherited in an autosomal dominant fashion, is clearly different from the classic acute-onset diabetes of juveniles. This collective evidence has been used in Table 2 to divide the class of diabetes mellitus into three distinct types, in each of which subtypes have been identified.

Heterogeneity within the diabetic syndrome has important implications for research and for the clinical management of diabetes: first, that different genetic and environmental etiologic factors can result in similar diabetic phenotypes; and second, that the distinct disorders grouped together under the rubric diabetes may differ markedly in pathogenesis, natural history, and responses to therapy and prophylactic measures.

Type I, insulin-dependent diabetes mellitus. The first subclass of diabetes, type I or insulin-dependent diabetes mellitus (IDDM), is usually characterized clinically by abrupt onset of symptoms, insulinopenia and dependence on injected insulin to sustain life, and proneness to ketosis. Classically, this type of disease occurs in juveniles, and it was formerly termed juvenile diabetes. However, it can be recognized and become symptomatic for the first time at any age; hence, diagnosis based on age at onset is inappropriate. In addition to the ketosis-prone stage, this type of diabetes can also be recognized in a preketosis-prone stage. For example, prospective testing in siblings of insulin-dependent diabetics has disclosed patients with normal fasting plasma glucose (FPG) levels but with abnormal glucose tolerance who progress rapidly to the ketotic form, usually within 2 yr after recognition, but occasionally after longer periods of time.[1] IDDM appears to be heterogeneous in terms of genetics and environmental factors that precipitate the disease.[2] Genetic determinants are thought to be important in most patients, as expressed by the associated increased or decreased frequency of certain histocompatibility antigens (HLA) on chromosome 6.[3,4] Abnormal immune responses and autoimmunity are also thought to play an etiologic role, and islet cell antibodies are frequently present at diagnosis in this type of diabetes.[5].

Type II, noninsulin-dependent diabetes mellitus. The

TABLE 2
Classification of diabetes mellitus and other categories of glucose intolerance

Class	Former terminology	Associated factors	Clinical characteristics	Diagnostic criteria
		Clinical Classes		
Diabetes Mellitus (DM)				
Insulin-dependent type (IDDM), Type I	Juvenile diabetes, juvenile-onset diabetes, juvenile-onset-type diabetes, JOD, ketosis-prone diabetes, brittle diabetes	Evidence regarding etiology suggests genetic and environmental or acquired factors, association with certain HLA types, and abnormal immune responses, including autoimmune reactions.	Persons in this subclass are dependent on injected insulin to prevent ketosis and to preserve life, although there may be preketotic, non-insulin-dependent phases in the natural history of the disease. In the preponderance of cases, onset is in youth, but IDDM may occur at any age. Characterized by insulinopenia. Islet cell antibodies are frequently present at diagnosis in this type.	Diagnosis of diabetes in adults should be based on: (1) unequivocal elevation of plasma glucose concentration together with the classical symptoms of diabetes. or (2) elevated fasting plasma glucose concentration on more than one occasion. or (3) elevated plasma glucose concentration after an oral glucose challenge on more than one occasion. Diagnosis of diabetes in children requires either (1) or (2) *and* (3). See Table 5 for diagnostic plasma glucose standards. See text for recommended procedure for performance of the oral glucose tolerance test. Additional criteria for NIDDM: See text and Table 6 for standards of obesity.
Noninsulin-dependent types (NIDDM), Type II 1. Nonobese NIDDM 2. Obese NIDDM	Adult-onset diabetes, maturity-onset diabetes, maturity-onset-type diabetes, MOD, ketosis-resistant diabetes, stable diabetes	There are probably multiple etiologies for this class, the common outcome being derangement of carbohydrate metabolism. Evidence on familial aggregation of diabetes implies genetic factors, and this class includes diabetes presenting in children and adults in which autosomal dominant inheritance has been clearly established (formerly termed the MODY type, maturity-onset diabetes in the young). Environmental factors superimposed on genetic susceptibility are probably involved in the onset of the NIDDM types. Obesity is suspected as an etiologic factor and is recommended as a criterion for dividing NIDDM into two subclasses, according to the presence or absence of obesity.	Persons in this subclass are not insulin-dependent or ketosis-prone, although they may use insulin for correction of symptomatic or persistent hyperglycemia and they can develop ketosis under special circumstances, such as episodes of infection or stress. Serum insulin levels may be normal, elevated, or depressed. In the preponderance of cases, onset is after age 40, but NIDDM is known to occur at all ages. About 60–90% of NIDDM subjects are obese and constitute a subtype of NIDDM; in these patients, glucose tolerance is often improved by weight loss. Hyperinsulinemia and insulin resistance characterize some patients in this subtype.	
Other types, including diabetes mellitus associated with certain conditions and syndromes: 1. Pancreatic disease 2. Hormonal 3. Drug or chemical induced 4. Insulin receptor abnormalities 5. Certain genetic syndromes 6. Other types	Secondary diabetes	This subclass contains a variety of types of diabetes, in some of which the etiologic relationship is known (e.g., diabetes secondary to pancreatic disease, endocrine disease, or administration of certain drugs). In others, an etiologic relationship is suspected because of a higher frequency of association of diabetes with a syndrome or condition (e.g., a number of the genetic syndromes). See Table 3 for a list of these conditions and syndromes.	In addition to the presence of the specific condition or syndrome, diabetes mellitus is also present.	In order to place an individual in the subclass Other Types, two diagnostic determinations must be made, the presence of diabetes (as described above) and the presence of the associated condition or syndrome.
Impaired Glucose Tolerance (IGT)				
Nonobese IGT Obese IGT IGT associated with certain conditions and syndromes, which may be (1) pancreatic disease, (2) hormonal,	Asymptomatic diabetes, chemical diabetes, subclinical diabetes, borderline diabetes, latent diabetes	Mild glucose intolerance in subjects in this class may be attributable to normal variation of glucose tolerance within a population. In some subjects, IGT may	Nondiagnostic fasting glucose levels and glucose intolerance of a degree between normal and diabetic. Some studies have shown increased preva-	Diagnosis is based on the oral glucose tolerance test after determining that fasting plasma glucose is <140 mg/dl. See Table 5 for diagnostic criteria and

TABLE 2 (Continued)

Class	Former terminology	Associated factors	Clinical characteristics	Diagnostic criteria
		Clinical Classes		
(3) drug or chemical induced, (4) insulin receptor abnormalities, (5) certain genetic syndromes		represent a stage in the development of NIDDM or IDDM although the majority of persons with IGT remain in this class for many years or return to normal glucose tolerance. See Table 3 for a list of associated conditions and syndromes.	lence of arterial disease symptoms and electrocardiographic abnormalities and increased susceptibility to atherosclerotic disease associated with known risk factors including hypertension, hyperlipidemia, adiposity, and age. Clinically significant renal and retinal complications of diabetes are absent.	text and Table 6 for standards of obesity.
Gestational Diabetes (GDM)	Gestational diabetes	Glucose tolerance with onset during pregnancy is thought to be due to complex metabolic and hormonal changes which are incompletely understood. Insulin resistance may be responsible in part for gestational diabetes.	Glucose intolerance that has its onset or recognition during pregnancy. Thus, diabetics who become pregnant are not included in this class. Associated with increased perinatal complications and with increased risk for progression to diabetes within 5–10 yr after parturition. Requires reclassification after pregnancy terminates into PrevAGT, DM, or IGT.	Diagnosis is based on the oral glucose tolerance test. See Table 5 for the 1964 diagnostic standards of O'Sullivan and Mahan which are widely used in North America. Different criteria are employed in other parts of the world.

Class	Former terminology	Description
		Statistical Risk Classes
Previous Abnormality of Glucose Tolerance (PrevAGT)	Latent diabetes, prediabetes	This class is restricted to those persons who now have normal glucose tolerance but who have previously demonstrated diabetic hyperglycemia or impaired glucose tolerance either spontaneously or in response to an identifiable stimulus. Individuals who have been gestational diabetics and returned to normal glucose tolerance after parturition form an obvious subclass of PrevAGT. Another small but important group of individuals in this class are former obese diabetics whose glucose tolerance has returned to normal after losing weight. Clinical studies have shown that many patients under acute metabolic stress due to trauma or injury experience transient hyperglycemia. Apart from studies of former gestational diabetics, there has been little systematic investigation of the later liability of persons who have exhibited glucose intolerance to develop diabetes. However, it is likely that this is increased and that there is utility in including all those with a history of glucose intolerance, now normal, in this separate class "Previous Abnormality of Glucose Tolerance."
Potential Abnormality of Glucose Tolerance (PotAGT)	Prediabetes, potential diabetes	This class includes persons who have never exhibited abnormal glucose tolerance but who are at substantially increased risk for the development of diabetes. Individuals who are at increased risk for IDDM include (in decreasing order of risk): persons with islet cell antibodies; monozygotic twin of an IDDM diabetic; sib of an IDDM diabetic, especially one with identical HLA haplotypes; offspring of an IDDM diabetic. Individuals who are at increased risk for NIDDM include (in decreasing order of risk): monozygotic twin of an NIDDM diabetic; first degree relative of an NIDDM diabetic (sib, parent, and offspring); mother of a neonate weighing more than 9 lb; obese individuals; members of racial or ethnic groups with a high prevalence of diabetes, e.g., a number of American Indian tribes. The degree of risk for any of these circumstances is not well established as yet.

second subclass of diabetes, type II or noninsulin-dependent diabetes mellitus (NIDDM), frequently presents with minimal or no symptoms referable to the metabolic aberrations of diabetes. Patients with NIDDM are not dependent on insulin for prevention of ketonuria and are not prone to ketosis. However, they may require insulin for correction of symptomatic, or persistent, fasting hyperglycemia if this cannot be achieved with the use of diet or oral agents. Such patients may develop ketosis under special circumstances, such as severe stress precipitated by infections or trauma. There may be normal levels of insulin, mild insulinopenia, or above normal levels of insulin associated with insulin resistance. The whole range of insulin responses to glucose from low to supranormal has been found in patients of this subclass, many of whom do not have fasting hyperglycemia. Patients with NIDDM may be asymptomatic for years or decades and show only slow progression of the disease. However, the typical chronic associations and complications of diabetes, namely, macroangiopathy, microangiopathy, neuropathy, and cataracts, may be seen in this type.[1] NIDDM undoubtedly is also heterogeneous in nature. Although in most patients who develop NIDDM the onset is after age 40, the NIDDM type also occurs in young persons who do not require insulin and are not ketotic. Consequently, age at onset is again not recommended as a criterion by which to classify an individual, and the terms adult-

onset diabetes and variations of this phrase, should be abandoned as classifying terms.

NIDDM also has a genetic basis, which appears to be stronger than in IDDM, as evidenced by a more frequent familial pattern of occurrence. Indeed, included within this type are families in whom diabetes presents in children, adolescents, and adults in which autosomal dominant inheritance has been well established (formerly referred to as maturity-onset-type diabetes of the young, or, MODY[1]). Environmental factors superimposed on genetic susceptibility are undoubtedly involved in onset of the NIDDM types. Intake of excessive calories leading to weight gain and obesity is probably an important factor in its pathogenesis. Although small changes in weight may be important, NIDDM has been subdivided according to the absence or presence of obesity, as 60% to 90% of all NIDDM patients are obese in Western societies (see Table 6 for proposed standards for obesity). Hyperglycemia and glucose intolerance are usually improved by weight loss. In persons with this type of diabetes, characteristic aggregation of HLA types and islet cell antibodies have not been found.

Other types of diabetes. In this subclass, diabetes forms part of certain other conditions and syndromes that often have many clinical features not generally associated with the diabetic state. In some instances the co-occurrence of glucose intolerance and the other features is known to be etiologically related. In others, the frequency of co-occurrence indicates that there is an, as yet unknown, causal relationship. Thus, this subclass has been divided according to the known or suspected etiologic relationships. For example, diabetes may be secondary to (1) pancreatic disease or removal of pancreatic tissue, (2) endocrine diseases such as acromegaly, Cushing's syndrome, pheochromocytoma, glucagonoma, somatostatinoma, and primary aldosteronism, or (3) the administration of certain hormones, drugs, and chemicals that cause hyperglycemia. Diabetes may also be associated with defects of insulin receptors, which may be caused by either abnormalities in numbers or affinity of insulin receptors or antibodies to receptors with or without associated immune disorders. Diabetes (or carbohydrate intolerance) is found in increased frequency with a large number of genetic syndromes.[6,7] Finally, this class contains room for certain special types of diabetes that occur only under specific, well-described environmental and clinical conditions, e.g., diabetes associated with malnourished populations. The heterogeneity of the diabetic syndrome is clearly illustrated by the variety of conditions listed in Table 3, with which glucose intolerance is associated.

Difficulties in assignment of a patient to a subclass of diabetes mellitus. Each of the types of diabetes described above has a set of features that distinguishes it from the other two. However, on occasion, it may be difficult to definitely assign an individual to one class because inadequate information is available on that patient. For example, distinguishing between an insulin-dependent diabetic and a thin NIDDM patient who has been prescribed insulin may require taking these patients off insulin and monitoring the course of their disease, which may be impractical. The additional examinations required to determine whether a patient has diabetes secondary to some other condition may not have been done, and some patients may be incorrectly classified as IDDM or NIDDM. Furthermore, there are stages in the natural history of each type of diabetes that mimic features of the other types, e.g., the remission phase of IDDM or the ketonuria an NIDDM patient develops under metabolic stress. If these discrete stages are considered alone rather than in the context of the historical progression of the disease, misclassifications will result. Furthermore, as will be described later, there will, on occasion, be patients whose PG levels in the fasting state or after an oral glucose challenge have been inadequately determined or are equivocal, such that they do not meet the required criteria for diabetes. In each of these situations, classification should be held in abeyance until adequate clinical and diagnostic information is obtained.

RECOMMENDED PROCEDURES FOR THE DIAGNOSIS OF DIABETES IN ADULTS

Diagnosis of diabetes should be based on (1) unequivocal elevation of PG concentration, together with the classic symptoms of diabetes; or (2) elevated FPG concentration on more than one occasion; or (3) elevated PG concentration after an oral glucose challenge on more than one occasion.

Figure 1 is a flow diagram illustrating the set of measurements and decisions needed to classify an individual.

The presence of such obvious diabetes' symptoms as polyuria, polydipsia, ketonuria, and rapid weight loss, together with gross and unequivocal elevation of the PG, is usually sufficient to make the diagnosis of diabetes. In the absence of these signs and symptoms, however, quantitative measurements of PG under carefully standardized conditions are the prescribed methods for making a clinical diagnosis of diabetes. These include measurement of the FPG concentration and, if FPG is not elevated, performance of the OGTT. The PG levels considered to be diagnostic of diabetes are shown in Table 5 and are discussed here later.

The OGTT is not necessary if the fasting PG meets the criteria for diabetes shown in Table 5. Indeed, in studies on individuals whose FPG was diagnostic of diabetes, subsequent OGTTs exhibited glucose values that met or exceeded the criteria for diabetes in over 90% of subjects.[8] Because of the reliance placed on the FPG level, it is essential that factors other than diabetes that elevate fasting blood glucose are carefully considered and are known to be absent in a subject.

The use of PG glucose levels in the fasting state or in response to an oral glucose challenge to establish a diagnosis of diabetes is associated with several well-recognized problems and limitations. Factors other than diabetes will elevate FPG or impair glucose tolerance, and these have been thoroughly discussed in the 1969 recommendations of the American Diabetes Association.[9] These include a variety of metabolic disturbances or stresses, such as illness, trauma, pregnancy, endocrinopathies, and certain drugs that induce hyperglycemia (Table 3). Physical inactivity or carbohydrate intake of less than 150 g per day for several days before the OGTT can produce abnormal glucose tolerance. Administration of the test in the afternoon can produce aberrant results. Lack of fasting (less than 10 h) can elevate PG level, and prolonged fasting (more than 16 h) can impair tolerance. In addition, abundant evidence exists that there is variability in a subject's response, in that repeat OGTTs done in the same individual under standard conditions may

TABLE 3
Conditions and syndromes associated with diabetes mellitus and impaired glucose tolerance*

1. Pancreatic Disease
- a. Neonatal
  - Congenital absence of the pancreatic islets
  - Transient diabetes of the newborn
  - Functional immaturity of insulin secretion
  - ? Converse of infants of diabetic mothers
- b. Postinfancy
  - Acquired—traumatic, infections, toxic, neoplastic
  - Inherited—cystic fibrosis, hereditary relapsing pancreatitis, hemochromatosis

2. Hormonal
- a. Hypoinsulinemic
  - Endocrine overactivity
    - Catecholamines, e.g., pheochromocytoma
    - Somatostatinoma
    - Mineralocorticoids, e.g., aldosteronoma
  - Underactivity
    - Hypoparathyroidism—hypocalcemia
    - Type-I isolated growth hormone deficiency
    - Multitropic pituitary deficiency
    - Laron dwarfism
    - Hypothalamic lesions—"Piqure" diabetes (of Claude Bernard)
- b. Hyperinsulinemic—states of insulin resistance
  - Overactivity
    - Glucocorticoids
    - Progestins and estrogens
    - Growth hormone—acromegaly
    - Glucagon
  - Underactivity
    - Type-II isolated growth hormone deficiency

3. Drugs and Chemical Agents†
- a. Diuretics and Antihypertensive Agents
  - Chlorthalidone (Hygroton, Combipres, Regroton)
  - Clonidine (Catapres, Combipres)
  - Diazoxide (Hyperstat, Proglycem)
  - Furosemide (Lasix)
  - Metalazone
  - Thiazides (Several forms, many trade names)
  - ‡ Bumetamide
  - ‡ Clopamide
  - ‡ Clorexolone
  - ‡ Ethacrynic acid (Edecrin)

  (Note: hyperglycemic response to diuretics may be independent of K^+ fluctuations)
- b. Hormonally Active Agents
  - Adrenocorticotropin (Acthar)
    - ‡ Tetracosactrin
  - Glucagon
  - Glucocorticoids (natural and synthetic)
  - Oral contraceptives
  - Somatotropin
  - Thyroid hormones (thyrotoxic doses)
    - Dextrothyroxine (Choloxin)
  - ‡ Calcitonin (Calcimar)
  - ‡ Medroxyprogesterone (AMEN, Depo-Provera, Provera)
  - ‡ Prolactin

Drugs and chemical agents (continued)
- c. Psychoactive Agents
  - Chlorprothixene (Teractan)
  - Haloperidol (Haldol)
  - Lithium carbonate (Eskalith, Lithane, others)
  - Phenothiazines
    - Chlorpromazine (Thorazine)
    - Perphenazine (Trilafon, Etrafon, Triavil)
  - ‡ Clopenthixol
  - Tricyclic Antidepressants
    - Amitriptyline (Elavil, Endep, Etrafon, Triavil)
    - Desipramine (Norpramin, Pertofrane)
    - Doxepin (Adapin, Sinequan)
    - Imipramine (Presamine, Tofranil, Imavate)
    - Nortriptyline (Aventyl)
  - ‡ Marijuana
- d. Catecholamines and Other Neurologically Active Agents
  - Diphenylhydantoin (Dilantin)
  - Epinephrine (Adrenalin Chloride, Asthma-Meter, Sus-Phrine)
  - Isoproterenol (Isuprel)
  - Levodopa (Bendopa, Dopar, Larodopa, Sinemet)
  - Norepinephrine (levarterenol, Levophed)
  - ‡ Buphenine (Nylidrin)
  - ‡ Fenoterol
  - ‡ Propranolol (Inderal)
- e. Analgesic, Antipyretic, and Anti-inflammatory agents
  - Indomethacin (Indocin)
  - ‡ Acetaminophen (overdose amounts) (Tylenol, Nebs, others)
  - ‡ Aspirin (overdose amounts)
  - ‡ Morphine
- f. Antineoplastic Agents
  - Alloxan
  - L-asparaginase
  - Streptozotocin
  - ‡ Cyclophosphamide (Cytoxan)
  - ‡ Megestrol Acetate (Megace)
- g. Miscellaneous
  - Isoniazid (INAH, Nydrazid, others)
  - Nicotinic acid (Cerebro-Nicin, Nicobid, others)
  - ‡ Carbon disulfide
  - ‡ Cimetidine
  - ‡ Edetic acid (EDTA)
  - ‡ Ethanol
  - ‡ Heparin
  - ‡ Mannoheptulose
  - ‡ Nalidixic acid (NegGram)
  - ‡ Nickel chloride
  - ‡ Niridazole
  - ‡ Pentamidine (Lomidine)
  - ‡ Phenolphthalein (Ex-Lax)
  - ‡ Rodenticide (Vacor)
  - ‡ Thiabendazole

4. Insulin Receptor Abnormalities
- a. Defect in Insulin Receptor
  - Congenital lipodystrophy
  - Associated with virilization, acanthosis nigricans
- b. Antibody to insulin receptor-associated immune disorders

TABLE 3 (Continued)

5. Genetic Syndromes

a. Inborn Errors of Metabolism
- Glycogen-storage disease type I
- Acute intermittent porphyria
- Hyperlipidemia
- Hyperglycerolemia

b. Insulin-resistant Syndromes
- Ataxia telangiectasia
- Myotonic dystrophy
- Mendenhall's syndrome
- Lipoatrophic syndromes

c. Hereditary Neuromuscular Disorders
- Optic atrophy—diabetes mellitus
- Diabetes insipidus, nerve deafness
- Muscular dystrophies
- Late onset proximal myopathy
- Huntington's chorea
- Machado's disease
- Herrman syndrome
- Friedreich's ataxia
- Alstrom syndrome
- Laurence-Moon-Biedl syndrome
- Retinopathy, hypogonadism, mental retardation, nerve deafness
- Pseudo-Refsum's syndrome

d. Progeroid Syndrome
- Cockayne syndrome
- Werner syndrome

e. Syndromes with Glucose Intolerance Secondary to Obesity
- Prader-Willi syndrome
- Achondroplasia

f. Miscellaneous
- Steroid-induced ocular hypertension
- Epiphyseal dysplasia and infantile-onset diabetes

g. Cytogenetic Disorders
- Down
- Turner
- Klinefelter

6. Other Types
- Diabetes associated with malnourished populations

* It is acknowledged that this list is not all-inclusive, and it is anticipated that it will change with future research advances.

† For many of these agents, it cannot be determined now whether the hyperglycemic response represents solely a pharmacologic action or is an interaction between a predisposition for abnormal glucose tolerance and the pharmacologic effects of the agent. Drugs exacerbating pre-existing diabetes have been excluded from this list. A number of agents shown to cause hyperglycemia in animals but with no reported effect in humans also are not listed.

‡ Association not clearly established for one of the following reasons: (1) confounded by the simultaneous administration of other drugs; (2) limited to a single case report; (3) conflicting or contradictory evidence; (4) drug has been reported to cause interference with laboratory test for serum glucose. See reference list for these drugs and chemicals.

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TABLE 3 (Continued)

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Phenolphthalein	Ann. Intern. Med. *70*:791, 1969; N. Engl. J. Med. *273*:1135, 1965.
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§ Agents and drugs not referenced are listed in at least one of the following well known sources: Physicians' Desk Reference, Goodman & Gilman, Martindale's Extra Pharmacopoeia, AMA Drug Evaluation, Side Effects of Drugs, Drug Interactions.

yield dissimilar results.[10–13] For example, in a group of 334 subjects, each given six 100-g OGTTs over a period of 1 yr, there were some individuals whose test results were consistent and others whose OGTTs showed variability, although average PG levels during the tests for the group as a whole remained the same over time.[14] Of importance is that, on single tests, some of the subjects exhibited abnormal or diabetic glucose levels, but in no case was this consistent over several tests. The individual variability could not be related to age, race, weight, or family history of diabetes. This difficulty in diagnosing diabetes from a single OGTT is also found in children who do not present with the acute signs of insulin-dependent diabetes.[15]

In light of the many factors other than diabetes that elevate FPG and impair glucose tolerance, it is imperative that elevated FPG or OGTT values be demonstrated on more than one occasion before a clinical diagnosis of diabetes is made.

Alternative methods to determine glucose intolerance, such as measurement of postprandial or random blood sugar or the performance of a GTT regardless of the time of the last meal, are not recommended as definitive procedures. Although such methods have been used as screening techniques, measurement of FPG or a confirmatory OGTT in the fasting state is necessary to arrive at a definitive diagnosis unless, as stated above, the classic symptoms of diabetes are present together with unequivocal elevation of PG.

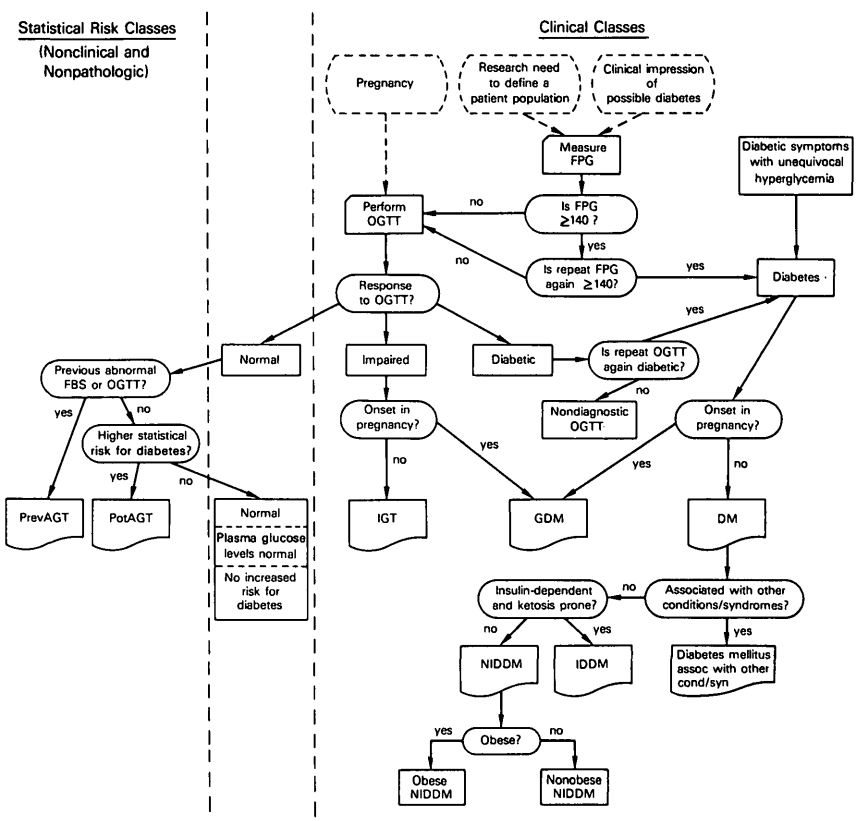

FIGURE 1. Procedure for classifying adult research subjects or clinical patients.

THE ORAL GLUCOSE TOLERANCE TEST (OGTT)

The procedure for administering the OGTT recommended by the American Diabetes Association[9] in 1969 (which is similar to that of the British Diabetic Association's[16] recommendations of 1964) is reendorsed, with a single change: The glucose dose now recommended for nonpregnant adults is 75 g (1.75 g/kg ideal body weight for children, up to a maximum of 75 g), which is midway between the dose of 50 g widely used in Europe and the dose of 100 g often used in the United States.

Several factors prompted this recommendation. First, it was deemed highly desirable to achieve international standardization on the administration of the OGTT. Second, a number of major research centers in the United States and abroad, as well as the current national survey of glucose tolerance in the United States[8] (now being conducted by the National Center for Health Statistics), use a 75-g glucose load. Third, it has been reported that a 50-g dose is not provocative enough to detect some individuals who exhibit impaired glucose tolerance with larger doses, while the 100-g dose has been reported to cause nausea in subjects. Finally, it has been shown that doses of 50 g or 100 g, administered under standardized conditions, result in virtually identical PG levels during the OGTT in normal subjects, the only significant difference being a 15 mg/dl higher PG level at 2 h after the 100-g dose.[17,18] Between 75- and 100-g doses, the differences were not significant. Individuals with impaired glucose tolerance do display a larger difference (up to 50 mg/dl) in the 2-h value between the 50- and the 100-g doses.[18]

The standard OGTT is often unnecessary for the diagnosis of diabetes, as, for example, when the fasting blood glucose concentration is elevated on more than one occasion. In addition, as discussed in the previous section, it should be administered only to patients who are otherwise healthy and ambulatory and who are known not to be taking drugs that elevate PG. Attention should also be given to the fact that certain drugs interfere with the laboratory determination of glucose (Table 4). When the OGTT is administered, it should be performed in the morning after at least 3 days of unrestricted diet (≥150 g CHO) and physical activity. The subject should have fasted for at least 10 h but no more than 16 h; water is permitted during this period. The subject should remain seated and not smoke throughout the test.

The dose of glucose administered should be 75 g (1.75 g/kg ideal body weight, up to a maximum of 75 g, for children). A commercially prepared carbohydrate load equivalent to this glucose dose is also acceptable. (To use the criteria for gestational diabetes in Table 5, a dose of 100 g of glucose is required.)

A fasting blood sample should be collected, after which the glucose dose in a concentration no greater than 25 g/dl of flavored water should be drunk in about 5 min. Zero time is the beginning of the drink, and blood samples should be collected at 30-min intervals for 2 h. (For pregnant subjects,

TABLE 4
Drugs reported to interfere with laboratory tests for serum glucose*

Drug	Effect on serum glucose value	Laboratory test
Acetaminophen	Increase	SMA 12/60
Aminosalicylic acid	Increase	Alkaline ferricyanide method
Ascorbic acid	Increase	O-toluidine procedure; alkaline ferricyanide procedure; neocuproine procedure
	Decrease	Glucose oxidase dianisidine procedure; coupled glucose oxidase method; glucomatic method
Chloropropamide	Decrease	Boehringer GOD-PERID method
Dextran	Increase	Alkaline ferricyanide method; HBAH procedure; o-toluidine procedure; glucose oxidase methods
Epinephrine	Increase	SMA 12/60 (at 10 mg/dl); alkaline ferricyanide method
Hydralazine	Increase	SMA 12/60
	Decrease	Glucose oxidase method of Boehringer
Iron dextran	Increase	Glucose oxidase method; O-toluidine method; p-HBAH procedure; alkaline ferricyanide method
Iron sorbitex	Increase	O-toluidine method; p-HBAH procedure; alkaline ferricyanide procedure; glucose oxidase methods
Isocarboxazid	Decrease	Glucose oxidase method of Boehringer
Isoniazid	Decrease	Glucose oxidase method of Boehringer
Isoproterenol	Increase	SMA 12/60
Levarterenol	Increase	Alkaline ferricyanide method
Levodopa	Increase	SMA 12/60; alkaline ferricyanide method
Mercaptopurine	Increase	SMA 12/60
Methyldopa	Increase	SMA 12/60
Nalidixic acid	Increase	Copper reduction methods
Nitrazepam	Decrease	Glucose oxidase method of Boehringer
Phenacetin	Decrease	GOD-PERID procedure
Phenazopyridine	Decrease	Delays coupled glucose oxidase reaction
Phenformin	Decrease	Boehringer GOD-PERID method
Propylthiouracil	Increase	SMA 12/60
Tetracycline	Increase	Hexokinase reaction; o-toluidine method; MBTH procedure of Neeley
Tolbutamide	Increase	Glucose oxidase methods

* Source: AMA Drug Evaluations, 3rd edit. Littleton, Mass., Publishing Sciences Group, 1977.

TABLE 5
Diagnostic criteria*

Diabetes Mellitus in Nonpregnant Adults

Any one of the following are considered diagnostic of diabetes:

A. Presence of the classic symptoms of diabetes, such as polyuria, polydipsia, ketonuria, and rapid weight loss, together with gross and unequivocal elevation of plasma glucose.
B. Elevated fasting glucose concentration on more than one occasion:

venous plasma ≥ 140 mg/dl (7.8 mmol/L)
venous whole blood ≥ 120 mg/dl (6.7 mmol/L)
capillary whole blood ≥ 120 mg/dl (6.7 mmol/L)

If the fasting glucose concentration meets these criteria, the OGTT is *not required.* Indeed, virtually all persons with FPG > 140 mg/dl will exhibit an OGTT that meets or exceeds the criteria in C below.

C. Fasting glucose concentration less than that which is diagnostic of diabetes (B, above), but sustained elevated glucose concentration during the OGTT on more than one occasion. *Both* the 2-h sample *and* some other sample taken between administration of the 75-g glucose dose and 2 h later must meet the following criteria:

venous plasma ≥ 200 mg/dl (11.1 mmol/L)
venous whole blood ≥ 180 mg/dl (10.0 mmol/L)
capillary whole blood ≥ 200 mg/dl (11.1 mmol/L)

Impaired Glucose Tolerance (IGT) in Nonpregnant Adults†

Three criteria must be met: the fasting glucose concentration must be below the value that is diagnostic for diabetes; the glucose concentration two hours after a 75-g oral glucose challenge must be between normal and diabetic values; and a value between ½-h, 1-h, or 1½-h OGTT value later must be unequivocally elevated.

Fasting value:

venous plasma < 140 mg/dl (7.8 mmol/L)
venous whole blood < 120 mg/dl (6.7 mmol/L)
capillary whole blood < 120 mg/dl (6.7 mmol/L)

½-h, 1-h, or 1½-h OGTT value:

venous plasma ≥ 200 mg/dl (11.1 mmol/L)
venous whole blood ≥ 180 mg/dl (10.0 mmol/L)
capillary whole blood ≥ 200 mg/dl (11.1 mmol/L)

2-h OGTT value:

venous plasma of between 140 and 200 mg/dl) (7.8 and 11.1 mmol/L)
venous whole blood of between 120 and 180 mg/dl (6.7 and 10.0 mmol/L)
capillary whole blood of between 140 and 200 mg/dl) (7.8 and 11.1 mmol/L)

Normal Glucose Levels in Nonpregnant Adults

Fasting value:

venous plasma < 115 mg/dl (6.4 mmol/L)
venous whole blood < 100 mg/dl (5.6 mmol/L)
capillary whole blood < 100 mg/dl (100 mmol/L)

2-h OGTT value:

venous plasma < 140 mg/dl (7.8 mmol/L)
venous whole blood < 120 mg/dl (6.7 mmol/L)
capillary whole blood < 140 mg/dl (7.8 mmol/L)

OGTT values between ½-h, 1-h, or 1½-h OGTT value later:

venous plasma < 200 mg/dl (11.1 mmol/L)
venous whole blood < 180 mg/dl (10.0 mmol/L)
capillary whole blood < 200 mg/dl (11.1 mmol/L)

Glucose values above these concentrations but below the criteria for diabetes or IGT should be considered nondiagnostic for these conditions.

Diabetes Mellitus in Children

Either of the following are considered diagnostic of diabetes:

A. Presence of the classic symptoms of diabetes, such as polyuria, polydipsia, ketonuria, and rapid weight loss, together with a random plasma glucose >200 mg/dl.
B. In asymptomatic individuals, *both* an elevated fasting glucose concentration and a sustained elevated glucose concentration during the OGTT on more than one occasion. Both the 2-h sample *and* some other sample taken between administration of the glucose dose (1.75 g/kg ideal body weight, up to a maximum of 75 g) and 2 h later must meet the criteria below.

Fasting value:

venous plasma ≥ 140 mg/dl (7.8 mmol/dl)
venous whole blood ≥ 120 mg/dl (6.7 mmol/dl)
capillary whole blood ≥ 120 mg/dl (6.7 mmol/dl)

2-h OGTT value and an intervening value:

venous plasma ≥ 200 mg/dl (11.1 mmol/L)
venous whole blood ≥ 180 mg/dl (10.0 mmol/L)
capillary whole blood ≥ 200 mg/dl (11.1 mmol/L)

Impaired Glucose Tolerance (IGT) in Children

Two criteria must be met: the fasting glucose concentration must be below the value that is diagnostic of diabetes, and the glucose concentration 2 h after an oral glucose challenge must be elevated.

Fasting value:

venous plasma < 140 mg/dl (7.8 mmol/L)
venous whole blood < 120 mg/dl (6.7 mmol/L)
capillary whole blood < 120 mg/dl (6.7 mmol/L)

2-h OGTT value:

venous plasma > 140 mg/dl (7.8 mmol/L)
venous whole blood > 120 mg/dl (6.7 mmol/L)
capillary whole blood > 120 mg/dl (6.7 mmol/L)

Normal Glucose Levels in Children

Fasting value:

venous plasma < 130 mg/dl (7.2 mmol/L)
venous whole blood < 115 mg/dl (6.4 mmol/L)
capillary whole blood < 115 mg/dl (6.4 mmol/L)

2-h OGTT value:

venous plasma < 140 mg/dl (7.8 mmol/L)
venous whole blood < 120 mg/dl (6.7 mmol/L)
capillary whole blood < 140 mg/dl (7.8 mmol/L)

TABLE 5 (Continued)

Gestational Diabetes‡

Two or more of the following values after a 100-g oral glucose challenge must be met or exceeded:

	venous plasma	venous whole blood	capillary whole blood
Fasting	105 mg/dl (5.8 mmol/L)	90 mg/dl (5.0 mmol/L)	90 mg/dl (5.0 mmol/L)
1 h	190 mg/dl (10.6 mmol/L)	170 mg/dl (9.5 mmol/L)	170 mg/dl (9.5 mmol/L)
2 h	165 mg/dl‡ (9.2 mmol/L)	145 mg/dl (8.1 mmol/L)	145 mg/dl (8.1 mmol/L)
3 h	145 mg/dl (8.1 mmol/L)	125 mg/dl (7.0 mmol/L)	125 mg/dl (7.0 mmol/L)

* See text for discussion of factors (other than diabetes) that elevate the fasting glucose level or impair glucose tolerance and for discussion of standardized procedure for performance of the OGTT.

† See text for modification of these criteria for epidemiologic studies.

‡ Several members of the workgroup recommended that a category of impaired gestational glucose tolerance be defined by a 2-h plasma glucose level between 120 and 164 mg/dl.

the criteria for gestational diabetes in Table 5 require sampling at fasting, 1, 2, and 3 h.) If possible, venous blood samples should be collected, and, unless glucose concentrations can be determined immediately using a rapid glucose analyzer, blood should be collected in a tube containing sodium fluoride (5 ml whole blood to 30 mg NaF). The sample should be centrifuged and separated within 4 h of collection, and the plasma should be frozen unless glucose levels are to be determined immediately.

PG is the preferred measurement by any of the following methods, which have been shown to be comparable when performed with adequate quality control procedures and with sufficient attention to the many factors that interfere with measurement of glucose in blood and plasma samples: glucose oxidase, hexokinase, o-toluidine, Somogyi-Nelson, AutoAnalyzer ferricyanide, or AutoAnalyzer neocuproine. Table 4 is a list of drugs reported to interfere with laboratory tests for PG. (*See also* Cooper, G. R.: Methods for determining the amount of glucose in blood. CRC Crit. Rev. Clin. Lab. Sci. *4*:101–45, 1974.)

CRITERIA FOR THE DIAGNOSIS OF DIABETES IN NONPREGNANT ADULTS

Based on the results of several long-term prospective studies conducted in the United States and Britain over the last 15 yr, it is increasingly apparent that the PG standards commonly used as diagnostic for diabetes in adults may have been set too low and the criteria for diabetes should be redefined. The recommended new standards, which are derived from these studies, are shown in Table 5. With these proposed diagnostic levels, it is felt that adjustment in the criteria for age of the subject is not necessary.

Interpretation of PG levels in the fasting state and during the OGTT has been based on a variety of criteria; West lists at least 17 sets of criteria for interpreting the OGTT.[19] Of these, the four commonly employed have been the criteria of the US Public Health Service (USPHS),[20] Fajans and Conn,[21,22] the British Diabetic Association,[16] and the World Health Organization (WHO).[23] In general, their diagnostic values for diabetes are a 1-h PG value of more than 180–195 mg/dl, and a 2-h level of more than 140–160 mg/dl. However, tests deemed abnormal by one set of these criteria can frequently be classified normal by another, resulting in widely varying estimates of the prevalence of diabetes.[24]

Substantial differences exist in the diagnostic criteria used in practice by diabetologists,[25,26] and there is no consensus as to the dividing line between normal and diabetic glucose levels. This lack of agreement is primarily caused by the fact that there is no clear division between diabetics and nondiabetics in their FPG concentration or their response to an oral glucose load. With rare exceptions, the frequency distribution in most populations shows a continuous unimodal distribution from low to high and skewed to the higher levels;[22,27] no features of this curve allow diabetics to be distinguished from nondiabetics. In contrast, PG levels in the Pima Indian[28] and the Nauruan[29] populations exhibit a bimodal distribution, and there is a distinction between nondiabetics, whose 2-h PG levels are below 200 mg/dl and fall in the first mode, and diabetics, whose 2-h levels are above 240 mg/dl and fall in the second mode. The same bimodal distribution occurs for FPG, where the value of about 140 mg/dl divides the lower mode from the upper mode. However, for other populations, no such bimodality has been described, and an arbitrary decision has been made as to what level justifies the diagnosis of diabetes. The Fajans-Conn[21] criteria had a statistical basis: individuals were termed diabetic if their 1-, 1½-, and 2-h PG levels were all greater than 2 SD above the mean for a group of healthy adults younger than 50 yr. The USPHS[20] criteria and the WHO[23] criteria were each based on a consensus of a group of experts. The British Diabetic Association[16] criteria were admittedly set arbitrarily, in anticipation of completion of several long-term prospective studies, which would provide a more scientific basis for establishment of diagnostic glucose levels.

These studies,[31–42] which are complemented by several conducted in the United States,[28,30] are long-term observations on groups of adults whose initial glucose intolerance was of a degree of severity often termed borderline diabetes or chemical diabetes. In general, the PG criteria used to define these study populations were FPG of less than 140 mg/dl and, 2 h after an oral glucose challenge, a PG level of between 140 and 200 mg/dl. None of this research has included children in the study populations; consequently, their conclusions can be applied only to adults at this time.

The general findings of these studies are (1) the overwhelming majority of individuals whose PG levels fall between normal values and diabetic levels should constitute a category separate from individuals with gross glucose intolerance; (2) in this group, development of overt diabetic symptoms, or decompensation to well-recognized abnormal glucose tolerance in the absence of symptoms, occurs at a rate of only 1%–5% per year; a large proportion of individuals shows spontaneous reversion to normal glucose tolerance and the remainder stay in the borderline category; (3) treatment with oral hypoglycemic agents has little influence on development of diabetes in this group; and (4) the visual and renal microvascular complications of diabetes generally do not develop; however, some studies show significantly increased frequency of morbidity and mortality from atherosclerotic disease for subjects in this borderline group.

The following are summaries of the long-term studies on which these findings are based.

O'Sullivan and Mahan[30] identified 352 chemical diabetics of 1013 nonpregnant ambulant women given annual 100-g OGTTs. The 352 subjects, who were asymptomatic and of average age 36 yr, were classified by three progressively higher criteria (all values are for venous whole blood): (A) 1-h glucose level greater than 151 mg/dl and less than 160 mg/dl and 2-h level greater than 101 mg/dl and less than 120 mg/dl; (B) 1-h glucose level greater than 160 mg/dl and less than 170 mg/dl and 2-h level greater than 120 mg/dl; (C) fasting glucose level greater than 110 mg/dl, 1-h level greater than 170 mg/dl, and 2-h level greater than 120 mg/dl.

The subjects were followed for 1–12 yr to determine which persons showed sufficient decompensation of carbohydrate control to be called unequivocally diabetic. The presence of any two of the following was used as criteria for decompensation: blood glucose level higher than 300 mg/dl at any time within 3 h after ingestion of 100 g glucose; blood glucose level higher than 180 mg/dl within 5 h of a meal; and fasting blood glucose level of 120 mg/dl or higher.

Diabetes was later diagnosed in 3.0% of persons who met criteria A, in 10.7% of persons who met criteria B, and in 25.9% of persons who met criteria C. Since the subjects were observed for varying periods of time, life-table calculations were made, which showed the percentages that would have progressed to decompensation if all individuals were followed for the full 10 yr. These were 8.9%, 27.3%, and 52.5%, respectively.

There was, thus, a direct relationship between initial blood glucose levels during the OGTT and subsequent decompensation to overt diabetes. However, even among group C, the rate of decompensation by life-table analysis was only 5% per year, and this rate is considerably smaller than anticipated if all individuals had had true diabetes. In addition, during the period of observation of group C, 45% reverted to normal tolerance and 30% remained in the initial, impaired tolerance category; the reversion to normal in groups A and B was as great as 70%, and 20% remained in the initial impaired glucose tolerance range.

The Diabetes Survey Working Party, in a study[31–34] in Birmingham, England, administered 50-g OGTTs to 808 subjects out of the population of 19,412 persons. Normal individuals were defined as those who had fasting glucose levels below 100 mg/dl, 1-h levels below 180 mg/dl, and 2-h levels below 135 mg/dl (capillary whole blood). Overt diabetics were defined as those having a fasting blood glucose level exceeding 130 mg/dl; 60% also had such symptoms as thirst, pruritis, weight loss, and tiredness. A borderline group (GTT diabetics) was defined as those whose fasting levels were below this but whose 1-h glucose levels exceeded 180 mg/dl and whose 2-h glucose levels exceeded 135 mg/dl; 16% of these had mild diabetic symptoms. Finally, the remainder of individuals was classed in several groups with more minor degrees of glucose intolerance; no symptoms were reported in this group. The persons found to have overt diabetes were referred to their physicians. Subjects in the other categories were told they were normal and no treatment was advised.

The latter subjects were followed-up at 5 and 10 yr after the original tests, and, at 10 yr, 382 subjects (83% of those still alive and available for testing) were readministered the OGTT. Over the 10-yr period, no individuals in the normal group converted to overt diabetes, 60% remained in the normal category, and the remainder showed only slight deterioration of their glucose tolerance. Fifty percent of the borderline group remained in their original category and 5% reverted to normal; 45% decompensated to overt diabetes, an average of 4.5% per year, similar to that found by O'Sullivan and Mahan, above. Of the persons in the group with glucose intolerance intermediate between normal and GTT diabetic, only 4% decompensated to overt diabetes during the 10-yr period; 30% reverted to normal, 16% progressed to GTT diabetes, and 50% remained in their original category.

A third long-term study[35–39] was conducted in Bedford, England, in which a modified OGTT (a single capillary blood glucose measurement two hours after a 50-g glucose dose) was carried out on a sample of 1509 individuals of the resident population of 38,400 persons older than age 21. In addition, full 2-h 50-g OGTTs were conducted on an age-stratified sample of 542 persons in the population. The 2-h blood glucose level (capillary whole blood) was used to divide the subjects into three groups: 128 individuals with 2-h blood glucose levels greater than 200 mg/dl were classified as definitely diabetic; 228 persons with 2-h blood glucose levels between 120 and 200 mg/dl were classified into a borderline group; the remainder, with 2-h levels below 120 mg/dl, were classified as normal. The frequency of arterial disease symptoms was compared in the three groups; there was a clear trend for the prevalence of arterial disease symptoms and electrocardiographic abnormalities among the diabetics to exceed normals by about two- to threefold, with the borderline group occupying an intermediate position. The borderline group was followed for 8½ yr with examinations at 6-mo intervals, and, at the end of this period, 8.5% had decompensated to overt diabetes, an average rate of 1% per year. Individuals with sustained impaired glucose tolerance did not develop the visual or renal complications of diabetes, although they showed increased susceptibility to atherosclerotic disease. This increased susceptibility, in large part, was associated with known risk factors for arterial disease, including hypertension, hyperlipidemia, adiposity, and aging.

In another British study,[40–42] 204 male civil servants whose 2-h postglucose capillary blood glucose levels fell

between 110 and 200 mg/dl were followed for 8 yr, with regular ophthalmoscopic examinations. During this period, the classic complication of diabetic retinopathy was not observed in this group of borderline diabetics.

In studies where postprandial blood glucose has been measured, it has been shown that the risk of decompensation to diabetes over time is related to the initial blood glucose level.[43] However, the rate of decompensation in persons even with the highest glucose levels (>170 mg/dl) averaged only 2% per year over the 20 yr of observation.

The systematic survey of the Pima Indians over the past 14 yr[28] has revealed that the PG levels 2 h after an oral glucose load can differentiate diabetics from nondiabetics. The population can be divided into two groups, one with a distribution of 2-h levels below 200 mg/dl, and the other with a distribution above 240 mg/dl. The presence of diabetic symptoms and the complications of retinopathy and nephropathy are largely confined to the second mode, i.e., in persons whose 2-h PG levels are 240 mg/dl or higher, indicating that this value represents a suitable division between true diabetes and lesser degrees of glucose intolerance. Individuals in the diabetic mode seldom regress spontaneously to lower 2-h levels, but persons in the first mode develop diabetes at a rate proportional to their initial 2-h PG level (e.g., risk of diabetes in persons whose initial 2-h levels were 160–199 mg/dl was about three times that of persons with lower 2-h levels). However, even in this population with the greatest known prevalence of diabetes, the highest age/sex-specific rate of decompensation to overt diabetes is only 3% per year.

When the 2-h levels in the Bedford population are plotted on a log/log scale,[44] there are indications of a second distribution curve, starting at a level of 200 mg/dl. Similar indications have come from a South African survey of nearly 3000 persons.[44]

In view of the relatively slow rate of progression of persons in the intermediate range of glucose intolerance to overt diabetes (only 1%–5% per year), the low frequency of diabetic symptoms in this group, the rarity of clinically significant microvascular disease, and the probability of persons in this group to revert to normal glucose tolerance or to remain in the intermediate ranges, it is difficult to justify the classification of these individuals as diabetic. Rather, these persons, many of them elderly, more logically fall into a category of impaired glucose tolerance and are at higher risk than the general population for developing diabetes (see below).

It is thus recommended that the term diabetes mellitus be restricted to those persons who have (1) overt diabetic symptoms and unequivocal hyperglycemia or (2) FPG levels higher than 140 mg/dl on more than one occasion or (3) if FPG is not elevated, PG levels during the OGTT that exceed 200 mg/dl both at 2 h after administration of the glucose dose and at some other time point between time 0 and 2 h, on more than one occasion.

It is anticipated that these criteria may change with future research advances. For example, although 140 mg/dl has been chosen as the FPG value that is definitely diagnostic of diabetes, fasting values between 125 (or 130) and 140 mg/dl probably indicate a degree of abnormal glucose tolerance that has not been assessed fully as yet.

IMPAIRED GLUCOSE TOLERANCE (IGT)

The long-term prospective studies described above provide a scientific basis for defining a condition of IGT, in which FPG concentration is less than that required for a diagnosis of diabetes (i.e., <140 mg/dl), and in which the PG response during the OGTT is intermediate between normal and diabetic. Thus, an OGTT is necessary to place a subject in this class. The detailed criteria are shown in Table 5.

While individuals in this class are not considered to be diabetic, they are at higher risk than the general population for the development of diabetes. In some patients, IGT represents a stage in the natural history of NIDDM (and less frequently of IDDM), and it can be expected that 1%–5% of persons with IGT will proceed to overt clinical diabetes per year. However, many will return to normal glucose tolerance spontaneously, and a proportion remain in this class for many years. Hence, to avoid the psychologic and socioeconomic stigma of the term diabetes, these individuals are more appropriately designated as having IGT, and it is recommended that the terms chemical, borderline, subclinical, asymptomatic, and latent diabetes, which have been applied to persons in this class, be abandoned.

A case for detection of IGT should rest on our ability to intervene in the progression to clinical diabetes, or, to detect diabetes early after it develops and prevent or ameliorate diabetic complications. However, evidence from the long-term prospective study in Bedford, England, gave no indication that treatment with tolbutamide will prevent the development of clinical diabetes in this group. Improvement in glucose tolerance can be effected over the short term by caloric restriction[15] or weight loss[30] in persons with IGT, although the long-term impact on development of clinical diabetes is not known. Although clinically significant renal and retinal complications of diabetes (microangiopathy) are absent in patients with IGT, many studies of such groups have shown an increased prevalence of arterial disease, electrocardiographic abnormalities, and death or increased susceptibility to atherosclerotic disease associated with other known risk factors, including hypertension, hyperlipidemia, and adiposity.[38] Thus, IGT, particularly in otherwise healthy and ambulatory individuals, may have prognostic implications and should not be ignored or taken lightly.

In analogy to the subclasses within diabetes mellitus, it is suggested that the researcher and clinician might find it advantageous to characterize IGT individuals with regard to the presence of conditions or syndromes suspected of inducing glucose intolerance and whether or not obesity is present.

The assignment of an individual to the IGT class requires that at least two blood samples be taken during the OGTT, the 2-h sample and some other sample between ingestion of the glucose dose and 2 h, and that the glucose concentrations in these samples and in the fasting state meet the criteria in Table 5. However, in epidemiologic studies on diabetes, it may frequently be impossible or impractical to meet these requirements. Consequently, a modification is recommended, whereby a fasting blood sample should be collected and an additional blood sample should be drawn 2 h after administration of the 75-g glucose dose. If these values meet the criteria in Table 5, the individual can be assigned to the IGT class for epidemiologic purposes.

NORMAL PG VALUES IN NONPREGNANT ADULTS

An FPG concentration equal to or greater than 140 mg/dl has been chosen as the value that is definitely diagnostic of diabetes. Similarly, an FPG concentration of less than 115 mg/dl is considered to be normal. However, it is probable that FPG concentrations between this value and that which is diagnostic of diabetes (≥140 mg/dl) are abnormal and should not be ignored.

Normal glucose tolerance, as measured by the OGTT, is considered to be present when the 2-h PG concentration is less than 140 mg/dl, with no value between time 0 and 2 h exceeding 200 mg/dl. Glucose concentrations above these values but below the criteria for diabetes or IGT should be considered nondiagnostic for those conditions.

DIABETES AND IGT IN CHILDREN*

The presence of the classic symptoms of diabetes, including polyuria, polydipsia, and glycosuria, together with a random PG in excess of 200 mg/dl, is sufficient to make the diagnosis of diabetes in children. In these subjects, an OGTT is not required for diagnostic purposes.

In the absence of these signs and symptoms, there should be clear indications for the need for an OGTT. In asymptomatic and aglycosuric children, routine glucose tolerance testing is not indicated for the detection and diagnosis of diabetes mellitus. When there are clear reasons for administration of the OGTT, it should be performed under the carefully standardized conditions recommended for adults, with a single exception: the dose of glucose administered should be 1.75 g per kilogram ideal body weight, up to a dose of 75 g. The diagnostic criteria under these conditions are more stringent than those recommended for adults: there must be an elevated FPG *and* sustained elevated PG levels during the OGTT, both ascertained on more than one occasion, for a definite diagnosis of diabetes. The criteria for diagnosis of diabetes in children are shown in Table 5.

Available evidence indicates no need for age adjustment of glucose responses to the OGTT (despite abundant evidence that insulin responses do increase with age in normal subjects).

The long-term studies in adults that have been used as a basis for the diagnostic criteria recommended in this paper for diabetes and IGT have not been performed with groups of children. However, a number of investigators who have followed children with chemical diabetes for up to 10 yr have found that between 0% and 10% progressed to diabetes. Those that developed the disease were likely to have had more severe impairment of glucose tolerance at the beginning of the study (although not severe enough to warrant a diagnosis of diabetes) and/or low insulin responses. Attempts have been made to distinguish between progression to IDDM or to NIDDM, and rates of progression to the latter were notably low. Consequently, it is believed that an analogy can be drawn between children and adults, and that IGT is a class to which both can belong.

Clearly, there is a need to examine, both prospectively and retrospectively, the significance of IGT in children and its relationship to development of frank disease and diabetic complications. In the absence of these studies, the recommended criteria for IGT in children are designed so that relatively fewer children will be diagnosed as diabetic. IGT is considered to be present in children with a venous FPG value less than 140 mg/dl and a 2-h postload value in excess of 140 mg/dl, *even if* the 2-h value and some other value between time 0 and 2 h exceeds 200 mg/dl. Thus, emphasis is placed on the fasting glucose value as a criterion for IGT.

GESTATIONAL DIABETES (GDM)

This class is restricted to pregnant women in whom the onset or recognition of diabetes or IGT occurs *during* pregnancy. Thus, diabetic women who *become* pregnant are not included in this class. In addition, after pregnancy terminates, the woman must be reclassified, either into diabetes mellitus or IGT, if her postpartum PG levels meet the criteria for those classes, or into previous abnormality of glucose tolerance (PrevAGT). In the majority of gestational diabetics, glucose tolerance returns to normal postpartum,[45] and the subject can be reclassified as PrevAGT.

GDM is recommended as a separate class because of the special clinical features of the diabetes developing in pregnancy. Patients with asymptomatic, newly diagnosed diabetes in pregnancy, in whom there is no prior adverse obstetric history and in whom good control can be maintained with diet alone, are still at increased risk for perinatal morbidity and mortality.[46] There is also an increased frequency of viable fetal loss.[47,48]

Clinical recognition of GDM is important because (1) in a setting where high risk pregnancies can be managed effectively, therapy can prevent much of the associated perinatal morbidity and mortality,[49] and (2) these women are at higher risk of developing diabetes 5–10 yr after parturition.[45] In about 1%–2% of all pregnancies, gestational diabetes will develop. Indications for giving an OGTT in pregnancy include glycosuria, a family history of diabetes in a first degree relative, a history of stillbirth or spontaneous abortion, the presence of a fetal malformation in a previous pregnancy, a previous heavy-for-date baby, obesity in the mother, a high maternal age, and a parity of five or more.[50] The presence of more than one of these factors is especially indicative of increased risk.

Deterioration of glucose tolerance normally occurs during pregnancy, particularly in the third trimester,[47] and the upper levels of normal are, thus, altered in relation to the values in nonpregnant individuals. The criteria for abnormal glucose tolerance in pregnancy, which are widely accepted in North America, were proposed by O'Sullivan and Mahan in 1964 and were based on data obtained from an unselected group of prenatal patients.[45] OGTTs were performed on 752 pregnant subjects, and the mean value and standard deviation for the fasting, 1-, and 2-h blood glucose were determined. The criterion for an abnormal glucose tolerance was defined as two or more blood glucose values greater than two standard deviations above the mean. These criteria are shown in Table 5. That these arbitrarily set criteria have physiologic significance for prediction of later diabetes was shown by long-term study of 1013 nondiabetic women in

* The international workgroup was fortunate to have members of the Lawson-Wilkens Pediatric Endocrine Society as consultants on the topic of diabetes in children. The above recommendations are the consensus of a number of the members of this Society.

whom OGTTs were performed in pregnancy and at intervals after parturition.[45] Life-table analysis of an 8-yr follow-up of women who met or exceeded the criteria in Table 5 showed that 29% became diabetic in contrast to 17% of those whose glucose levels were below these criteria. The more abnormal the OGTT during pregnancy, the higher the risk of later diabetes. Of those women whose glucose levels during the OGTT were three standard deviations above the mean, the development of diabetes was greatest, 60% becoming diabetic over the 8-yr period. In addition, fetal loss was greatest in pregnancies where the criteria in Table 5 were exceeded.[47]

Although new criteria for the diagnosis of GDM[51,52] have recently been proposed, the workgroup felt that these have not been widely tested. Consequently, no new recommendations are made in this paper for diabetes developing in pregnancy, and the 1964 criteria of O'Sullivan and Mahan are reiterated as the guidelines most commonly accepted in North America.

Certain members of the workgroup felt that greater attention should be paid to pregnant subjects whose PG levels at the 2-h point during the OGTT were between 120 mg/dl and 164 mg/dl. They recommended that such values define a class called impaired gestational glucose tolerance.

TABLE 6
Standards for obesity*

Height (m)	Men: Average† weight (kg)	Men: Weight for body mass index of 27 and for percent desirable weight of 120% (kg)	Women: Average† weight (kg)	Women: Weight for body mass index of 25 and for percent desirable weight of 120% (kg)
1.45			46.0	54
1.48			46.5	55
1.50			47.0	56
1.52			48.5	58
1.54			49.5	59
1.56			50.4	61
1.58	55.8	68	51.3	62
1.60	57.6	69	52.6	64
1.62	58.6	71	54.0	66
1.64	59.6	73	55.4	67
1.66	60.6	75	56.8	69
1.68	61.7	77	58.1	71
1.70	63.5	78	60.0	72
1.72	65.0	80	61.3	74
1.74	66.5	82	62.6	76
1.76	68.0	84	64.0	77
1.78	69.4	86	65.3	79
1.80	71.0	87		81
1.82	72.6	89		83
1.84	74.2	91		84
1.86	75.8	94		86
1.88	77.6	95		88
1.90	79.3	97		90
1.92	81.0	99		92
(ft) (in.)	(lb)	(lb)	(lb)	(lb)
4 10			102	119
4 11			104	123
5 0			107	128
5 1			110	132
5 2	123	149	113	138
5 3	127	153	116	142
5 4	130	158	120	146
5 5	133	162	123	150
5 6	136	167	128	155
5 7	140	173	132	160
5 8	145	178	136	165
5 9	149	184	140	170
5 10	153	189	144	175
5 11	158	194	148	180
6 0	162	200	152	185
6 1	166	205		190
6 2	171	211		195
6 3	176	216		200
6 4	181	222		206

* Based on height without shoes and weight without clothes.
† Recommended weight in relation to height derived from the medium-frame ideal body weight estimates of the Society of Actuaries, Fogarty International Center, NIH, Conferences on Obesity, 1973 and 1978.

PREVIOUS ABNORMALITY OF GLUCOSE TOLERANCE (PrevAGT)

This class is restricted to those persons who now have normal glucose tolerance but who have previously demonstrated diabetic hyperglycemia or IGT either spontaneously or in response to an identifiable stimulus.

The terms latent diabetes and prediabetes have been used in the past to describe persons in this class; however, PrevAGT individuals are not diabetic, and it is recommended that the use of these terms be abandoned, particularly in light of the psychosocial and economic sanctions that would erroneously be placed on these individuals by use of the term diabetes.

Individuals who have been gestational diabetics and have returned to normal glucose tolerance after parturition form an obvious subclass of PrevAGT. Indeed, pregnancy is probably the most commonly encountered metabolic stress associated with the appearance of IGT, and the importance of this state is such that a separate class (GDM) has been recommended for glucose intolerance developing *during* pregnancy. However, after termination of pregnancy, the individual must be reclassified: if glucose tolerance returns to normal, the person should be reclassified into PrevAGT; if it remains at diabetic or impaired levels, the person should be reclassified according to the criteria in Table 5. O'Sullivan and Mahan, in their 8-yr study of 1013 pregnant women, showed that, of gestational diabetics who return to normal glucose tolerance after parturition, it can be predicted that about 30% will become diabetic within 5–10 yr.[45]

Another small, but important, group of individuals in this class are former obese diabetics whose glucose tolerance has returned to normal after losing weight.

Several clinical studies have demonstrated that a large proportion of patients in the acute phase of myocardial infarction have hyperglycemia or impaired glucose tolerance.[53] Hyperglycemia is also common after other traumatic events, including burns,[54] accidents resulting in bone injury,[55] war wounds,[56] abdominal surgery,[57] and infections.[58] Generally, these individuals return to normal glucose tolerance as time elapses after termination of the metabolic stress and should be reclassified as PrevAGT. Since interpretation of the OGTT applies only to otherwise healthy and ambulatory individuals under carefully standardized conditions and not to individuals with acute or chronic illnesses, the initial interpretation of abnormal or impaired glucose tolerance in the states described above has to be questioned.

Apart from studies of former gestational diabetics, there has been little systematic investigation of the later liability of persons who have exhibited transient glucose intolerance to develop diabetes. However, it is likely that this is increased and that there is utility in including all those with a history of glucose intolerance, now normal, in the separate class PrevAGT.

POTENTIAL ABNORMALITY OF GLUCOSE TOLERANCE (PotAGT)

This is a statistical risk class that includes persons who have never exhibited glucose intolerance, but who are at increased risk over that of the general population for development of diabetes for a variety of reasons. PotAGT should never be applied as a diagnosis to a patient, although knowledge of factors that increase risk for diabetes may be of value in counseling nondiabetic patients. The purpose of PotAGT in this classification lies primarily in identifying groups of individuals who could be used in prospective research studies.

Individuals who are at increased risk for NIDDM include (in decreasing order of risk) the monozygotic twin of an NIDDM diabetic; another first degree relative of an NIDDM diabetic—sibling, parent, or offspring; obese individuals; mothers of neonates weighing more than 9 lb; and members of racial or ethnic groups that have a high prevalence of diabetes, such as a number of American Indian tribes. Individuals who are at increased risk for IDDM include (in decreasing order of risk) persons with islet cell antibodies; the monozygotic twin of an IDDM diabetic; the sibling of an IDDM diabetic—HLA identical, haploidentical, and HLA nonidentical; offspring of an IDDM diabetic. The degree of risk for any of these circumstances is not well established as yet, and further studies on groups of persons with these characteristics are needed.

The terms prediabetes and potential diabetes have been used to describe persons in this class. However, glucose

TABLE 7
Recommendations for data to be collected on clinical patients and research subjects

Data Required to Classify an Individual
FPG (fasting plasma glucose)
OGTT (if FPG is normal)
Insulin dependence, ketosis proneness
Height/Weight
Onset during pregnancy (for class GDM)
Previously demonstrated glucose intolerance (for class PrevAGT)
Presence of higher statistical risk for glucose intolerance (for class PotAGT)
Presence of conditions/syndromes in Table 3
Recommendations for Additional Data to be Collected to Describe Clinical Patients or Research Subjects
Age/date of birth
Sex
Race/ethnic origin
Socioeconomic status
Age of onset and date of diagnosis
Duration of diabetes
Type of therapy
Immediate family history of diabetes, specifying whether IDDM, NIDDM, etc.
Degree and type of obesity
Metabolic perturbation, e.g., pregnancy, trauma, infection
Nature and extent of complications
Source of medical care
Suggestions for Other Data Desirable to More Fully Describe Research Subjects
Adherence to therapy (compliance)
Degree of control of hyperglycemia
Extended family history of diabetes, specifying type of diabetes
Insulin secretory response
Glucagon secretory response
Insulin antibodies
Insulin resistance
C-peptide
Islet cell antibodies
HLA type
Other investigations as may be locally available

tolerance is normal in these individuals, and the terms prediabetic or potential diabetic are not recommended, since these convey the meaning that a clinical form of diabetes exists in these persons, which invokes unjustified social, psychological, and economic sanctions. Prediabetes should be used in a retrospective fashion exclusively, referring to the period of life before diagnosis of diabetes.

STANDARDS FOR OBESITY

The definition of obesity is complex and no satisfactory index of obesity has been devised. It has been shown that, of measures employing height and weight, the body mass index (BMI) has the highest correlation with both skinfold thickness and body density. In addition, BMI is linearly related to the index of percent desirable weight (PDW; Figure 2). The latter is derived from the medium frame Ideal Body Weight estimates of the Society of Actuaries, which have been endorsed by several conferences on obesity as recommended standards for weight in relation to height. A PDW of 120% corresponds to a BMI of 25 for men and 27 for women, and it is recommended that obesity be defined as those values equal to or greater than these criteria. Table 6 lists weights for heights that correspond to these criteria. Researchers may wish to report finer divisions of obesity than simply obese and nonobese.

The BMI is not a satisfactory method for assessing obesity in children, since BMI increases with age in nonobese children up to about age 15. Other standards for weight and height in children have been promulgated.[59]

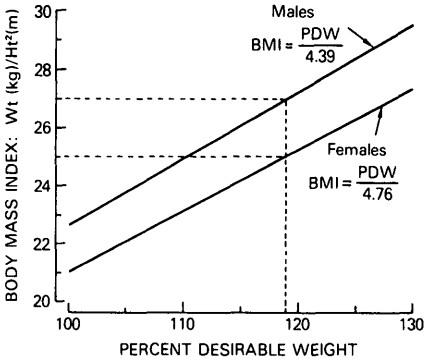

FIGURE 2. Comparison of body mass index (BMI) and percent desirable weight (PDW).

RECOMMENDATIONS FOR COLLECTION OF CLINICAL AND RESEARCH DATA

There is a hierarchy of measurements that can be made on an individual—from the simple set of data and measurements needed to classify a person into one or another of the classes in Table 2—through the demographic and clinical data that more fully describe a subject, which are useful in clinical patient management and are almost necessary for research purposes—to the sophisticated types of measurements, such as islet cell antibodies or insulin secretory dynamics. These levels of information are reflected in Table 7, which delineates the minimal data required to classify an individual, as well as listing recommendations for additional data that more fully describe a subject in a clinical or research setting. It seems both appropriate and potentially

TABLE 8
Provisional research subclassification

	Diabetes Mellitus		
	Association with organ-specific autoimmune disease or autoimmune phenomena	Presence of islet cell antibodies (in relation to onset of insulin dependency)	Characteristics that offer promise of being used to subclassify but require further research
I. Insulin-dependent type (IDDM)			
Subclass a	Positive	Usually persistent	Possible viral etiology; mode of inheritance; genes on chromosome 6 that influence development of IDDM; prevalence of HLA types (elevated or reduced relative to the general population), such as Dw2, Dw3, Dw4, B7, B8, B15, etc.; antibody response to exogenous insulin
Subclass b	Negative	Usually transient	
Subclass c	Negative	Undetected	
II. Noninsulin-dependent types (NIDDM)			
Subclass nonobese Subclass obese	No subclassifying characteristics other than obesity are well enough established at the present time to differentiate within NIDDM diabetes		Insulin levels in the basal state and after stimulation; insulin resistance; receptor defects; alcohol-induced flushing after chlorpropamide

Potential Abnormality of Glucose Tolerance

Individuals at increased risk to develop IDDM (in decreasing order of risk)	Individuals at increased risk to develop NIDDM (in decreasing order of risk)
1. Individuals who are islet cell antibody positive	1. Monozygotic twin of an NIDDM diabetic
2. Monozygotic twin of an IDDM diabetic	2. Other first degree relative of an NIDDM diabetic—sibling, parent, or offspring
3. Sibling of an IDDM diabetic	3. Obese individuals
a. HLA identical sibling (shares both haplotypes)	4. Mother of a neonate weighing more than 4.5 kg
b. Haploidentical sibling (shares one haplotype)	5. Members of racial or ethnic groups that have a high prevalence of diabetes
c. HLA nonidentical sibling (shares no haplotypes)	
4. Offspring of an IDDM diabetic	

useful to collect as much information as is feasible concerning the characteristics in Table 7, in conjunction with standard tests of glucose metabolism, such as the OGTT. Of course, this table represents contemporary knowledge, and it can be expected to change with further research. Table 8 contains subclassifications of IDDM and PotAGT based on recent research findings.[2,60–67] These subclasses should be considered provisional until additional research confirms their identity as distinct subclasses.

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