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CE Issue

New Recommendations for the Diagnosis and Classification of Diabetes Mellitus

New recommendations about the diagnosis and classification of diabetes mellitus have been published in the July 1997 issue of Diabetes Care, *marking the first changes since 1979. These recommendations (summarized below by the American Diabetes Association) were made by an expert panel and have been accepted and are supported by the American Diabetes Association, the National Institute of Diabetes and Digestive and Kidney Diseases, and the Centers for Disease Control and Prevention, Division of Diabetes Translation. Comments from two Indian Health Service consultants follow this summary.*

Summary of Major Recommendations

Classification

- Eliminate the terms "insulin-dependent diabetes mellitus" (IDDM) and "non-insulin-dependent diabetes mellitus" (NIDDM).
- *Keep the terms "type 1" and "type 2,"* but use Arabic, rather than Roman, numerals.
- Type 1 diabetes is characterized by beta cell destruction, usually leading to absolute insulin deficiency. It has two forms: Immune-Mediated Diabetes Mellitus and Idiopathic Diabetes Mellitus. Immune-mediated diabetes mellitus results from a cellular-mediated autoimmune destruction of the beta cells of the pancreas. Idiopathic type 1 refers to forms of the disease that have no known etiologies.
- Type 2 diabetes is defined as a term for individuals who have insulin resistance and usually have relative (rather than absolute) insulin deficiency. People with type 2 diabetes can range from predominantly insulin resistant with relative insulin deficiency to predominantly deficient in insulin secretion with insulin resistance.
- *A new stage of impaired glucose homeostasis called "impaired fasting glucose" (IFG) has been defined* as a fasting plasma glucose of ≥110 mg/dl but <126 mg/dl. *The stage called "impaired glucose tolerance" (IGT) is retained*, defined as an oral glucose tolerance test value of ≥140 mg/dl but less than 200 mg/dl. Both IFG and IGT refer to metabolic stages of impaired glucose homeostasis that are intermediate between normal glucose homeostasis and diabetes. Although not clinical entities in their own right (in the absence of pregnancy), they are associated with future diabetes and cardiovascular disease.
- *Gestational Diabetes Mellitus (GDM) is retained*; however, selective screening, rather than universal screening, for glucose intolerance in pregnancy is now recommended (see "IHS Consultants Respond" on page 124). Low-risk women are: less than 25 years of age, normal body weight,

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Table 1. Diagnosing diabetes.

STAGE	TEST: Fasting Plasma Glucose (FPG) (preferred)*	TEST: Casual Plasma Glucose	TEST: Oral Glucose Tolerance Test (OGTT)
Normal	FPG ‹110 mg/dl		Two-hour plasma glucose (2-hour PG) ‹140 mg/dl
Impaired Glucose Homeostasis	Impaired fasting glucose (IFG) = FPG ≥ 110 and <126 mg/dl		Impaired glucose tolerance (IGT) =2-hour PG ≥ 140 and <200 mg/dl
Diabetes	FPG ≥ 126 mg/dl (7.0 mmol/l)†	Casual plasma glucose ≥200 mg/dl (11.1 mmol/l) plus symptoms‡	2-hour PG ≥ 200 mg/dl§

* The FPG is the preferred test for diagnosis, but any one of the three listed is acceptable. In the absence of unequivocal hyperglycemia with acute metabolic decompensation, one of these three tests should be used on a different day to confirm diagnosis.
† Fasting is defined as no caloric intake for at least 8 hours.
‡ Casual = any time of day without regard to time since last meal: symptoms are the classic ones of polyuria, polydipsia, and unexplained weight loss.
§ OGTT should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. The OGTT is not recommended for routine clinical use.

have no family history of diabetes mellitus, and are NOT a member of an ethnic/racial group with a high prevalence of diabetes (Hispanic, African American, Native American, Asian). No change is recommended to the current diagnostic criteria for GDM.

- A fasting plasma glucose of 110 mg/dl has been chosen as the upper limit of "normal" range.

Diagnostic Criteria

- Diagnostic criteria have been modified from those previously recommended (see Table 1). Three ways to diagnose diabetes are possible, but one (the fasting plasma glucose, FPG) is preferred. At this time, hemoglobin A1c (HbA1c) is not recommended for diagnosis.
- An FPG value ³126 mg/dl (confirmed by repeat testing) is diagnostic for diabetes. This recommendation is based on new population-based data showing a sharp rise in adverse outcomes (i.e., microvascular complications) at or near this blood glucose level and an increased risk for macrovascular disease.
- The revised criteria are for *diagnosis* and are *not* treatment criteria or goals of therapy.

Obtaining the Report

To obtain a copy of the complete report ("Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus", *Diabetes Care*, July 1997;20(7):1183-1197) you can call 1-800-DIABETES (1-800-342-2383) or you can access the July issue of *Diabetes Care* through the Internet at www.diabetes.org □

Table 2. Criteria for testing in asymptomatic, undiagnosed individuals.*

Type 1 Diabetes: Testing presumably healthy individuals for the presence of any immune markers, outside of a clinical trial setting, is not recommended.

Type 2 Diabetes: In asymptomatic, undiagnosed individuals, testing for diabetes should be considered in all individuals at age 45 years and above and, if normal, it should be repeated at 3-year intervals.

Testing should be considered at a younger age, or be carried out more frequently, in individuals who:

- are obese ≥120% desirable body weight or a body mass index (BMI) ≥27 kg/m²].
- have a first-degree relative with diabetes.
- are members of a high-risk ethnic population (African American, Hispanic, Native American, Asian).
- delivered a baby weighing ›9 lb, or were diagnosed with GDM.
- are hypertensive (≥140/90).
- have an HDL cholesterol level ≤35 mg/dl and/or a triglyceride level ≥250 mg/dl.

The FPG is the preferred diagnostic test because of its ease of administration, convenience, acceptability to patients, and lower cost.

* Adapted from *Diabetes Care*, Volume 20, Number 7, July 1997, p.1193.

Continuing Education Available In This Issue

The Indian Health Service (IHS) Clinical Support Center (CSC) has been in the business of providing independent study continuing education activities (through the mail, on request) to physicians and nurses caring for American Indians and Alaska Natives for over 15 years. We have often considered making such continuing education available in conjunction with articles published in *The Provider*.

With this issue, the IHS CSC is initiating this type of continuing education (CE) activity, as the articles this month are particularly suitable for this type of endeavor. Readers can read "New Recommendations for the Diagnosis and Classification of Diabetes Mellitus," "IHS Consultants Respond," and "Preserving the Diabetic Kidney," complete the post test and evaluation on page 135 , and mail, with your name and address, to the IHS Clinical Support Center, 1616 East Indian School Road, Suite 375, Phoenix, AZ 85016 (or fax to 602-640-2138). Those passing the post test (passing score = 70%) will receive a certificate of continuing education in the mail.

In the future, whenever appropriate, the editors will make such continuing education available free to physicians, nurses, physician assistants, nurse practitioners, and nurse midwives who work at IHS or urban Indian programs, or at tribal facilities that have contracted or compacted and have *not* taken their share from the CSC budget.

For those individuals who work for a compacted tribe that *has* taken their share of the CSC budget, there will be a $15 fee for participation in each module. The payment of this fee must come from the tribe.

Additional copies of the post test and evaluation are available from the CSC Fax Retrieval Service. To obtain these, call 602-640-2140, then request transfer to the Fax Retrieval Service (or press 8 during any telephone auto attendant greeting). For the post test and evaluation form, press 5010 when asked to select a document; listen to the instructions, then press the pound sign if you selected the correct document. You will need to have your fax number handy. When requested to do so, enter your phone extension number (since no name will be on the fax sent) and then the fax number; the form will be faxed to you within minutes.

Currently, only individuals employed by the IHS or the tribes may participate in the continuing education activity.

Dates:
Continuing education credit for this activity is valid anytime from August 15, 1997 through August 14, 1998.

Goal:
To update knowledge about the diagnosis and classification of diabetes, and the preservation of the diabetic kidney.

Objectives:
At the completion of this activity, participants will be able to:
1. describe changes of clinical importance in the diagnosis and classification of diabetes.
2. describe the stages, causes, and diagnosis of diabetic nephropathy.
3. discuss prevention and treatment of diabetic nephropathy.

Accreditation:
The Indian Health Service (IHS) Clinical Support Center (CSC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing education for physicians. The IHS CSC designates this continuing education activity for 1 hour of Category 1 credit toward the Physician's Recognition Award of the American Medical Association.

This Category 1 credit is accepted by the American Academy of Physician Assistants and the American College of Nurse Midwives.

The IHS CSC is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation. This activity has been awarded 3.6 contact hours for nurses.

IHS Consultants Respond
Diagnosis and Classification of Diabetes Mellitus

Brenda A. Broussard, RD, MPH, Acting Director, IHS Diabetes Program, Albuquerque, New Mexico.

The IHS Diabetes Program supports and adopts the new recommendations for the diagnosis and classification of diabetes announced June 23, 1997 by the American Diabetes Association. William Knowler, MD, DrPH, Principal Investigator for the Southwest American Indian Diabetes Prevention Program (DPP), National Institutes of Health (Phoenix, Arizona), served on the international expert committee on the diagnosis and classification of diabetes mellitus, working under the sponsorship of the American Diabetes Association.

What do these changes mean for you, the provider, and the Native American peoples and communities you serve?

1. *New Terms*. Familiar terms to you, type 1 and type 2 diabetes replace the confusing terms, IDDM and NIDDM. *Note: Arabic numerals*.
2. *New diagnostic recommendations* urge a simpler, quicker test (fasting plasma glucose, FPG) to screen for diabetes, with the cutoff point lowered to 126 mg/dl (7 mmol/dl) rather than 140 mg/dl used previously. FPG is much easier to obtain and less subject to day-to-day variation than is the oral glucose tolerance test. A fasting blood sugar of ≥126 mg/dl is consistent with a 2-hour postprandial value ≥200 mg/dl and is likely to identify people with "early" microvascular complications of diabetes.
3. The *Native American population*, in general, is *at high risk* for diabetes.
4. *Testing recommendations* urge providers to be "thinking diabetes" when routinely assessing the health and well-being of all adult patients. Because Native Americans are at high risk for diabetes, having a high index of suspicion is even more important.

Today, diabetes has reached epidemic proportions among Native Americans. Early diagnosis and tight control of blood glucose levels, as close to normal range as possible, are essential to help people live well with diabetes and reduce their risk of diabetic complications.

Patient education is critical. People with diabetes can reduce their risk for complications if they are educated about their disease, learn and practice the skills necessary to better control their blood glucose levels, and receive regular checkups from their health care team.

Bernadine Tolbert, MD, PhD, Chief Medical Officer, IHS Oklahoma Area, Oklahoma City, Oklahoma.

We have known for some time that several complications of diabetes begin to develop prior to the diagnosis of diabetes; it is only logical to assume that the diagnosis of diabetes is not occurring early enough. It is hoped that by detecting diabetes early, with a fasting blood glucose of 126 mg/dl instead of 140 mg/dl, we may get a 3- to 5-year jump on the development of complications. After all, the complications of diabetes are what make the disease so serious.

The designations type 1 and type 2, instead of IDDM and NIDDM, should decrease some of the confusion that exists between the two types. More importantly, it shifts the emphasis from the treatment modality to disease etiology. It could be argued that a shift to a focus on disease etiology will be accompanied by an emphasis on treatment approaches that addresses etiology (i.e., insulin resistance and an insulin secretory defect in type 2 diabetes).

The new criteria for testing for diabetes emphasize the importance of testing asymptomatic Native Americans and other high-risk ethnic populations before 45 years of age.

We are seeing increasing numbers of adolescents and children with type 2 diabetes; hence we must be on constant alert for diabetes in any symptomatic patient, regardless of age.

Despite the recommendation for selective screening for gestational diabetes, all American Indian and Alaska Native women should continue to have blood glucose measured during the first prenatal visit, since an elevated level may detect undiagnosed pre-existing type 2 diabetes. The IHS Diabetes Program Standards of care also recommend a blood glucose during the first prenatal visit *and* a screening oral glucose tolerance test at 24-28 weeks of gestation.

Finally, for those who are concerned about "labeling people as having diabetes," it is better to diagnose the condition early in the course of the disease and prevent complications with good glycemic control than to wait until its too late. □

Preserving the Diabetic Kidney

Steve Poirier, MD, Director, Zuni Diabetes Program, Zuni, New Mexico; and Ray Shields, MD, IHS Portland Area Diabetes Control Officer, Portland, Oregon.

Background

Diabetes is the most common cause of end stage renal disease (ESRD) in American Indians and Alaska Natives. This is also true for the US population as a whole, but among Indians the rates are much higher. In Zuni, for instance, the rate of ESRD due to diabetic nephropathy is over 12 times the US rate for all races (personal communication, A. Narva, MD, August 1996). The IHS Kidney Disease Program, using 1996 data from the USRDS (US Renal Data System), has calculated that there is a doubling of new cases of ESRD every 5 years among American Indians.[1] The prognosis for patients with diabetes needing renal replacement therapy in the United States is rather discouraging in that the mortality rate is 50% greater for ESRD patients with diabetes than for those without diabetes.[2-4] However, survival data for American Indians on dialysis are better than for the general US population (personal communication, A. Narva, MD, August 1996).

Providers within the IHS can have an impact on these sobering statistics by supporting diabetes prevention activities and by intervening at the earliest sign of diabetic kidney disease.

Evaluating Renal Preservation Efforts at Your Facility

For a number of years, the IHS Diabetes Program has directed an annual chart audit that examines many process and outcome parameters related to diabetes care. The audit program provides a summary report to each participating facility, as well as Area-wide and IHS-wide summaries. Data on renal insufficiency were previously limited in that the only related parameter recorded was the percentage of patients with diabetes with a serum creatinine >2.0 mg/dl. This may underestimate the number of patients with renal insufficiency in that a serum creatinine of 1.5 mg/dl represents a significant decrease in the glomerular filtration rate (GFR) of a 70 year old 5' 2" woman, for example. In the past year, a supplemental report has been developed to allow a more detailed look at diabetic kidney disease screening and treatment efforts using data that are already present as part of the diabetes audit. It is referred to simply as the Renal Preservation Report; a copy of this report can be obtained from your Area Diabetes Control Officer (see page 131).

The first page of the report looks at various subcategories of blood pressure control and describes the audited population's mean arterial pressure distribution. It identifies the proportion of patients with both controlled and uncontrolled blood pressure who are prescribed an angiotensin-converting enzyme inhibitor (ACE inhibitor). Further, the report describes the distribution of the population's estimated creatinine clearance, and enumerates the proportion of patients who have already begun to advance toward ESRD (i.e., those whose serum creatinine is ≥2.0 mg/dl).

The second page examines the proportion of patients who have had a standard dipstick test for proteinuria, and how many of those found to have proteinuria have been started on an ACE inhibitor. The report also looks at the proportion of those without proteinuria who have been screened for microalbuminuria (see box for definitions), as well as how many with the combination of microalbuminuria and hypertension are on an ACE inhibitor. It compares the ACE inhibitor use by those with microalbuminuria OR proteinuria with those who have neither. It also looks at the glycemic control level for those patients in whom blood glucose control is most critical, namely, those who are without overt nephropathy. Finally, the report includes graphs of the diabetic population's mean diastolic and mean arterial pressures.

It is hoped that this new report will enable a more detailed assessment of the state of kidney function and renal protective efforts in individual service units, individual Areas, and IHS-wide. Service units can target for intervention those areas in which the Renal Preservation Report shows them to be not

Definitions

- **Normal albumin secretion:** (Stage I, II) Albumin excretion of *<30 mg/24 hours* or *<30 mg/g creatinine.*
- **Microalbuminuria:** (Stage III) Albumin excretion of *30-300 mg/24 hours* or *30-300 mg/g creatinine.*
- **Macroalbuminuria/Proteinuria/Nephropathy:** (Stage IV) Albumin/protein excretion *>300 mg/24 hours* or *>300 mg/g creatinine.* Even a "trace" positive urine dipstick is indicative of proteinuria in the absence of contamination or urinary tract infection.

performing ideally. Subsequent reports can serve as outcome measures for changes in renal preservation efforts. It is also hoped that this report will enable service units, Areas, and the IHS as a whole to more accurately estimate the future ESRD disease burden.

Stages of Diabetic Nephropathy

The progressive stages of diabetic kidney disease are well described in Narva's 1994 *IHS Provider* article.[1] Altered renal blood flow and subtle morphologic changes characterize **Stages I and II**, but these are clinically silent. The onset of microalbuminuria, **Stage III**, is the first clinically detectable stage. This stage is sometimes referred to as "incipient nephropathy" and is thought to be arrestable and perhaps partially reversible. **Stage IV** represents nephropathy, and is the stage when the dipstick is positive for protein. **Stage V** is end stage renal disease, which by definition requires dialysis or transplantation for survival.

In a Micral test, an albumin concentration of 20 mg/l or more is positive

Prevalence of Micro/ Macroalbuminuria

The prevalence of microalbuminuria in patients with type 2 diabetes (non-Indian) is 19%-37%.[5] However, in one study among a population of Pima Indians, 8% of those with normal glucose, 15% of those with impaired glucose tolerance, and 47% of those with diabetes had microalbuminuria or proteinuria.[6] Thus the physiologic changes that precede the diagnosis of diabetes may contribute to the development of microalbuminuria. Fifty-six percent of Pima type 2 patients who had diabetes more than 5 years had microalbuminuria.[6] **1996 IHS diabetes audit data showed that 28% of patients with diabetes had overt proteinuria, and 3% had creatinines of greater than 2.0** (which corresponds to a substantial decrease of GFR, especially in older and thinner patients).

What Causes Micro/Macroalbuminuria?

Prospective studies have shown that poor metabolic control, hypertension, longer duration of diabetes, and cigarette smoking are all risk factors for the development of microalbuminuria.[2,6-9] Conversely, intensive glycemic control in type 1 patients in the DCCT (Diabetes Control and Complications Trial), and in type 2 patients in the Kumamoto study, reduced the occurrence of microalbuminuria by 39% and 70%, respectively.[10,11] Pima studies show that pre-diabetic blood pressure and albumin excretion predict the presence of microalbuminuria after the onset of type 2 diabetes.[12,13] The level of albumin excretion in pre-diabetic patients may indicate renal susceptibility that only becomes manifest in the presence of diabetes. There may also be an inherited susceptibility to renal disease among Pima Indians; proteinuria occurred among 14% of diabetic offspring if *neither* parent had proteinuria, 23% if *one* parent had proteinuria, and 46% if *both* parents had proteinuria.[14,15]

Prognostic Value of Micro/Macroalbuminuria

Patients with microalbuminuria are between 9 and 20 times more likely to progress to nephropathy than patients without microalbuminuria.[2,4,16] All-cause mortality increases 148%, and cardiovascular mortality increases up to 15 fold.[7,17-21] Pima type 2 patients with proteinuria had a death rate 3.5 times as high as those without proteinuria.[22] In one 11-year follow-up study, nearly 70% of patients with diabetes with microalbuminuria developed retinopathy as opposed to none in the group without microalbuminuria.[23]

Screening

The National Kidney Foundation[2] and the IHS Diabetes Program recommend annual screening for the presence of microalbuminuria for all those who are dipstick negative for proteinuria. Recent heavy exercise, nonsteroidal anti-inflammatory drug (NSAID) use, and urinary tract infection may give a false positive test for albuminuria. Quantitative tests include 24-hour urines for albumin, and spot urines for albumin/creatinine ratio. Not as accurate, but easier to obtain in some settings, a Micral® or Micral II® dipstick can be a sensitive screening test to detect microalbuminuria (sensitivity 94% and specificity 87% compared to ELISA, according to package insert). Ward et al[24] found the Micral test to be reliable when compared to 24 hour urine tests for albumin.

In a Micral test, an albumin concentration of 20 mg/l or more is positive. Since the Micral is a screening test, confirmatory testing of a positive result is recommended to establish the diagnosis of microalbuminuria, especially if the use of ACE inhibitors is contemplated. Confirmatory testing is generally done with a timed (4- to 24-hr) urine albumin or urine albumin/creatinine ratio, although other methods may be acceptable.

Results of Intervention Trials

Glycemic Control. The Kumamoto study randomized 110 type 2 patients to intensive or conventional insulin treatment for 6 years. Intensive glycemic control prevented the onset of microalbuminuria compared to conventional treatment, and for those with microalbuminuria, it prevented the progression to proteinuria. The glycemic threshold to achieve this prevention benefit was a HbA1c of <6.5% (see Figures 1 and 2).[10] When compared to the DCCT,[11] the risk reduction in this group of type 2 patients was even more striking than in type 1 patients (70% vs. 39-54% for primary prevention of microalbuminuria). As a comparison, in the 1996 IHS diabetes audit, only 28% of patients with diabetes had a HbA1c <7.5.

Blood Pressure Control. The Modification of Diet in Renal Disease (MDRD) study showed that renal disease pro-

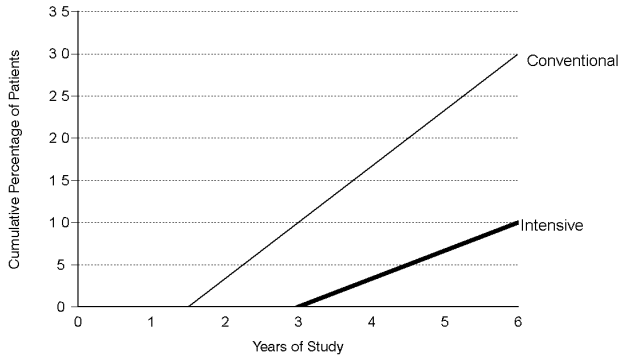
gressed more slowly if the patients' mean arterial blood pressure was kept near 92 (~125/75). This level of blood pressure control may be more important for those with >1g/day of proteinuria than for those with less significant proteinuria.[25] In fact, **in patients with significant proteinuria, blood pressure control cannot be over-emphasized.** It is the single most important element in the preservation of renal function in those with proteinuria and renal insufficiency. In untreated hypertensive patients with diabetic nephropathy, GFR declines approximately 1 ml/min per month; antihypertensive treatment can slow this rate of decline by about two-thirds.[1] The "normal" blood pressure of 140/90 is associated with the progression of renal disease.

All agree on the need for careful control of blood pressure in hypertensive, microalbuminuric, type 2 patients. The goal for patients with diabetes is to maintain a blood pressure <130/85, with further reduction as the patient tolerates.[26] ACE inhibitors are recommended as first line therapy since they lower glomerular capillary pressure through dilation of the efferent arteriole and preserve GFR more than can be explained by their antihypertensive effects.[21,27-29] For those who cannot tolerate an ACE inhibitor, agents such as diltiazem, verapamil, amlodipine, and nicardipine have beneficial effects on albumin excretion, while nifedipine has deleterious effects.[4,27,28,30] Alpha blockers have also been shown to have a beneficial effect on renal function in patients with diabetic nephropathy.[21] Although such agents are too new to have undergone scrutiny, it is expected that the angiotensin-II receptor antagonists will have similar effects to ACE inhibitors in those who cannot tolerate ACE inhibitors because of cough, etc.[31]

Dietary Protein Reduction. Several studies have indicated that dietary protein restriction decreases proteinuria and slows the decline in GFR in patients with type 1 diabetes compared to controls.[32] However, the one controlled trial designed to look at this question (the MDRD study) showed no benefit from protein restriction (although only 3% of the patients had ESRD secondary to diabetic nephropathy and 44% were on ACE inhibitors, which may have obscured the dietary effect). In addition, most of the patients were already consuming 1g/kg/day of protein or less, which is substantially less than most Americans consume.[25] It would presumably be beneficial to reduce the 2 g/kg per day that many Native American patients with diabetes eat to less than 1 g/kg perday; the American Diabetes Association recommends reductions to 0.6 g to 0.8 g/kg per day. This would also help promote weight loss since most animal protein consumed is accompanied by a considerable amount of fat. Other studies have determined that animal protein is more detrimental than vegetable protein.[33]

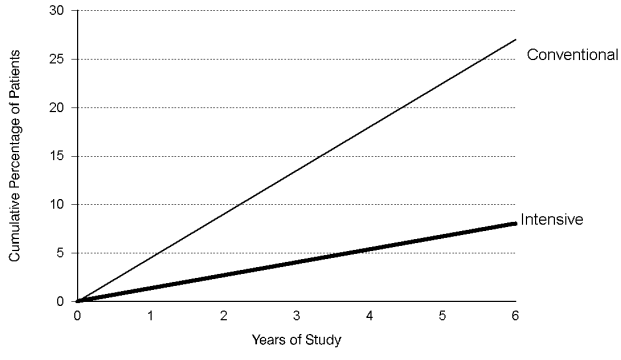
ACE Inhibitor Trials. Ravid et al[34] randomized 94 normotensive patients with type 2 diabetes with microalbuminuria to enalapril 10 mg/day or placebo (double blind) and followed them over 5 years. The enalapril treated patients showed stabilization of their urinary albumin excretion and maintained stable creatinine levels as compared with controls. Enalapril treatment resulted in an absolute risk re-

Figure 1. Nephropathy progression in conventional vs. intensive insulin injection therapy, Primary Prevention Cohort.*



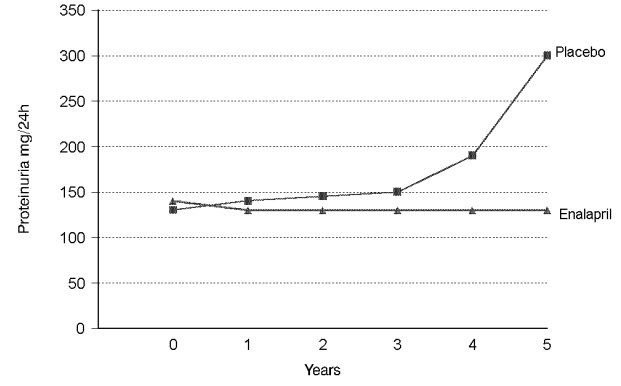
*Adapted from Chkubo, et al[10]

Figure 2. Nephropathy progression in conventional vs. intensive insulin injection therapy, Secondary Prevention Cohort.*



*Adapted from Chkubo, et al[10]

Figure 3. Effect of enalapril treatment on the development of proteinuria in [in normotensive type 2 diabetic patients].



Each point on the curve represents the annual group average of 3 to 4 determinations per patient. Less proteinuria occurred in the enalopril group compared with placebo after the second year ($P < 0.05$ for the second year, $P < 0.01$ for the third year, and $P < 0.005$ for the fourth and fifth years).
*Adapted from Ravid, et al.[34]

duction of 30% for the development of overt proteinuria. The mean blood pressures did not differ between the two groups (see Figure 3).

The authors published a follow-up study 2 years later[35] that showed that patients who stayed on enalapril had albumin excretion rates that were unchanged for the full 7 years of the study; the group that stopped the enalapril had increased albumin excretion. The placebo group that started enalapril for the last 2 years fared better than the group that never got enalapril. This seems to indicate that the earlier an ACE inhibitor is started, the better, and it is never too late to get beneficial effects from an ACE inhibitor. Other researchers have found similar results with both normotensive and controlled hypertensive type 1 and type 2 patients when placed on captopril or enalapril.[36-41] A more recent study shows ACE inhibitors provide protection against progression of renal insufficiency in patients with a variety of renal diseases, not just diabetic nephropathy.[42]

Guidelines for Treatment of Microalbuminuria

The National Kidney Foundation convened an expert panel that reviewed 425 publications to establish practice guidelines for patients with diabetes and microalbuminuria. Their treatment strategy is depicted in Figure 4.

After reviewing these and other recommendations, Mogensen et al[43] concluded that "early ACE inhibition may slow the progression of renal disease in such patients with microalbuminuria, even when blood pressure is 'normal.'" Blood pressure in excess of 130/85 should be considered abnormal, and evidence points to benefits in reductions of blood pressure to a lower level (<120/80 or mean arterial pressure of 92) (see Table 1).[44] Despite these lower target blood pressures, the **1996 IHS diabetes audit showed that at least 34% of diabetics had blood pressures ≥140/90.**

Conclusion

Given the extraordinarily high rate of ESRD among American Indians and the estimated doubling of new cases every 5 years, the most aggressive approach that is supported by the medical literature should be taken to stem this epidemic. This includes support and advocacy for diabetes prevention activities, and screening and treatment for those diabetic patients with micro- and macroalbuminuria. For the normotensive patient with type 2 diabetes with microalbuminuria, the minimal treatment should be aggressive attempts at control of glycemia with a goal of HbA1c < 7.0 in appropriate patients.

Table 1. Evidence-based treatment strategies for microalbuminuria in patients with type 2 diabetes.

	Normotensive	Hypertensive
Microalbuminuria	Glycemic Control Consider ACE inhibitors Close BP monitoring	Glycemic Control BP goal <130/85 ACE inhibitors
Proteinuria	Glycemic Control ACE inhibitors Protein ~10% of calories Close BP Monitoring	Glycemic Control ACE inhibitors; **BP goal <130/85** Protein ~10% of calories <2 g Na diet
Chronic Renal Insufficiency*	ACE inhibitors† Protein ~10% of calories Close BP Monitoring	ACE inhibitors†; **BP goal <125/75**[45] Protein ~10% of calories <2 g Na diet Loop diuretic helpful[46]

Note: NSAIDs and cigarettes should be avoided in all patients. Tight glucose control has been shown to slow disease progression at all stages up to and including proteinuria.[15,47,48]

* Use ACE inhibitors with caution (if at all) in those with creatinine > 3 mg/dl.

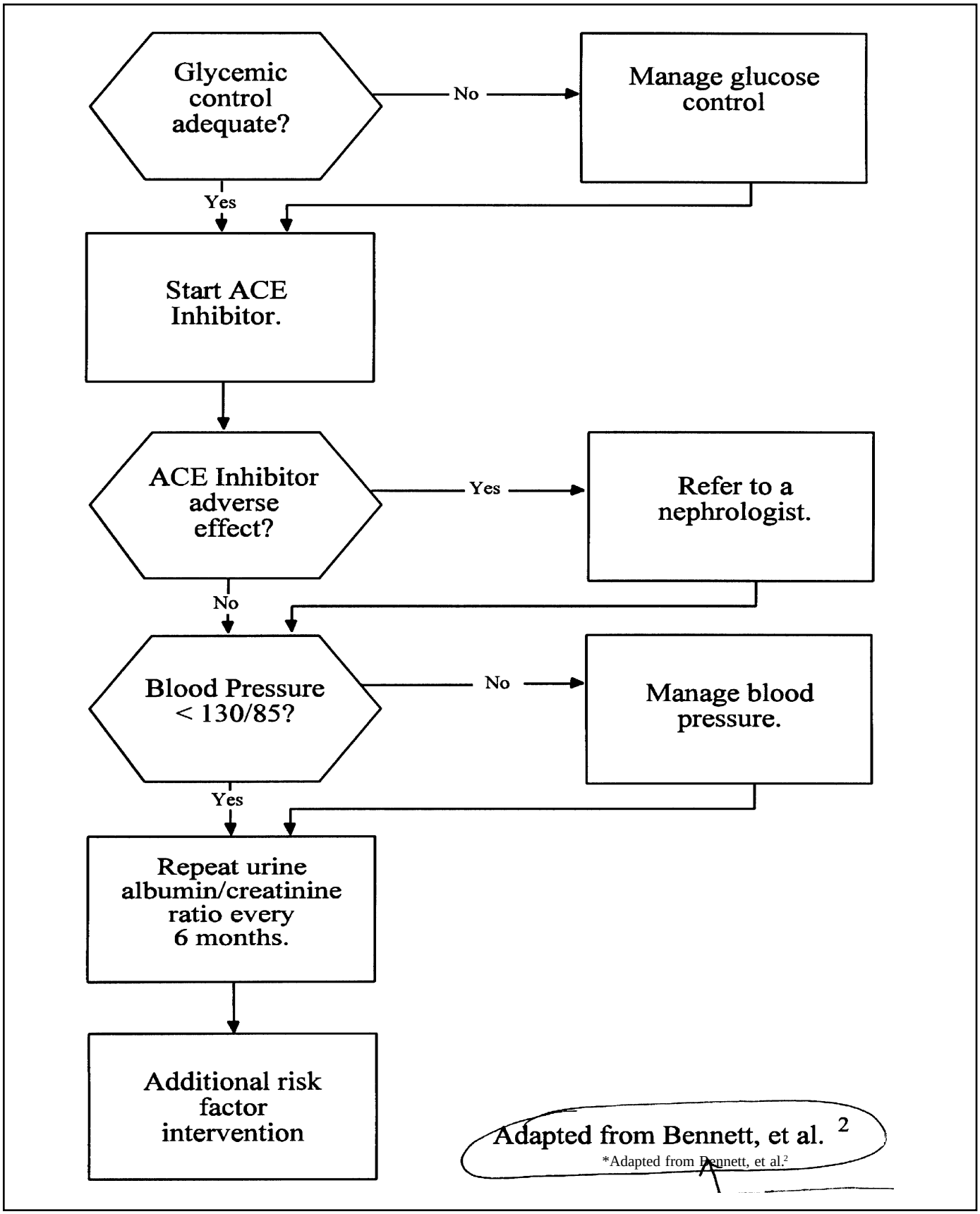
† Chronic renal insufficiency is defined as a serum creatinine >1.5 mg/dl or a calculated creatinine clearance of < 80% of expected. A creatinine of 1.5 mg/dl for example, would calculate to a creatinine clearance of only 27 ml/min in a 5' 2" 70 year old woman using the following formula:

$$\text{Males: CR Cl (ml/min)} = \frac{(140\text{-age})\ (\text{LBW}^{\ddagger})}{(72)\ (\text{Serum Cr})}$$

Females: As above x 0.85

‡ LBW (lean body weight): Males = 50 kg/5 ft + 2.3 kg/inch; Females = 45 kg/5ft + 2.3 kg/inch

Figure 4. Treatment strategy for microalbuminuria.*



*Adapted from Bennett, et al.[2]

There is support in the literature for the treatment of these patients with an ACE inhibitor, although at present the research data are not adequate to mandate this as a standard of care. Blood pressures of greater than 130/85 should be considered abnormal, and every attempt should be made to reduce blood pressures in patients with diabetes below this value. Patients with renal insufficiency should have a blood pressure goal of less than 125/75. □

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Cancer Prevention Fellowship Program

The *Cancer Prevention Fellowship Program*, sponsored by the National Cancer Institute (NCI), offers a unique opportunity for physicians, other clinicians, and PhDs to train in the field of cancer prevention and control. The program offers Master of Public Health training during the first year at accredited universities, followed by independent research opportunities within the Division of Cancer Prevention and Control, NCI, located in the Rockville, Maryland area. The program is 3 years, with the MPH option; up to 3 years without.

Applications for the 1998 Cancer Prevention Fellowship Program must be received by September 1, 1997 (the appointment begins July 1, 1998).

The *Summer Cancer Prevention and Control Academic Course* is a part of the Fellowship Program, but is also open to physicians and scientists from cancer centers, universities, health departments, and industries interested in specialized instruction on the principles and practices of cancer prevention and control. The course is divided into modules that can be attended in their entirety or individually. Prior experience or training in epidemiology is recommended.

To receive a fellowship application catalog or for details on the academic course, contact Douglas L. Weed, MD, MPH, PhD, Director, Cancer Prevention Fellowship Program, Division of Cancer Prevention and Control, Executive Plaza South, Suite T-41, 6130 Executive Boulevard MSC 7105, Bethesda, MD 20892-7105 (phone: 301-496-8640; fax: 301-402-4863).

Free MEDLINE

On June 26, 1997, the National Library of Medicine (NLM) began to provide all Americans with free access to MEDLINE, the world's most extensive collection of published medical information, over the World Wide Web. The web address for NLM is: www.nlm.nih.gov. Prior to June 26th, only registered users who paid for the service could search MEDLINE, an index of over 8.8 million articles from over 3800 biomedical journals. The opening of MEDLINE at no cost to all who can access it means that individuals can search for medical information on topics of interest to them and their families. As consumers become more informed about diseases and the courses of treatment available, they can use that knowledge in making health care choices.

To access MEDLINE, you need a computer, modem, and a service that links you to the Internet.

"PubMed," a free on-line service, will provide direct Web links between MEDLINE abstracts and the publishers of full-text articles.

Training on MEDLINE is currently being discussed. If you are interested in MEDLINE training, send an e-mail to Lois Steele, MD at lsteele@smtp.ihs.gov or call 520-295-2478 so we can assess the amount of interest in this training.

Note: This does not change the prearranged Lonesome Doc access for the IHS *Information Portal Project* participants.

Continuing Education Test Number 1

Diabetes Update

1. One of the two forms of type 1 diabetes, idiopathic diabetes mellitus has no known etiology.
   A. True.
   B. False.

2. Type 2 diabetes is defined as a term for individuals who have insulin resistance and usually have relative insulin deficiency.
   A. True.
   B. False.

3. Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) refer to metabolic stages of impaired glucose homeostasis and are associated with future diabetes and cardiovascular disease.
   A. True.
   B. False.

4. Testing for diabetes in asymptomatic persons from high-risk ethnic populations, including Native Americans, should begin at age 40.
   A. True.
   B. False.

5. The fasting plasma glucose (FPG) is the preferred test for screening for diabetes. Identify *ALL* that apply to FPG:
   A. Low in cost.
   B. An FPG level of ≥126 ma/dl is diagnostic for diabetes.
   C. Convenient.
   D. Less subject to day-to-day variation than the oral glucose tolerance test.

6. The Renal Preservation Report enables a more detailed assessment of the state of kidney function and renal protective efforts at the local sevice unit.
   A. True.
   B. False.

7. In discussing blood pressure control as it relates to preserving the diabetic kidney, please circle all that apply:
   A. It is the single most important element in those patients with proteinuria and renal insufficiency.
   B. The goal for patients with diabetes is to maintain a blood pressure ≤130/85.
   C. ACE inhibitors are recommended as first line therapy as they lower glomerular capillary pressure.
   D. Alpha blockers have been shown to have a negative effect on renal function in patients with diabetic nephropathy.

8. Patients with renal insufficiency should have a blood pressure goal of less than 125/75.
   A. True.
   B. False.

9. It is estimated that the number of end stage renal disease (ESRD) cases in Native Americans doubles every 5 years, calling for providers to adopt the most aggressive approach that is supported in the medical literature.
   A. True.
   B. False.

10. Women at low risk for gestational diabetes mellitus (GDM) include all the following *EXCEPT*:
    A. Under 25 years of age.
    B. Have no family history of diabetes mellitus.
    C. Are of normal body weight.
    D. Non-Caucasian.

11. The hemoglobin A1c is recommended for diagnosing diabetes.
    A. True.
    B. False.

12. Serum creatinines above this amount may represent a significant decrease in glomerular filtration rate (GFR).
    A. 1.2 mg/dl
    B. 1.5 mg/dl
    C. 2.0 mg/dl
    D. 3.0 mg/dl

13. Risk factors related to the development of microalbuminuria include all of the following *EXCEPT*:
    A. Poor metabolic control.
    B. Male sex.
    C. Hypertension.
    D. Cigarette smoking.
    E. Longer duration of diabetes.

14. A urinary tract infection may give a false positive test for albuminuria.
    A. True.
    B. False.

15. For diabetic patients with microalbuminuria, there is support in the literature for use of ACE inhibitors, although research data, to date, do not warrant their use as a standard of care.
    A. True.
    B. False.

Continuing Education Test Number 1

Diabetes

The Indian Health Service Clinical Support Center offers this continuing education free to physicians, nurses, physician assistants, nurse practitioners, and nurse midwives who work at IHS or urban Indian programs, or at contracted or compacted tribal facilities that have *not* taken their share from the CSC budget.

For those individuals who work for a compacted tribe that *has* taken their share of the CSC budget, there will be a $15 fee for participation in each module. The payment of this fee must come from the tribe by check made out to the Clinical Support Center.

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6. _____	14. _____
7. _____	15. _____
8. _____	16. _____

Rate each question below on a scale of 1 to 5.

1	2	3	4	5
Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

1. ___ I find this method of learning (independent study) effective.
2. ___ The content of the articles was relevant to the objectives.
3. ___ As a result of reading these materials, I feel I am better able to:
   - ___ (a) describe changes of clinical importance in the diagnosis and classification of diabetes.
   - ___ (b) describe the stages, causes, and diagnosis of diabetic nephropathy.
   - ___ (c) discuss prevention and treatment of diabetic nephopathy.
4. ___ The test questions helped reinforce my learning.
5. ___ The total time it took me to read the articles **and** take the test was: _____Hours/minutes
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