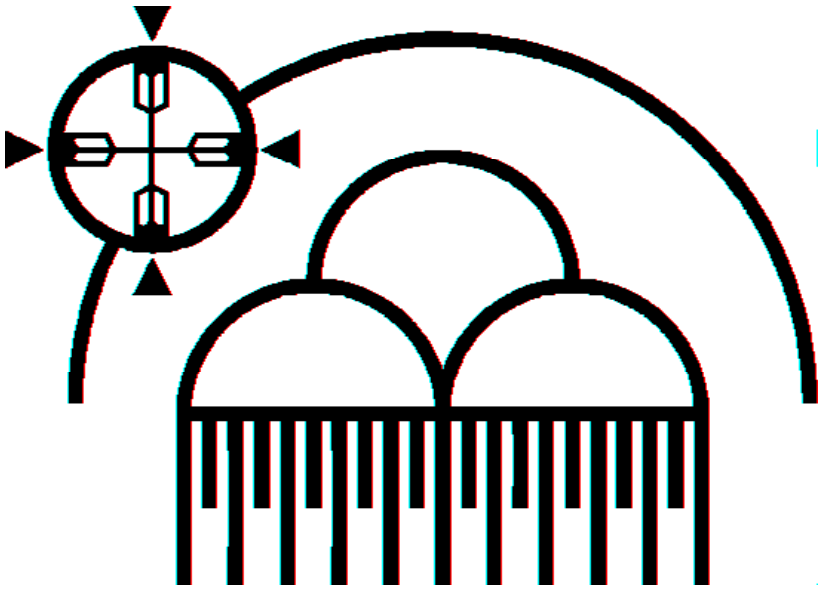
Guidelines
for the Treatment of Dyslipidemias in Native Americans



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December 11-13, 2000, Scottsdale, Arizona

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(issued November 2001)

These guidelines will help reduce the impact of cardiovascular disease in Indian communities," HHS Secretary Tommy G. Thompson said. "Despite improvements in many areas, serious health disparities continue to affect ethnic and racial minorities, including American Indians and Alaska Natives. HHS is working to reduce these disparities through prevention and education efforts like this one." *January 2002*

"In light of the rapid and significant increase in CVD rates among American Indians and Alaska Natives, these guidelines are an important component of the Indian health system efforts to prevent and effectively treat CVD in the Indian population," said Dr. Michael H. Trujillo, Director of the Indian Health Service (IHS). "This is part of a coordinated CVD prevention and treatment effort to help Indian people deal with these issues directly in their communities." *January 2002*

PART I:

Guideline Development Conference

The Treatment of Dyslipidemias in Native Americans

December 11-13, 2000 Scottsdale, Arizona

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Introduction

While the mortality rate for cardiovascular disease (CVD) in the general United States population has declined by more than 50% since the mid-1960's, incidence rates in Native American populations have, unfortunately, increased remarkably during this period. Recent studies of the incidence of coronary artery disease have demonstrated a marked and concerning upward trend with rates now almost double that of the general United States population.

The prevalence of many of the classic risk factors for CVD have likewise been noted to be increasing and appear responsible for this worrisome trend in CVD. Clearly, a number of recent reports have noted a significant increase in the prevalence of hypertension. Tobacco use among Native Americans, especially in the teen years, appears to be increasing. As obesity becomes more prevalent, the presence of the "insulin resistance syndrome," currently referred to as the "metabolic syndrome" is increasing and fuels the current epidemic of diabetes among Native Americans. This epidemic of diabetes, in turn, adds another powerful CVD risk factor. Diabetes appears to be the major risk factor contributing to the rapidly rising rates of CVD in Native Americans.

Many of us working in the field serving Native Americans have noted these events with alarm. We have also noted the simultaneous and significant development of dyslipidemia in this population, as a component of the "metabolic syndrome." Current evidence suggests that dyslipidemias play a major role in the development of CVD and may be more easily amenable to intervention than some of the other risk factors. As a sense of urgency was noted related to these trends in CVD, many of the clinical leaders in Indian Health throughout the nation came together on December 11, 12 and 13, 2000, in Scottsdale, Arizona to address the special issues of lipid management in adult Native American populations and developing a consensus on the optimal approach.

Over 50 of the national leaders in Indian Health were present, primarily physicians, including cardiologists, endocrinologists, internists, nephrologist, and family physicians, as well as nurses, physician assistants, nurse practitioners, nutritionists, dietitians, health educators, and pharmacists. A number of Native American providers and clinicians were present as well as a traditional healer, Mr. Gerard Kisto, were present to assist us in the development of these guidelines. Our efforts were joined by nationally renowned outside faculty, including Dr. Barbara Howard, one of the authors of the American Heart Association Scientific Guidelines of Diabetes and Heart Disease (as well as a Principal Investigator of the Strong Heart Study) as well as Wm. James Howard, MD and Jacque Rossouw, MD, two committee members working on the National Cholesterol Education Program (NCEP) ATP III guidelines. We were also honored to have Drs. Eliot Brinton, Peter Reaven and Johnathan Krakoff work with us in this effort. Over the next eight months, this document has undergone a number of subsequent rounds of clarification and refinement for the development of an optimal set of guidelines through contributions from the participants.

While dyslipidemia intervention is considered vitally important, the group acknowledged there are many additional aspects of CVD and diabetes prevention also requiring additional attention and would be addressed both as part of this conference as well as in future guideline conferences and major preventative efforts.

Several major issues became evident as the conference developed, including the economic impact of the therapeutic interventions considered. Although concerns related to the health care costs have had significant impact nationally related the general US population, the funding limitations within the Indian Health Service are even more stringent. In fact, congressionally allocated funding available for the delivery of health care within the Indian Health Service is only at 71% of the average cost of a mainstream health plan and is $1.3 billion short of parity with a benchmark mainstream health plan in 1999.

However, regardless of funding limitations, the care provided to Native Americans clearly **must** be held to the same standard as the general US population. Unfortunately, due to the high incidence of diabetes in Native Americans, a higher percentage of the population require intervention and preventative therapy than the general US population - with its attendant costs. Nevertheless, due to the high risk of this population, intervention is more cost effective as well.

General overview recommendations from the conference

The participants expressed strong support for the following:

1. Additional and separate line item congressional budgetary funding within the IHS budget to eliminate the disparities between Native American and non-Native American communities in the availability of standard of care medications (in addition to increased general funding support).

2. A **team approach** to CVD risk reduction, incorporating Tribal health directors, nutritionists, dietitians, nurses, pharmacists, educators, physicians and other appropriate staff through well organized and funded interventional programs.

3. The development of a culturally sensitive **public education/health** campaign related to CV (and other chronic disease) risk factor reduction.

Acknowledgements:

The following document is the result of a significant effort by multiple individuals. This consensus statement has been developed through many hours of hard work in an attempt to stem the rising tide of CVD in Native Americans. This manuscript is a tribute to the participants and all those who have spent many hours dedicated to the completion of this project. These efforts are greatly appreciated. This document is dedicated to the Native American people we serve.

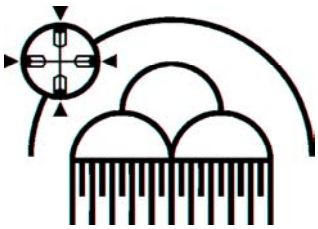
Preface

Several differences will be noted between these guidelines and the recently released Third Report of the National Cholesterol Education Program Adult Treatment Panel III (ATP III), despite having membership crossover in both guideline development panels. A major difference between these two is that our guidelines focus substantially more on the metabolic syndrome than ATP III due to its high prevalence and its major contribution to the increasing incidence and prevalence of CVD among Native Americans. In that light, the lipid goals for those with impaired fasting glucose and the triglyceride goal for those with both diabetes and cardiovascular disease are more stringent than those in ATP III.

Another substantial difference is that we chose to continue to use the risk factor counting approach in determining lipid goals and treatment choices as opposed to the ATP III Framingham risk factor assessment. This preference was made for simplicity of use and because there is no directly applicable risk assessment tool yet available for Native Americans. Additionally, the Framingham risk factor assessment underestimates the calculated CVD risks in Native Americans.

In addition, our committee's setting of an LDL goal of <130 after lifestyle modification for all adults with 2 or more risk factors constitutes a somewhat more aggressive approach than ATP III, as ATP III recommends drug treatment if LDL > 160 after lifestyle modification (with the same goal of < 130) for patients with 10-year risk of less than 10%, although the guidelines have identical recommendations if the individual with 2 risk factors has a 10-year risk of between 10 and 20%. Similarly, our setting a goal of LDL <160 after lifestyle modification for all with 0-1 RF without having a requirement threshold of an LDL >190 constitutes a more aggressive approach than was used in ATP III.

Our committee clearly recognizes that the guidelines we have produced present a somewhat more aggressive approach to the treatment of hyperlipidemia. As the rates of cardiovascular risk factors continue to grow and the incidence of CVD in Native Americans now approaching twice that of the general US population, we feel that this approach is not only justified, but essential to improve the health and prevent the mortality and disability of CVD among Native Americans.



PART 2:
EXECUTIVE SUMMARY
The Treatment of Dyslipidemias in Native Americans

Introduction

The *Lipids Guidelines Conference* addressed the global issues of dyslipidemia in the adult Native American population through several central sessions. More specific, detailed topics were covered in multiple breakout sessions. Each of the breakout groups developed a rough set of guidelines for presentation to the conference group as a whole. These guidelines were then integrated into a set of consensus recommendations. The results of each breakout group, after modification and approval by the entire group, are presented in detail later in this text. Following are the abbreviated summaries of the materials covered and recommendations developed for each breakout subject area and includes the revisions, modifications and endorsements of the entire conference.

Initial Evaluation

Initial evaluation of hyperlipidemia should investigate secondary causes and should include a thyroid stimulating hormone (TSH) measurement, urinalysis, liver function tests, review of current medications, fasting plasma or serum glucose and a history of alcohol use.

Elevated LDL-C

The most effective clinically proven drugs to lower LDL-Cholesterol (LDL-C) are the HMG-CoA reductase inhibitors (statins). Other agents useful in lowering LDL cholesterol include bile-acid binding resins, fibric acid derivatives, and nicotinic acid (niacin).

Recommendations

- The use of the direct LDL-C measurement should be considered for those with diabetes, triglycerides > 250 mg/dL (due to inaccuracy of LDL-C calculations with triglycerides above this level), or when fasting lipids are difficult to obtain. The direct LDL-C measurement is now widely available, relatively inexpensive, and does not require patients to fast. For effective evaluation, fasting lipid levels are also necessary to assess other parameters, including HDL-C and triglycerides, however.

- The following LDL-C goals and actions to meet those goals are recommended:

Risk Level	LDL-C Goal	Action
IFG/IGT/DM/CVD*	<100 mg/dL	Diet/lifestyle/pharmacologic agents
2+ risk factors**	< 130 mg/dL	Diet/lifestyle/pharmacologic agents
0-1 risk factors**	< 160 mg/dL	Diet/lifestyle

**CVD includes patients with a global risk assessment of >20% 10-year risk of CHD. See Risk Assessment module.*
IFG = impaired fasting glucose; IGT= impaired glucose tolerance; DM= diabetes mellitus; CVD= cardiovascular disease
***Risk factors other than LDL-C include: cigarette smoking, high blood pressure (>140/90 mm Hg or on treatment), low HDL (< 40 mg/dL), family history of premature CVD (in first degree males age <55 years and first degree females age < 65 years), age (men > 45 years and women > 55 years or premature menopause without estrogen replacement).*

- The following drug choices (in order of priority) are recommended for primary LDL-C lowering.

1. Statin
2. Resin (if non-diabetic and absence of triglyceride elevation)
3. Niacin formulation (depending on glucose control)

Low HDL & High Triglycerides: The Metabolic Syndrome

The triad of low HDL cholesterol, high triglycerides, and abnormal levels of small, dense LDL cholesterol forms are the dyslipidemias that form part of the metabolic syndrome. A crucial understanding to any discussion of lipid treatment for primary and secondary prevention for CHD is the fact that **diabetes alone (without CHD) represents a CHD risk equal to or greater than known prior CHD. Due to this fact, diabetes is generally considered a "CHD risk equivalent".** Because of the tremendous increases in diabetes and cardiovascular disease noted in Native Americans, early recognition and a low intervention threshold are essential to prevent cardiovascular disease. Because of the increased risk for the entire population of Native Americans, interventions should be considered against a backdrop of the larger intervention of community and individual lifestyle changes.

Recommendations:

Lipoprotein evaluation in patients with known atherosclerosis, diabetes, IGT, IFG, and multiple risk factors should consist of a full lipid profile, including total cholesterol, triglycerides, LDL-C, and HDL. If the patient is diabetic, has significant triglyceride elevation (above 250), or difficulty in obtaining fasting lipids, a direct LDL-C should be considered, rather than a calculated LDL-C from the lipid profile. For effective

evaluation, fasting lipid levels are also necessary to assess other parameters, including HDL-C and triglycerides, however.

The following medications are potential agents for addressing the metabolic syndrome in Native American populations.

- Statins are primarily beneficial when triglycerides are < 400 mg/dL.
- Resins are generally not recommended as primary therapy if triglyceride levels are borderline or high (although they may be used adjunctively when triglycerides are controlled). However, new agents are being released that may prove to be useful in patients with mild hypertriglyceridemia.
- Fibric acid derivatives may be the first choice for patients with triglyceride elevations of greater than 400 mg/dL and some may be considered in combination with statins.
- The use of niacin have been controversial due to concerns over precipitation of diabetes or worsening of glycemic control, although two recent studies have suggested that these issues may be minor.

The group recommends the following treatment goals for Native American patients with the metabolic syndrome:

HDL-C/TG/LDL-C goals	HDL-C		TG	LDL-C
	Male	Female		
Normal Glucose Tolerance	> 40	> 45	< 200	< 130
IGT, IFG, DM without CVD*, CHD without DM	> 40	> 45	< 150	< 100
DM and CVD*	> 40	> 45	< 100**	< 100

**CVD includes: CHD, PVD, and/or other known atherosclerotic events*
All patients with dyslipidemia should be assessed for reversible etiologies, including thyroid abnormalities (assess with a thyroid stimulating hormone, TSH), liver function abnormalities (assess liver function tests), nephrotic syndrome (assess with urine analysis) and, if not already assessed, diabetes as well as levels of alcohol intake and medication use (check for potential dyslipidemic effects).
***Some authors felt that a TG of 150 or less would be a more reasonable goal in this category.*
Diet, weight loss, and physical activity must be integral parts of treatment.

Risk Assessment Methodologies Session

It is often helpful to patients and their providers to have a reasonable assessment of CHD risk for individual risk level identification as well as a motivational tool for patient compliance. In addition, the level of intervention aggressiveness is most appropriate if they are matched to the risk of the individual. It has been suggested that the optimal approach is to divide the 10-year risk of cardiac events into three categories as determined by level of risk: high risk (greater than 20%), intermediate risk (10%-20%), and lower risk (less than 10%). Efforts are underway to develop a more accurate global

risk score for Native Americans. Until this information is available, a global risk score evaluation based on the Framingham data will give us a useful estimate (although likely an underestimate) of the risk of individual Native American patients and may help providers more appropriately treat cardiac risk factors and help public health workers tailor interventions.

Recommendations

- Risk assessment evaluations should optimally be based on 10-year global risk of cardiovascular disease, categorizing patients into high (>20%), intermediate (10%-20%), and lower risk (<10%). However, in the absence of a global risk score for Native Americans, a risk factor counting methodology is indicated and reasonable to initially assess CVD risk.
- Development of a global risk score specific for the Native American population based on the data from the Strong Heart Study, with assessment of the value of a separate global risk score for diabetic patients.
- Lipid levels and risk evaluation in general adult population should be performed at least once every 5 years. For diabetics, lipid levels and risk evaluation should be performed at least annually. More frequent evaluations may be necessary based on clinical considerations such as use of lipid lowering therapy and intervening change in clinical status.
- All non-diabetic patients greater than 45 years of age with cardiovascular risk factors and without contraindications should be on aspirin 81 – 325 mg/day. Diabetic patients over 30 years of age should be on 162 – 325 mg daily, unless contraindicated, due to the increased thrombotic tendencies associated with diabetes.

Cardiovascular Health Promotion Programs Session

Since cardiovascular morbidity and mortality are related to CHD risk factors, it has been postulated that by targeting and aggressively treating secondary and high-risk primary prevention patients to modify or control risk factors, the result would lead to long-term reduction of CHD rates in American Indians. It has been shown that physician directed multidisciplinary programs, where CHD risks were managed by clinical pharmacists, registered nurses or advance practice nurses, were more effective than individual physician management efforts.

Recommendations

- Health promotion programs that effectively “team manage” patient CHD risks are excellent methods to address these concerns in American Indian communities.
- These teams should be multidisciplinary and involve, where possible, physicians and mid-level providers (clinical pharmacy specialists, nurse practitioners, clinical nurse specialists, and/or physician assistants) as well as dietitians and appropriate ancillary staff (diabetes educator, exercise physiologist, etc.).
- Mid-level providers must be certified and current in risk reduction practice.

- Certificate programs should be established and implemented specifically designed to train and update practitioners, covering American Indian cultural, psychological and social values, motivational interviewing, exercise physiology, medical nutrition therapy, weight loss, tobacco cessation, diabetes, hypertension and Dyslipidemias using available national consensus clinical practice guidelines.

Effective Lifestyle Modifications in a Cultural Context Session

Healthy lifestyles that include regular physical activity and balanced nutrition are essential and may be paramount to the health of Native Americans. Lives that incorporate healthy habits on a daily basis will not only improve dyslipidemia, but decrease morbidity and mortality from cardiac disease, prevent other significant medical illnesses, and promote improved mental health and a general sense of well being. The American Heart Association and the American Diabetes Association have both developed guidelines emphasizing weight management, regular physical activity, and individualized dietary recommendations. These recommendations are relevant to Native Americans; however, they need to be tailored to the specific traditions and cultures of Native American communities. In general, a teamwork approach is encouraged. This should include available health professionals, such as dietitians, pharmacists, nurses, physicians, physical therapists, certified diabetes educators, and ancillary heath care staff, as well as local Tribal members. The development of support for these efforts with the Tribal health board and, where appropriate, the Tribal council among other local community is essential.

The Diabetes Prevention Program has recently released their results revealing a striking 58% reduction in the onset of type 2 diabetes mellitus with diet and lifestyle interventions, when compared to an untreated control group. These results were seen in a mixed U.S. population group, including Native Americans, selected for the presence of impaired glucose tolerance as a marker of high risk for the development of type 2 diabetes mellitus.

Dietary Recommendations

- The 2000 AHA Dietary Guidelines should be followed while accommodating the local diets. Specific foci include the following:
  - General reductions in sugar-based beverages.
  - Reductions in total calorie intake.
  - Reductions in total fat, saturated fat, and trans fatty acids.
  - Increases in dietary fiber and complex carbohydrates (whole grains).
  - Increase intake of vegetables and whole fruit.

Implementation of Dietary Changes

- Referral of dyslipidemic and other high-risk patients to a registered dietitian for medical nutrition therapy
- Modeling of healthy food options at hospitals and community facilities.
- Easily understandable community education.

Physical Activity Recommendations

- Guidelines for physical activity from both the Surgeon General and the AHA should be followed with an emphasis upon lifestyle modifications from a culturally appropriate perspective.
- If no contraindications exist, the level of physical activity should be assessed and goals tailored towards a gradual increase working up to 30 to 60 minutes of activity on most, if not all, days per week. In addition, emphasis should be placed on increasing routine non-strenuous physical activity, such as stair climbing (rather than elevator use) and walking, throughout the day.

Obesity Management and Other Lifestyle Recommendations

- It is important to include tobacco cessation as a routine part of health maintenance.
- All patients with a BMI $\geq$ 30.0 or BMI $\geq$ 25.0 with other risk factors or co-morbidities should be offered a formal weight management program.
- Behavior modification, including avoidance of inappropriate use of food
- Diagnosis and treatment of psychopathology (depression, anxiety, etc.) and emotional needs (loneliness, boredom, etc.) through direct, non-caloric means.
- Combined efforts are strongly encouraged; for instance, a combination of moderate physical activity and good nutrition can make substantial contributions to the treatment of hyperlipidemia.
- Two medications appear initially to be safe and effective adjuncts to the above measures for obesity management, orlistat and sibutramine. They could be considered for use in high-risk patients for weight loss and especially long-term maintenance of weight loss.

Public Health and Community Education Session

Community education for dyslipidemia in Native American communities is an essential aspect of an overall effort to reduce the rising tide of CVD in Native Americans. Such education must be addressed at several levels to insure an appropriate and effective campaign.

Recommendations

- The inclusion and guidance of national Native American leaders and organizations is vital.
- Community level education is greatly enhanced by the inclusion and support of local leaders. These may include tribal leaders, tribal council members, traditional healers/medicine people, community health representatives, local health board members, educators, athletes, entertainers, etc.

- The following measures should be taken at the local level:
  - Emphasize proactive/positive message of wellness through lifestyle, diet, etc.
  - Utilize patient role models as examples of treatment successes along with patient support groups for those with established CHD/CVD.
- Identify unique potential settings in which community education can occur.
- Providers must be considered an integral part of the community, both as role models for healthy lifestyles and as participants in the educational process.
- In communities with established medical facilities, we recommend the consideration of the appointment of one health care professional with special interest in cardiovascular risk reduction as a dyslipidemia coordinator (DC), analogous to the diabetes coordinator position already established at many IHS facilities.
- Consider privileging other staff within the hospital to order lipid profiles. RNs, pharmacists and others are in a unique situation to identify patients at high cardiovascular risk and, if allowed to order lipid tests, may help assure that adequate lipid screening is occurring.
- Periodic evaluation of educational program efficacy should be performed, including at least semi-annual assessment of rates of lipid profile and risk factor assessment as well as intervention.

Secondary Prevention Session

Lipid lowering in patients with known coronary artery disease (CAD) is termed "secondary prevention." A crucial understanding to any discussion of lipid treatment for secondary prevention of CHD is the fact that **diabetes alone (without CVD) represents a CHD risk equal to or greater than known prior CHD, and, due to this fact, diabetes is often considered a "CHD risk equivalent." Thus, lipid management goals for diabetics without CAD should be at the levels established for secondary prevention, even without known CAD.** Furthermore, because the risk increases even further in diabetes with established CAD, many suggest that even lower goals could be considered. Previously, coronary atherosclerosis was considered to be a relentless progressive disease, where disability and death from CAD were almost inevitable. In the last decade, numerous multi-center, randomized clinical trials have conclusively proven that lowering elevated low density lipoprotein (LDL) cholesterol levels in patients with established CAD sharply reduces the risk of future MI, revascularization procedures, death from CAD, stroke and death from all causes. The intensity of lipid therapy and its cost effectiveness depends on the patient's clinical risk status, and those patients at higher risk should receive the more aggressive interventions.

Recommendations

- For the diagnosis and management of patients needing secondary prevention a complete lipid profile is required, including total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. If there is diabetes, significant triglyceride elevation (above 250), or difficulty in obtaining fasting lipids, a direct LDL-C should also be strongly considered.

- The goals for lipid lowering therapy in patients needing secondary prevention are listed below.

Lipid Profile Goals in Secondary Prevention.

1. Lower LDL cholesterol to < 100 mg/dL.
2. Raise HDL cholesterol to ≥ 40 mg/dL in men and ≥ 45 mg/dl in women.
3. Reduce triglycerides to ≤ 150 mg/dL (≤ 100 mg/dL if diabetic and CVD*)

* Some authors felt that TG of 150 mg/dl was more appropriate in those with DM and CVD.

- All secondary prevention patients should be referred to a registered dietician for medical nutrition therapy to improve lipid levels and lower the risk of MI and CAD death.
- If no contraindications exist, the level of physical activity should be assessed and goals tailored to a gradual increase, working up to 30 to 60 minutes of activity on most, if not all, days. In addition, emphasis should be placed on increasing routine non-strenuous physical activity, such as stair climbing (rather than elevator use) and walking throughout the day.
- Most patients receiving secondary prevention will require pharmacological intervention in addition to dietary and lifestyle intervention to adequately lower their risk of future CAD events. A summary of lipid therapy recommendations is shown on the following table:

<table>
<tr><td colspan="8">LIPID THERAPY SUMMARY FOR SECONDARY PREVENTION.</td></tr>
<tr><td>LDL-C <
100 mg/dL</td><td colspan="3">LDL-C 100 – 130 mg/dL
Add drug therapy to diet and physical activity as follows:</td><td colspan="3">LDL-C > 130 mg/dL
Add drug therapy to diet and physical activity as follows:</td><td>HDL < 40 mg/dL</td></tr>
<tr><td rowspan="2">Diet and physical activity.
Consider low dose statin.</td><td>TG<200 mg/dL</td><td>TG 200 – 400 mg/dL</td><td>TG>400 mg/dL</td><td>TG<200 mg/dL</td><td>TG 200 – 400 mg/dL</td><td>TG>400 mg/dL</td><td rowspan="2">Emphasize weight loss and physical activity.
Advise smoking cessation.
Consider niacin, fibrates or statins as necessary based on remainder of profile.</td></tr>
<tr><td>Statin. Could also use Resin.</td><td>Statin or Fibrates or combination*, if needed. Could also consider Niacin.</td><td>Fibrates. May combine* with Statins if necessary. Could also consider Niacin.</td><td>Statins.</td><td>Statins. May be combined* with Fibrates (or niacin) if necessary.</td><td>Fibrates. May be combined* with Statins if necessary.</td></tr>
</table>

** with appropriate monitoring, especially liver function tests*

- Patients considered for secondary prevention should be evaluated for ischemia and left ventricular (LV) dysfunction.
- Patients indicated for secondary prevention should take aspirin (unless contraindicated or not tolerated) and often have indications for non-lipid lowering drugs such as beta-blockers, and angiotensin II antagonists.
- Aggressive glycemic and blood pressure control is warranted in patients with diabetes.
- Time must be taken for discussion of clinical concepts and should include the reasons for treatment and therapy goals, in understandable terms. Native-speaking health educators, dietitians, pharmacists and other professionals, as well as key family members, should always be included when possible.

Compliance Development and Recommendations for Counseling Session

Successful treatment of dyslipidemia in Native American individuals requires the development of an interpersonal trust between the provider and the patient as well as similar beliefs related to the importance and effect of the goal. Successful outcomes will result if a variety of methods are used to enhance patient adherence, tailored to the individual, and efforts should be undertaken by local providers to tailor these recommendations according to the local culture and belief systems as well as the availability of resources and the needs of the community.

Recommendations

- Treating patients with dyslipidemia should involve a holistic approach. Providers should treat the whole patient with attention to physical, mental, cultural, and spiritual dimensions.
- Patient education and treatment strategies should be developed which take into account patients learning styles, traditions, values and personal goals.
- Providers should empower patients and encourage self-management.
- Goals for lifestyle change should be developed with the patient, and providers should be attentive to cultural, psychosocial and socioeconomic issues that may present barriers to achieving these goals.

Hypertensive Therapeutic Interventions Session

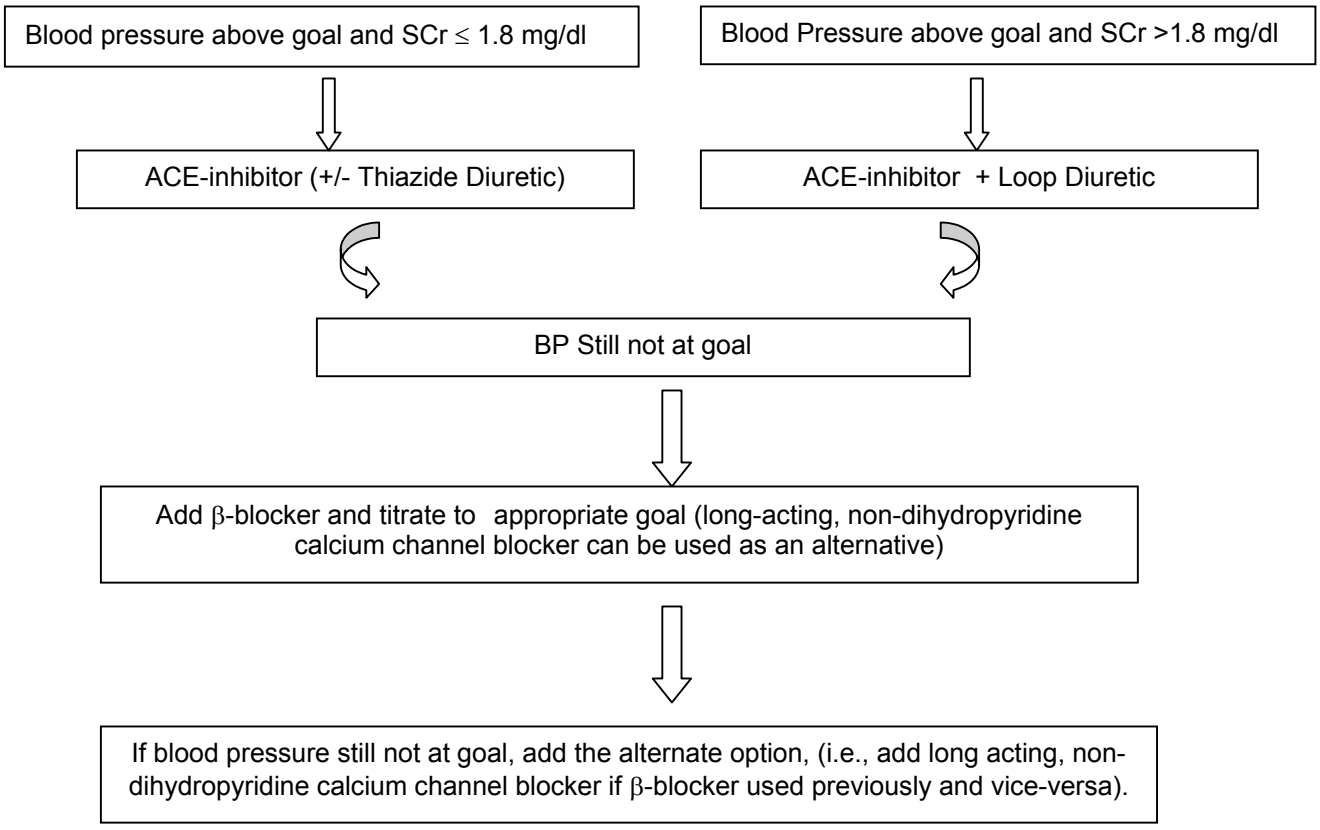
Hypertension is another significant CHD risk factor (which is also a part of the metabolic syndrome) that requires close attention for the prevention of CHD. In fact, results from the UKPDS show that “tight” blood pressure control has a dramatic and beneficial reduction on the incidence of CHD, even to a significantly greater degree than “tight” glucose control. In hypertensive patients, angiotensin converting enzyme inhibitors (ACEI’s) provide a significant additional benefit when compared to other anti-hypertensives with the same level of blood pressure control and, in addition, have generally become the first line agent in hypertensive diabetic patients unless contraindicated or another agent specifically indicated.

A recent NIH-sponsored management conference recommended that ACE inhibitors be initiated in adult diabetic patients with any one of the following: hypertension (>140/90), creatinine>1.5, or proteinuria > 300 mg/day. There is also evidence that treatment of normotensive Type II DM patients with microalbuminuria may benefit from treatment with ACE inhibitors. Angiotensin converting enzyme inhibitors are also indicated for patients post-MI with significant LV dysfunction, or clinical congestive heart failure, as well as diabetic patients with hypertension and/or nephropathy. The recent HOPE Trial suggests that patients at high risk for atherosclerosis, including diabetics, should be strongly considered for ACE inhibitors.

In Type 2 diabetes, if the maximal dosage of the ACE-I (with or without diuretics) does not control the blood pressure to the desired goal of 130/80, the addition of beta blockers, unless contraindicated, is generally preferred over long acting non-dihydropyridine calcium channel blockers by the participants at our conference, unless contraindicated or not tolerated.

The consensus statement attempts to synthesize evidence in the literature into a cost-effective algorithm for non-diabetics and to provide optimal renal and cardiovascular protection to the diabetic patient. Key elements developed at this conference and based, in part, on the NIH consensus were: 1) Blood pressure goal of <130/80 for diabetics, <140/90 in non-diabetics 2) Use of ACE inhibitor as first line agents with appropriate renal monitoring (generally using concurrent if renal dysfunction), and 3) the utility of beta-blockers as second line (unless contraindication or specific indication for another medication), 4) Frequent necessity to use multiple drugs (including diuretics) in diabetics if initial blood pressure is >15/10 mm Hg above goal.

Figure 12. Blood Pressure Goals and Treatment Regimen



PART 3:
The Treatment of Dyslipidemias in Native Americans

FULL GUIDELINES

(November 20, 2001)

I. Elevated LDL-C

Introduction and rationale

LDL-C is the main cholesterol-bearing lipoprotein in the plasma; it transports cholesterol to cells in the vessel wall. Numerous studies have shown that lowering LDL-C cholesterol reduces atherosclerotic plaque and risk for cardiovascular morbidity and mortality. In diabetes, LDL-C concentrations are often not elevated, but LDL-C is altered in size and composition. In association with elevated triglycerides, LDL-C particles are often smaller and more dense. These changes promote entry and retention in the artery wall, as well as oxidation, glycation, and other pro-atherosclerotic modifications and effects.

American Indians have lower average LDL cholesterol levels than the U.S. population. However, there are convincing data in both nondiabetic and diabetic American Indians that LDL cholesterol concentration is a strong predictor of cardiovascular events, and there is a linear relationship between LDL-C and increasing risk for cardiovascular disease (CVD) for LDL-C concentrations >70 mg/dL.[1] In diabetic (compared to nondiabetic) American Indians, LDL-C has been shown to be denser and thus more atherogenic.[2] In comparison to Framingham Heart Study data, the regression line between LDL cholesterol and CVD events is much steeper, indicating that similar levels of LDL cholesterol in American Indians confer greater risk for CVD. (Personal communication, B. Howard and E. Lee, 2001)

Evidence for the benefits of LDL-C lowering

Although no studies have been conducted specifically in American Indians on the safety and efficacy of cholesterol-lowering drugs, there are very convincing data in other populations. The most effective drugs to lower LDL-C are statins. Five large, long-term clinical trials — three for secondary prevention and two for primary prevention — have established their efficacy in lowering LDL cholesterol and cardiovascular and total mortality.[3,4,5,6,7] Secondary analyses in diabetic subgroups confirmed that LDL-C lowering reduced cardiovascular and total mortality to an extent at least approaching, if not greater than, that of nondiabetic individuals. Other agents that are known to lower LDL cholesterol include bile-acid binding resins, fibric acid derivatives, and nicotinic acid/niacin. Of these three classes of agents, colestipol (a bile acid resin),[8] gemfibrozil[9] and fenofibrate[10] (both fibric acid derivatives), and nicotinic acid/niacin[11] were shown in long-term studies to reduce cardiovascular mortality.

Recommendations

1. **Recommendation for use of direct LDL-C measure**
   The use of the direct LDL-C measurement should be strongly considered for those with diabetes, triglycerides > 250 mg/dL (due to inaccuracy of LDL-C calculations above this level), or when fasting lipids are difficult to obtain. The direct LDL-C measurement is now widely available, relatively inexpensive, and does not require patients to fast. For optimal evaluation, fasting lipid levels remain necessary to assess other parameters, including HDL-C and triglycerides.

2. **Recommendations for LDL-C goals and actions to meet goals**

- The following LDL-C goals and actions to meet those goals are recommended.***

Figure 1. LDL-C Goals

Risk Level	LDL-C Goal	Action
IFG/IGT/DM/CVD*	<100 mg/dL	Diet/lifestyle/pharmacologic agents
2+ risk factors**	< 130 mg/dL	Diet/lifestyle/pharmacologic agents
0-1 risk factors**	< 160 mg/dL	Diet/lifestyle

**CVD includes patients with a global risk assessment of >20% 10-year risk of CHD.*
IFG = impaired fasting glucose; IGT= impaired glucose tolerance; DM= diabetes mellitus; CVD= cardiovascular disease
***Risk factors other than LDL-C include: cigarette smoking, high blood pressure (>140/90 mm Hg or on treatment), low HDL (< 40 mg/dL), family history of premature CVD (in first degree males age <55 years and first degree females age < 65 years), age (men > 45 years and women > 55 years or premature menopause without estrogen replacement).*
****Notes:*

- *Appropriate glucose control should be instituted for all diabetics.*
- *Patient input should assist in the determination of the balance of diet vs. pharmacological intervention.*
- *Pharmacologic therapy should be monitored closely in women who may become pregnant.*
- *If CVD and/or diabetes is present, start pharmacologic therapy at same time as diet.*
- *Pay particular attention to women with history of gestational diabetes. Six-month follow-up is important. Such women should receive aggressive lifestyle intervention.*

3. **The following drug choices (in order of priority) are recommended for primary LDL-C lowering**

Figure 2. Drug Choices for LDL-C Lowering:

1. Statin
2. Resin (if nondiabetic and without triglyceride elevation)
3. Niacin (depending on of glucose control)

Notes:
Medications should be based on total lipid profile.
Timing and dose escalation depends of extent of LDL-C increase, CVD, and other risk factors. Consider hepatic function, alcohol use, pregnancy and uric acid levels during drug selection.

II. Low HDL & High Triglycerides: The Metabolic Syndrome

Introduction

Forty percent of patients with myocardial infarctions have an LDL cholesterol (LDL-C) < 130mg/dL. Many of these patients had a triad of low HDL cholesterol (HDL-C), high triglycerides (TG), and excess small dense LDL-C. This triad composes an atherogenic phenotype.[12] These lipid abnormalities are often associated with hypertension, central obesity, and insulin resistance. Together, this combination has been called the metabolic syndrome.

Low HDL-C is a risk factor for coronary heart disease (CHD) independent of LDL-C, hypertension, body mass index (BMI) and smoking.[13,14,15,16] Framingham data suggest that individuals with HDL-C < 35 mg/dL have an eight-fold increased risk of CHD compared to those with an HDL-C > 65 mg/dL. Low HDL-C confers excess risk across all levels of LDL-C.

The case for TG as a risk factor for CHD independent of other risks has been more difficult to establish. In many populations, elevated TGs are a strong risk factor in univariate analysis, but not in multivariate analysis when HDL-C is included in the models. Nevertheless, a recent meta-analysis of 17 population-based prospective studies, which included 46,000 men and 11,000 women, demonstrated a 30% and 75% excess risk for men and women respectively for every 88 mg/dL increase in TG.[17] The excess risk diminished but was still significant after adjustment for HDL-C. The Copenhagen Male Study found increasing risk of cardiovascular events along tertiles of TG even after stratifying by HDL-C.[18] The atherogenic potential of elevated triglyceride levels likely is determined by the particular triglyceride-rich lipoprotein that is in excess. IDL and other remnant particles appear atherogenic, while large VLDL and large chylomicrons appear less so.

Small dense LDL enters the arterial wall more readily and is more easily oxidized than normal-sized LDL.[19] Distinguishing small dense LDL as an independent risk for CHD is difficult because LDL size is highly correlated with TG level.[20] Nevertheless, several studies have found small dense LDL to be a risk factor independent of TG.[21,22]

Rationale

While there are established guidelines for primary and secondary prevention for LDL-C lowering, the treatment of low HDL-C and high TG have been less well studied. The Helsinki Heart Study (HHS) used gemfibrozil for primary prevention of CHD (defined as fatal and non-fatal MI and sudden death).[9] Those treated had a 35% decrease in TG, 9% increase in HDL-C and 8% decrease in LDL-C. Over the 5 year study period CHD was reduced by 34% with most of the reduction occurring in the low HDL/high TG group. Later data analysis suggested that for every 1% increase in HDL, there was 3% decrease in CHD.

The available evidence on secondary prevention in patients with low HDL-C and high TG come from trials using the fibric acid derivatives, which lower TG and raise HDL-C but have modest effects on LDL-C. The Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT) studied young, post-infarct patients with a 90% stenosis and total cholesterol levels of greater than 200mg/dL and TG levels greater than 140mg/dL

randomized to placebo or bezafibrate.[23] HDL-C rose and TG fell but LDL-C did not change in the intervention group. Coronary luminal diameter was stabilized in those treated while coronary diameter narrowing was noted in the placebo group.

The Lopid Coronary Angiographic Trial (LOCAT) randomized subjects post CABG with low HDL-C (< 42.5 mg/dL) to gemfibrozil or placebo.[24] In the gemfibrozil treated group, HDL-C increased 21% and TG decreased by 36%. The number of new lesions in venous grafts was reduced significantly in the treated group. The Bezafibrate Infarction Prevention (BIP) Trial randomized subjects with known CHD aged 45-74 years with HDL-C <40 mg/dl and TG < 300mg/dl to bezafibrate or placebo.[25] There was a nonsignificant trend toward decreased CHD events in the overall intervention group (9% reduction). However in the subgroup with elevated TG > 200 mg/dl, a significant decrease was noted (p=0.002). The VA-HDL-C Intervention Trial (VA-HIT) is the most convincing evidence for use of fibric acid derivatives in secondary prevention.[26] This study recruited 2531 men under age 74 with a history of CHD and HDL-C < 40 mg/dl, LDL-C < 140 mg/dl, and TG <300 mg/dl. Subjects were randomized to gemfibrozil or placebo. The gemfibrozil group had a 22% risk reduction (RR) in fatal and non-fatal MIs; HDL-C rose 6%, TG declined 31% and LDL-C did not change in the intervention group. VA-HIT compares favorably to secondary prevention trials in statins (CARE, LIPID)[4,5] on a numbers needed to treat basis. VA-HIT also had impressive reductions in new stroke (25% RR) and transient ischemic attacks (59% RR). A non-significant trend (11%) toward lower overall morality was also found. Subsequent analysis of VA-HIT has suggested that the RR may be primarily due to the HDL-C effect (S. Robbins; presentation at American Heart Association, 1999). Another study which provides additional support of the aggressive treatment of individuals with diabetes (and in this case CVD as well) is the DAIS study which found that the use of fenofibrate (vs placebo) produced a 23% reduction in combined coronary events with few serious adverse events.[27]

Treatment levels for HDL-C/TG

Defining treatment thresholds and goals for HDL-C and TG is difficult because of the relative lack of clinical trial data in this regard. Therefore, decisions regarding target levels for HDL-C and TG must rely in part upon knowledge of physiology and epidemiologic data. Data from Framingham suggest that low HDL-C is associated with CHD risk across all levels of LDL-C. As HDL increased, the CVD risk decreased in all LDL-C groups.[28] At HDL-C > 45 mg/dl risk of CHD diminished across LDL-C sub-groups and risk for CHD fell even further when HDL was > 65 mg/dl. The feasibility of achieving HDL > 65 mg/dl with current treatment regimens is limited, but HDL-C goals of 40 mg/dl for men and 45 mg/dl for women are more readily achieved and should provide a reduction in CHD risk across all LDL-C levels. VA-HIT findings show that for every 1 mg/dl increase in HDL-C there was an 11% decrease in CHD endpoints.[29] Therefore, even modest increases in HDL offer clinical benefit.

Defining treatment targets for TG is even more difficult. TG level is important in determining LDL-C size and physiologic evidence suggests that change in TG over a range as small as 80-250 mg/dl correlates with a downward shift in LDL-C size. By the time TG levels reach 250mg/dl, 90% of subjects will have a predominance of small,

denser LDL-C particles.[12] Furthermore, data from the Copenhagen Male Study suggest that in men in the middle and highest tertiles of TG had relative CHD risks of 1.5 and 2.2 even after adjustment for such factors as HDL-C and LDL-C. The average TG levels in these tertiles were 78, 118, and 217 mg/dl, suggesting that even TG over 100 conferred excess risk in this population.[18]

Crucial to any discussion of lipid treatment for primary and secondary prevention for CHD is the CHD risk equivalence of diabetes. Diabetes is clearly associated with a marked increase in CHD[30] and likely explains, to a large degree, the rising rates of CHD in Native Americans. The rates among Native Americans are now greater than rates in other community studies.[31] Haffner and colleagues compared the 7-year incidence of myocardial infarction (fatal and nonfatal) in a population of Finnish subjects ages 45-65 with and without diabetes.[32] The 7 year cumulative incidence of MI in subjects without diabetes but with prior history of MI was 18.8%; for subjects with diabetes but no prior MI the rate was 20.2%; for subjects with prior MI and diabetes the rate was 45%. Thus, the conclusion from this study is that subjects in this age group with diabetes should be treated as aggressively from the standpoint of lipid lowering as subjects who have had a prior MI. In addition, diabetics frequently have silent (and often unrecognized) ischemic events and increased post-event mortality as well as higher rates of sudden death compared to non-diabetics.

Approaches to treatment of evaluation/ treatment of high TG and low HDL

Evaluation of patients with high TG and low HDL should be an important part of the treatment plan. Their fasting glucose should be measured to rule out diabetes or impaired fasting glucose. Inquiries into use of other medications (oral estrogens and systemic glucocorticoids in particular), thyroid function testing, liver function tests, urine protein testing, and screening for alcohol use should also be considered. The optimal agent for the initiation of therapy depends on the overall lipid profile and concomitant disorders. LDL-C should continue to receive primary consideration for treatment.

Statins

Statins lower TG in direct proportion to the amount of LDL-C lowering and the baseline TG level.[33,34] The mechanism of TG lowering by statins is likely the same as that for LDL-C lowering, that is, increased removal of TG-rich particles by the upregulated LDL receptor.

Resins

Currently, resins are not recommended if the TG level is borderline or high as these agents tend to increase VLDL synthesis and further raise TG levels. [20]

Fibric acid derivatives

Fibric acid derivatives bind to a family of nuclear hormone receptors called the peroxisome proliferator activated receptors (PPARS).[35] Via these receptors, fibrates induce expression of lipoprotein lipase and decrease expression of apo C-III, enhancing clearance of TG rich particles and VLDL.[36,37] Thus, they are potent TG lowering

medications. They also increase HDL-C via increase in production of the major HDL-C apoproteins.[38,39]

Fibrates are excellent medications for treatment of the high TG/low HDL-C disorder. They may be considered first line agents in patients with low LDL-C or in patients with severe TG elevations (400-1000 mg/dL). Use of fibrates in combination with statins is relatively safe except for the combination of cerivastatin and gemfibrozil, which has prompted the recent withdrawal of cerivastatin from the market. A recent review suggests that the combination of most statins and fibrates results in a rate of myositis of approximately 1%.[20]

Nicotinic acid/Niacin

The use of niacin in patients with the metabolic syndrome is somewhat controversial. Niacin lowers LDL-C, raises HDL-C and lowers TG,[40] but the concern remains the precipitation of diabetes or worsening of glycemic control.[41] Recent data from the ADMIT trial[42] suggest that niacin was safe in subjects with diabetes, raised HDL-C by 29%, decreased TG by 23% and LDL-C by 8%. Subjects with and without diabetes had a small increase in average glucose levels. Diabetic subjects on niacin did not have a change in their hemoglobin A1c (HgbA1c) over the course of the 48 week study period, but their HgbA1c was slightly higher at the end of the study (a difference of 0.3%, p=0.04) compared to the group on placebo.

Glycemic control

Patients with diabetes can have marked lowering of TG with improvement in glycemic control, particularly when the HgbA1C is > 9.0%. TG lowering is less dramatic with lowering of HgbA1C less than 9.0%; lipid lowering agents are generally more beneficial in this group.

Recommendations

These recommendations are based on the concept that much of the cardiovascular disease in Native Americans has as its roots the metabolic syndrome. Because of the tremendous increases in diabetes and cardiovascular disease, early recognition and a lower threshold for intervention may be essential to prevent cardiovascular disease. Because of the increased risk for the entire population of Native Americans, interventions should be considered against a backdrop of the larger intervention of community and individual lifestyle changes. We suggest that the percent of the population “at risk” for this syndrome, and particularly diabetics, is large and lipid values should be judged in that context. For the sake of simplicity and because of the high risk these patients have of developing diabetes as well as the presence of these entities within the metabolic syndrome, we have combined patients with impaired glucose tolerance (IGT) and impaired fasting plasma glucose (IFG) in with diabetic patients. Patients with diabetes and pre-existing CHD remain a distinct category owing to the extreme risk of recurrent events in this group. It should also be noted that diet, weight loss, and physical activity should be integral parts of treatment.

Figure 3. HDL-C/TG Goals.	HDL-C		TG	LDL-C
	Male	Female		
Normal Glucose Tolerance	> 45	> 45	< 200	< 130
IGT, IFG, DM without CVD*, CHD without DM	> 45	> 45	< 150	< 100
DM and CVD*	> 45	> 45	< 100**	< 100

**CVD includes: CHD, PVD, and/or other known atherosclerotic events*

**Some authors felt that less than 150 mg/dl was more reasonable in this category.*

III. Primary Prevention - Risk Evaluation Methodologies

Introduction and rationale

It is often helpful to patients and their providers to have a reasonable assessment of risk for cardiovascular disease for the individual risk level identification as well as a motivational tool for patient compliance. In addition, the level of intervention aggressiveness is most appropriate if matched to the risk of the individual. In particular, lipid treatment guidelines are optimally based on overall risk of cardiac events. The National Cholesterol Education Program Guidelines I and II recommended that lipid treatment be based on three broad categories – those with known coronary artery disease, those with two or more other cardiac risk factors, and those with one or no other cardiac risk factor.[43,44] More recently, several investigators and expert panels have recommended that treatment guidelines be based on not only the presence but the severity of risk factors with the development of a graded, quantitative global risk of future cardiac events.[45,46,47]

Experts suggest that the optimal approach is to divide the 10-year risk of cardiac events into three categories as determined by level of risk: high risk (greater than 20%), intermediate risk (10%-20%), and lower risk (less than 10%). To determine 10-year cardiac risk for individuals without known CVD (i.e. primary prevention), our participants agreed upon the utilization of the subsequently published NCEP Adult Treatment Panel III Framingham Risk Point Scores.[48] Although these are the best data available for this purpose, the data for this risk assessment were derived from the Framingham, Mass. community population a number of years ago utilizing a predominantly white population. This may not accurately reflect the current risks among a different population with a varying prevalence of risk factors and disease incidence, such as Native Americans.[46] In fact, Howard and colleagues have demonstrated that the standard Framingham risk estimates underestimate the risk among Native Americans. (Personal communication, B. Howard and E. Lee, 2001)

A more accurate global risk score for Native Americans is being developed using Strong Heart Study and other study data. In particular, this risk score may incorporate additional markers, such as insulin resistance, triglyceride levels, obesity, and/or

physical inactivity, which may be more relevant for Native Americans. Until this information is available, a global risk score evaluation based on the Framingham data will give us a useful estimate (although likely an underestimate) of the risk of individual patients and may help providers more appropriately treat cardiac risk factors and help public health workers tailor interventions. Below are assessment tools utilized by the National Cholesterol Education Panel ATP III.[48]

Estimating 10-Year Risk for Men and Women

Risk assessment for determining the 10-year risk for developing CHD is carried out using Framingham risk scoring (Figure 4 for men and Figure 5 for women). The risk factors included in the Framingham calculation of 10-year risk are: age, total cholesterol, HDL cholesterol, systolic blood pressure, treatment for hypertension, and cigarette smoking. The first step is to calculate the number of points for each risk factor. For initial assessment, values for total cholesterol and HDL cholesterol are required. Because of a larger database, Framingham estimates are more robust for total cholesterol than for LDL cholesterol. Note, however, that the LDL cholesterol level remains the primary target of therapy. Total cholesterol and HDL cholesterol values should be the average of at least two measurements obtained from lipoprotein analysis. The blood pressure value used is that obtained at the time of assessment, regardless of whether the person is on anti-hypertensive therapy. However, if the person is on anti-hypertensive treatment, an extra point is added beyond points for the blood pressure reading because treated hypertension carries residual risk. The average of several blood pressure measurements, as recommended by the Joint National Committee (JNC), is needed for an accurate measure of baseline blood pressure. The designation “smoker” means any cigarette smoking in the past month. The total risk score sums the points for each risk factor. The 10-year risk for myocardial infarction and coronary death (hard CHD) is estimated from total points.

Figure 4. Estimate of 10-Year Risk for Men (Framingham Point Scores)

Age	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Total Cholesterol	Points at Age 20-39	Points at Age 40-49	Points at Age 50-59	Points at Age 60-69	Points at Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

	Points at Age 20-39	Points at Age 40-49	Points at Age 50-59	Points at Age 60-69	Points at Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Point Total	10-Year Risk (%)	Point Total	10-Year Risk (%)
<0	<1	9	5
0	1	10	6
1	1	11	8
2	1	12	10
3	1	13	12
4	1	14	16
5	2	15	20
6	2	16	25
7	3	≥17	≥30
8	4		

FIGURE 5. Estimate of 10-Year Risk for Women (Framingham Point Scores)

Age	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Total Cholesterol	Points at Age 20-39	Points at Age 40-49	Points at Age 50-59	Points at Age 60-69	Points at Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
≥280	13	10	7	4	2

	Points at Age 20-39	Points at Age 40-49	Points at Age 50-59	Points at Age 60-69	Points at Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

Point Total	10-Year Risk (%)	Point Total	10-Year Risk (%)
<9	<1	18	6
9	1	19	8
10	1	20	11
11	1	21	14
12	1	22	17
13	2	23	22
14	2	24	27
15	3	≥25	≥30
16	4		
17	5		

Recommendations

1. Risk assessment evaluations should be based on 10-year global risk of cardiovascular events, categorizing patients into high (>20%), intermediate (10%-20%), and lower risk (<10%), currently utilizing the Framingham risk scoring. Due to the underestimation of risk utilizing these methods, risk factor counting methods will be primarily utilized for determining appropriate lipid interventions in Native Americans.
2. Development of a global risk score specific for the Native American population based on the data from the Strong Heart Study, with assessment of the value of a separate global risk score for patients with diabetes mellitus. As this becomes available, this will replace the Framingham risk assessment for Native Americans.
3. Lipid levels and risk evaluation in the general adult population should be done at least once every 5 years. For diabetics, lipid levels and risk evaluation should be performed at least annually. More frequent evaluations may be necessary based on clinical considerations such as use of lipid lowering therapy and intervening change in clinical status.
4. All non-diabetic patients greater than 45 years of age with cardiovascular risk factors and without contraindications should be on aspirin 81–325 mg/day. Diabetic patients over 30 years of age should be on 162–325 mg daily, unless contraindicated, due to the increased thrombotic tendencies associated with diabetes.

IV. Cardiovascular Health Promotion Programs

Introduction and rationale

CHD is the leading cause of death in American Indians/Alaska Natives (AI/AN), with rates exceeding other US populations.[31] Since cardiovascular morbidity and mortality are related to CHD risk factors, it has been postulated that by targeting and aggressively treating patients to modify or control risk factors, the result would lead to long-term reduction of CHD rates in American Indians.[31,49,50,51] Healthy People 2010 specifically supports this concept with a goal to "improve cardiovascular health and quality of life through prevention, detection, and treatment of CHD risk factors".[52]

Recommendations

Reinventing the approach to risk management

It has been shown that physician directed multidisciplinary programs, where CHD risks were managed by clinical pharmacists, registered nurses or advance practice nurses, were more effective than individual physician management.[53,54,55,56,57] In the AI/AN population, effective risk management has been demonstrated by the clinical pharmacy specialist/dietitian team.[49,58] The success of these programs is related to variables such as number of visits with the providers, time spent with the patient at each visit, amount of patient education provided, and aggressive risk/goal oriented management.

An optimal intervention includes the development and implementation and of effective health promotion programs that are multidisciplinary in nature, where patients have their CHD risks "team managed". These programs should involve physicians and

mid-level providers (clinical pharmacy specialists, nurse practitioners, clinical nurse specialists, and/or physician assistants) utilizing medical staff approved protocols with appropriate peer review performed by the designated physician consultant. This team should include a dietitian and appropriate ancillary staff (diabetes educator, exercise physiologist, etc.). It is essential for the medial staff to actively endorse cardiovascular health promotion programs, including team approaches with medical staff guidance, and provide a referral base. The support of tribal leadership, the health board, community health representatives, and the service unit administration are also essential to the success of these programs.

Practitioner training and certification

It is essential that mid-level providers be certified and current in risk reduction practice for the team concept to be effective. The Indian Health Service should support the establishment of a certificate program specifically designed to train and update practitioners. Minimally this program will cover the following topics: American Indian cultural, psychological and social values, motivational interviewing, exercise physiology, medical nutrition therapy, weight loss, tobacco cessation, diabetes, hypertension and dyslipidemias using available national consensus clinical practice guidelines. When initiating strategies, certification allows team consensus on cardiovascular health goals, identification, and treatment of high-risk patients.

V. Effective Lifestyle Modifications in a Cultural Context

Introduction and rationale

Healthy lifestyles incorporating regular physical activity and balanced nutrition are essential to the health of Native Americans. Along with weight reduction, improved glycemic and blood pressure control, and an increase in HDL cholesterol will be seen.[68] Through dietary and lifestyle modification one can significantly improve dyslipidemia, minimizing the need for pharmacotherapy or significantly reduce the dosage needed to reach LDL-C goals.[59] LDL-C response to dietary intervention is variable but generally quite modest in Caucasian populations, typically with a 3 to 15% reduction reported.[59,60] However, The Native American Cardiovascular Risk Reduction Program found a 12 to 23% LDL-C reduction through diet and exercise in their population.[59] The American Heart Association (AHA) has established and revised specific well supported recommendations that emphasize weight management, regular physical activity, and "individualized dietary recommendations, involving medical nutrition therapy for specific subgroups."[61] The new 2000 AHA Dietary Guidelines have replaced the previously used AHA Step 1 and Step 2 diets. The American Diabetes Association has also suggested lifestyle modifications that are widely accepted. In addition, the Diabetes Prevention Program has recently released their results revealing a striking 58% reduction in the onset of type 2 diabetes mellitus with diet and lifestyle interventions, when compared to an untreated control group. These results were seen in a mixed U.S. population group, including Native Americans, selected for the presence of impaired glucose tolerance as a marker of high risk for the development of type 2 diabetes mellitus.[62]

These recommendations are relevant to Native Americans. However, they need to be tailored to the specific traditions and culture of Native American communities. For

maximal benefit and compliance, goal implementation should be developed around the strong sense of culture and family. The future health of the individual patient and his family both would greatly improve through family directed lifestyle modifications. Particular attention focusing on educational approaches in the school system would further reinforce these guidelines. The cultural aspects of health care for Native Americans have many advantages that can be mobilized to encourage lifestyle modification. In general, a teamwork approach is more acceptable and encouraged. The broad team of health care professionals, should include dietitians, pharmacists, nurses, physicians, physical therapists, certified diabetes educators, and ancillary heath care staff. Well-validated materials and programs promoting diet and lifestyle modifications for the general US population are available and should be appropriately adapted for local use in the Native American population. Consistency within and between patient-based and community-based education is desirable. This teamwork should strive to achieve community acceptance and should utilize Tribally elected officials and other Tribal leaders. Well-established programs directed at lifestyle modifications exist within Native communities and should be utilized.

Recommendations

Nutrition

Patients with dyslipidemia should be referred to a Registered Dietitian for Medical Nutrition Therapy. The 2000 AHA Dietary Guidelines[61] should be followed while accommodating the local diets. Some specific recommendations that should be consistent across the Indian health care system are as follows:

1. Reduce intake of total fat, saturated fat and trans fatty acids.
2. Reduce the total caloric intake, especially empty calories from simple sugars. In this vein, a general reduction in sugar based beverages is essential, and non-calorie containing beverages with specific attention to water should be emphasized.
3. Increase the intake of dietary fiber and complex carbohydrates (whole grains), fruits and vegetables.
4. Hospitals and community facilities should set examples. Some specific examples are providing healthier options in vending machines and at tribal and community events. Providing lower-fat dairy products and healthy meals for patients, staff and visitors should be considered.
5. Individual and community education should emphasize easily understandable materials and techniques. For example, one teaching aide uses a pie chart to represent a dinner plate in which half of the plate is filled with vegetables and fruit, one quarter with a starchy food, and the remaining quarter with lean protein.[63]
6. Contact the Indian Health Service and the National Diabetes Program for educational materials.[64]

Physical activity

Guidelines for physical activity from both the Surgeon General and the AHA should be followed with an emphasis upon lifestyle modifications.[61,65] Any individual with known disease will need physician written approval before beginning an exercise program and, ideally, all high risk individuals should have physician consultation prior to

exercise program initiation as well.[66] If no contraindications exist, the level of physical activity should be assessed and goals tailored towards a gradual increase working up to 30 to 60 minutes of activity on most, if not all, days per week.[67] The physical activity sessions can also be broken up during the day to equal the total 30 to 60 minutes. In particular, these changes should be directed at lifelong changes and should begin as early in life as possible. In addition, emphasis should be placed on increasing routine non-strenuous physical activity, such as stair climbing and walking, throughout the day. Physical Education throughout school should be required from kindergarten to completion of high school, while involvement in competitive and recreational sports should be encouraged. Finally, identification and resumption of traditional fitness activities should be highly promoted.

Tobacco cessation

Prevention and cessation of tobacco is critical to effective health promotion. All people who abuse tobacco must be counseled to stop. The level of addiction and readiness to quit should also be assessed. Medications for assistance in cessation are effective, and should be encouraged as a routine part of smoking cessation efforts. If available, refer to a smoking cessation program. Tobacco prevention and cessation education efforts should begin with children and adolescents. Finally, while specific efforts for smoking cessation may be directed at the individual, community efforts should be continuously emphasized. We encourage that all public buildings be smoke free and economic dependence on the sale of tobacco should be de-emphasized.

Obesity prevention and treatment

The Body Mass Index (BMI) should be used to identify obesity and guide its treatment. BMI $\geq$ 25.0 but $\leq$ 29.9 is defined as overweight, BMI $\geq$ 30 but $\leq$ 40 is defined as obese, and BMI $\geq$ 40.0 is defining as extreme obesity.[68] In addition to BMI, the presence of other comorbidities to obesity needs to be assessed. Accurate measurements of height are required. Waist circumference measurements should be made initially and repeated if significant change in weight is noted. Waist circumference over 40" for men or over 35" for women greatly increases the adverse impact of obesity on health. An assessment of depression should also be performed in all obese patients, with appropriate medication initiation and referral to mental health.

All patients with a BMI $\geq$30.0 or BMI $\geq$25.0 with other risk factors or comorbidities should be offered a formal weight management program. Initial weight loss goal should begin with a 10% reduction of total body weight in a 6- month time frame.[68] A reasonable target weight loss goal of 1 to 2 pounds per week is set. Emphasis should include an increase in physical activity and a reduction of total calories. Referral to a Registered Dietitian and/or a Certified Lifestyle and Weight Management Consultant is essential to assist in the implementation of these changes.

Figure 6. Nutritional Recommendations

MODALITY	NATIONAL RECOMMENDATIONS	INDIAN HEALTH SUPPLEMENTATION
Diet	*These recommendations are appropriate for all individuals > 2 years of age* • 6 or more servings a day of a variety of grain products, including whole grains. • 5 or more servings a day of a variety of fruits and vegetables. • 2 – 4 servings a day of nonfat or low-fat milk and nonfat or low-fat dairy products. • Limit to 6 ounces a day of fish, skinless poultry or lean meat. Include at least 2 servings of fish per week. • Limit intake of sugars (and refined carbohydrates) – particularly in insulin resistance, glucose intolerance, and hypertriglyceridemia. • Limit saturated fat to < 10% calories and limit trans-fatty acids. Substitute mono- and poly-unsaturated fats and increase omega 3 fatty acids.	*Refer patients at risk to a Registered Dietitian for Medical Nutrition Therapy* • Encourage whole wheat flour in homemade breads and tortillas; oatmeal; enriched whole grain cereals; and brown rice. • Encourage use of whole pieces of fruit instead of juice, encourage vegetables and salad at lunch and dinner meals. • Use low-fat dairy products for those over 2 years of age, and include low-fat or non-fat dairy products in schools. • Encourage low-fat preparation techniques for meat, poultry and fish. (Baking, broiling, roasting, grilling). • Remove skin from poultry and trim off visible fat from meat. • Encourage less frequent usage and smaller portions of high fat meats such as bacon, sausage, salt pork, potted meat, Spam, Vienna sausage. • Encourage increased water intake and limited sugar-sweetened beverages such as soda pop, fruit punches, Kool-Aid; Gatorade. • Limit intake of sweets and candy. Serve fruit as dessert. • Encourage use of oil, preferably canola or olive oil in place of lard, shortening, margarine and butter. • Encourage use of fatty fish (sardines, mackerel, herring, salmon, tuna) twice weekly, and small portions of nuts and seeds
Physical activity	• Contraindications should be assessed • Assess current level of physical activity • Short range goal: increase level of physical activity • Long range goal: 30 – 60 minutes on most if not all days of the week	• Require physical education in schools • Encourage identification and resumption of traditional fitness activities • Provide tribal physical activity facilities
Obesity	• Begin formal weight reduction program if BMI ≥ 30 or ≥ 25 with comorbidities	• BMI should be used to assess weight status • Weight should be documented at all regular clinic visits • Measure waist circumference initially and upon significant weight change.
Tobacco Use	• Assess level of nicotine addiction • Assess readiness to quit • Pharmacotherapy with > 10 cigarettes/day	• Routinely document tobacco use in health record. Refer to smoking cessation program

VI. Public Health and Community Education

Introduction and rationale

Community education for dyslipidemia in Native American communities is an essential aspect of an overall effort to reduce the rising tide of CVD in Native Americans. Such education must be addressed at several levels to insure an appropriate and effective campaign. Native communities exist on several levels

including national, regional, tribal and local. Education and involvement at each of these levels may provide different but equally important influences on the goal of reducing dyslipidemia. Clearly, without community leadership and direction as well as enthusiastic support, any intervention in this regard will be unsuccessful.

Recommendations

National Native American Community Involvement

The inclusion of national Native American leaders and organizations is vital. Their endorsement and collaboration with local communities will help insure thorough coverage and acceptance of these guidelines by Indian communities throughout the U.S. These may include such groups as the Association of American Indian Physicians, the National Indian Health Board, the National Indian Council on Aging, and the National Congress of American Indians. These respected organizations and others may help underscore the vital need for local communities to act. Also national publications such as *Indian Country Today* could be helpful in this regard.

Local Community Level Involvement

Community level education is greatly enhanced by the inclusion and support of local leaders. Participants at this conference felt it vital to include all positive role models and leaders in this activity. A key first step is the identification of champions within the community. These may include tribal leaders, tribal council members, traditional healers/ medicine people, community health representatives, local health board members, educators, athletes, entertainers, etc. Individual communities should identify those in the community who are most influential and enthusiastic about such activities and encourage their involvement. Obviously, it is not necessary for these leaders to be members of the medical community.

Local community success requires the integration of local traditional and community beliefs and values that support the goals of the educational program. This fosters community ownership of the program and will increase relevance to the community. Our work group has identified the following issues as central on the local level.

1. Emphasize proactive/positive message of wellness through lifestyle, diet, etc. Messages should be simple. Special emphasis on the benefits of dyslipidemia therapies (lifestyle and medication) should be prominent. Focus on the potential benefits for both present and future generations.
2. Use of traditional media plays an important role, even in extremely rural communities and may include local publications, handouts, brochures, posters, billboards, as well as public service announcements on local radio.
3. Utilize patient role models as examples of treatment successes along with patient support groups for those with established CHD/CVD to provide culturally appropriate education in multiple venues (i.e., schools, clinics, etc.).
4. Identify unique potential settings where community education can occur. Take advantage of existing activities and organizations within the community. These may include schools, health fairs/walks/races etc., WIC, Indian Centers, HeadStart, churches, clinics, and rodeos. Urban settings may include large employers (such as casinos), social gathering places, powwows, fairs, and clinics among others.

Professional Education and Organization

The participants at this conference recognize that appropriate therapy for dyslipidemia is as dependent upon health provider education and motivation as it is upon that of the client. Providers have a unique opportunity to intervene both therapeutically and educationally at each patient encounter. Providers must be considered an integral part of the community, both as role models for healthy lifestyles and as participants in the educational process.

In communities with established medical facilities, we recommend the consideration of one health care professional with special interest in cardiovascular risk reduction being specified. This individual could be considered the **dyslipidemia coordinator** (DC), analogous to the diabetes coordinator position already established at many IHS facilities. This individual should work closely with the diabetes coordinator, or even function concurently as the diabetes coordinator at smaller facilities, to provide direct patient and provider information regarding dyslipidemia and its therapy. Consideration of the establishment of dyslipidemia clinics should be made, coordinated by the DC. This would serve to underscore the importance of the issue both to patients and other providers and improve the follow-up of patients already on therapy or requiring initiation of therapy. The DC's interest and expertise in dyslipidemia should be widely disseminated within the community to ensure that individual providers and patients have a resource for questions and concerns.

In addition, consideration of the liberalization of lipid testing is recommended. RNs, NPs, PAs, and pharmacists are all in a unique situation to identify patients at high cardiovascular risk and may assure that adequate lipid screening is occurring. In addition, these health care professionals can assist to ensure adequate follow-up of patients currently on therapy and provide patient education on risk factor reduction.

Program Evaluation

Periodic evaluation of the educational program efficacy should be performed. This may be both formal and informal, and include at least a semi-annual assessment of rates of lipid profile and risk factor assessment as well as intervention. Both provider and patient feedback should be sought to assure continuous quality improvement.

On a broader level, comparison to current data from the Diabetes Audit will allow reassessment of the status of lipid evaluations within participating service units.

VII. Secondary Prevention

Introduction and rationale

Lipid lowering therapy in patients with known coronary artery disease (CAD) is termed "secondary prevention."[69,70,71] This concept refers to the observation that the presence of CAD in a patient confers a very high risk of subsequent coronary events and CAD mortality. Indeed, men and women with proven CAD have a 5- to 7-fold increased risk of developing subsequent myocardial infarction (MI) or coronary death, with a greater than 20% ten-year risk for subsequent CHD event.[71] Native American patients are similarly afflicted, and CAD prevalence in American Indians now exceeds rates in other U.S. populations, possibly related to the high prevalence of type 2 diabetes mellitus (DM2).[31]

Previously, coronary atherosclerosis was considered to be a relentless progressive disease, where disability and death from CAD were inevitable. This was especially true for DM2 patients who experienced acute MI.[72,73,32] However, numerous multi-center, randomized clinical trials have proven conclusively that lowering elevated low density lipoprotein cholesterol (LDL-C) levels in patients with established CAD sharply reduces the risk of future MI, revascularization procedures, death from CAD, stroke and death from all causes.[3,74,75] The benefit of cholesterol lowering therapy has been shown to extend even to patients with "average" cholesterol levels.[5,76] Most patients with CAD demonstrate one or more of the various abnormalities of cholesterol metabolism.

Other clinical atherosclerotic syndromes (cerebrovascular disease, carotid artery disease, peripheral arterial disease, and aortic aneurysm) identify patients at high risk for subsequent MI and CAD death as well.[69,70] Hence these patients, even without known CAD, are considered equally eligible for "secondary prevention" lipid therapy as CHD risk equivalents.

Diabetes has been a risk factor for CAD for many years; however recent reviews have clarified the extent of increased risk.[77] Patients with DM2, without known CAD have a risk of MI and CAD death equal to or greater than non-diabetic patients with recent MI.[32] Over 80% of deaths in diabetics are due to MI, stroke, or peripheral atherosclerosis.

Diabetes is not only a metabolic disease, but also a vascular disease. Thus, in accord with National Cholesterol Education Program (NCEP)[69,70], American Heart Association (AHA),[71,77] and American Diabetes Association (ADA) guidelines,[72] all patients with DM2 are treated with "secondary prevention" diet and drug intensity. The various clinical syndromes which indicate "secondary prevention" therapy are listed in Figure 7.

Figure 7. Patients Indicated for Secondary Prevention.

- Coronary Artery Disease
  - *current angina pectoris*
  - *history of coronary revascularization (CABG or PTCA)*
  - *history of acute coronary syndrome (Acute MI or unstable angina)*
  - *non-invasive or catheterization documented CAD*
- Cerebrovascular Disease
  - *stroke or trans-ischemic attack*
  - *carotid artery disease or increased internal wall thickness on carotid doppler*
- Peripheral Arterial Disease
  - *Absent or significantly reduced lower extremity pulse or ABI < 0.9*
  - *lower extremity revascularization*
  - *non-invasive or angiographically documented PAD*
- Type 2 Diabetes Mellitus
  - *Patients with proteinuria, neuropathy, and known CAD are at particularly high risk.*

Additionally, certain clinical coronary syndromes identify those at very high risk for recurrent MI and CAD death. These include patients with recent acute coronary syndromes (acute MI or unstable angina), patients with both symptomatic coronary ischemia and congestive heart failure (CHF), and diabetic patients with known CAD, even if asymptomatic post CABG or PTCA.[76,77,78] Those at highest risk for CAD death are listed in Figure 8.

Figure 8. Patients at Highest Risk for MI and CAD Death.

- Recent unstable coronary artery syndrome (acute MI or unstable angina)
- Type 2 diabetes patients with known CAD (current angina pectoris, previous MI, or history of CABG or PTCA, even if asymptomatic)
- Patients with active angina pectoris symptoms or ischemia by non-invasive testing and evident CHF.

In summary, the intensity of lipid therapy depends on the patient's clinical risk status, and those patients at higher risk should receive the more aggressive interventions.[79,83,92]

Recommendations

Lipid testing and hyperlipidemia

For the diagnosis and management of patients needing secondary prevention a complete lipid profile is required, including total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides.[69] A "direct LDL-C" should be strongly considered for patients with diabetes, triglycerides over 250 mg/dL, or for those individuals in whom a fasting sample would be difficult to obtain.[72] Ideally a lipid panel should be drawn in the fasting state, although total and HDL cholesterol can be tested accurately in the post-prandial state. Patients with acute coronary syndromes may have a lipid profile drawn on hospital admission within 4 hours of admission. After that, lipid values pseudo-normalize, but can be accurately repeated 8 to 12 weeks later. A review of previous lipid values and repeat testing of lipids is encouraged. Diagnosis of hyperlipidemia and dyslipidemia should follow NCEP guidelines.[69] In addition, fasting glucose and hemoglobin A1C should be ordered, as well as a TSH, a complete metabolic profile, and a urinalysis to complete the patient's risk profile.

General therapy goals

The goals for cholesterol lowering for patients needing secondary prevention are listed in Figure 9. Although the primary effort is LDL-C lowering, all parts of the cholesterol profile should be treated to "normal" if possible.[29,69,71,72,80] These profile goals and specific diet, lifestyle, and drugs must be adjusted to individual patient characteristics.

Figure 9. Lipid Profile Goals in Secondary Prevention.

1. Lower LDL cholesterol to < 100 mg/dL.
2. Raise HDL cholesterol to $\geq$ 40 mg/dL in men and $\geq$ 45 mg/dl in women.
3. Reduce triglycerides to $\leq$ 150 mg/dL ($\leq$ 100 mg/dL if diabetic and CVD*)

*Some authors felt that less than or equal to 150 mg/dl was more reasonable in those with DM and CVD.

Diet and lifestyle efforts

All secondary prevention patients should be referred to a registered dietician for medical nutrition therapy to improve lipid levels and/or lower the risk of MI and CAD death. Diet instruction should include AHA 2000 Dietary Guidelines diet, emphasizing a decrease in saturated fat (< 7% of calories), trans-fatty acids and dietary cholesterol.[69] Stricter dietary restriction of fat is often difficult to achieve and produces diminishing benefits. The recently described Lyon "Mediterranean" diet, which emphasizes an increased intake of monounsaturated fat, is an alternative. In post-MI patients, lipid profiles were not affected by this diet, but its use was associated with a dramatic fall in subsequent cardiac events.[81] In addition, this diet can improve glycemic control and assist in reducing elevated triglycerides. Because of the saturated fat and caloric density, "fast foods" are particularly discouraged.

All patients with a BMI greater than or equal to 25 should be offered a formal weight management program. Initial weight loss goal should begin with a 10% reduction of total body weight in a 6-month time frame.[66] A reasonable target weight loss goal of 1 to 2 pounds per week is set. Emphasis should include an increase in physical activity and a reduction of total calories. A registered dietitian and/or a Certified Lifestyle and Weight Management Consultant is essential to assist in the implementation of these changes.

Guidelines for physical activity from both the Surgeon General and the AHA should be followed with an emphasis upon lifestyle modifications.[60,80] With physician approval, and if no contraindications exist, the level of physical activity should be assessed and goals tailored towards a gradual increase, working up to 30 to 60 minutes of activity on most, if not all, days. Elderly patients or those with conditions such as arthritis or diabetic foot conditions can often do limited exercises, yoga, or other similarly low-level activities. Diet and physical activity efforts are most effective if both are pursued simultaneously.[82]

Drug therapy planning

Most patients receiving secondary prevention will require diet and drug therapy to lower their risk of future CAD events. It has been shown repeatedly that in CAD patients, treatment of even relatively normal levels of cholesterol reduces the future risk of CAD morbidity and mortality.[3,5,76] Drug therapy follows the current NCEP, AHA, and ADA guidelines.[3,69,71] Lipid goals are shown in Figure 9, in descending order of importance, and suggested drug therapy is outlined in Figure 10.

While any of the lipid drug groups (statins, fibrates, niacin, and bile acid binding agents) may be utilized, statins are preferred considering their profound benefits evident in clinical trials.[69,70,72,83] Benefit has been demonstrated for men as well as for women, for diabetics and non-diabetics,[70,84] and the elderly as well as middle aged patients.[79] Fortunately, these drugs are also remarkably safe. Although relatively expensive, the use of statins in secondary prevention has been shown to be very cost beneficial, and in the highest risk groups, cost saving.[83,85] The use of combination therapies of cholesterol lowering drugs in patients with severe dyslipidemia, especially combined dyslipidemia and diabetic dyslipidemia, is often required to normalize lipids and achieve maximal clinical benefit.[86] First generation statins (lovastatin, pravastatin, and simvastatin) may be used with fibrates or niacin; this combination therapy is associated with a small but definite risk of myositis, rhabdomyolysis and hepatitis, and should be

done cautiously, with frequent blood testing (LFTs), or with consultation.[87] Niacin has recently been shown to be usable in type 2 diabetics if close attention to glycemic status is observed.[42]

- Because of the profound effects statins have on cholesterol as well as on endothelial function and plaque biology, all patients at "higher risk" (see Figure 8) should be considered for statin therapy, even if LDL-C is less than 100 mg/dL or lipid levels are not available.[88,89,90,91,92] The starting dose should be proportional to the level of LDL cholesterol elevation. Prescribing a clinically effective dose is more important than the specific statin chosen. A summary of lipid therapy is shown in Figure 10.

FIGURE 10. LIPID THERAPY SUMMARY FOR SECONDARY PREVENTION.

LDL-C < 100 mg/dL	LDL-C 100 – 130 mg/dL Add drug therapy to diet and physical activity as follows:			LDL-C > 130 mg/dL Add drug therapy to diet and physical activity as follows:			HDL < 35 mg/dL
Diet and physical activity. Consider low dose statin.	TG<200 mg/dL	TG 200 – 400 mg/dL	TG>400 mg/dL	TG<200 mg/dL	TG 200 – 400 mg/dL	TG>400 mg/dL	Emphasize weight loss and physical activity. Advise smoking cessation. Consider niavcin, ffibrates or statins as necessary based on remainder of profile.
	Statin. Could also use Resin.	Statin or Fibrates or combo*, if needed. Could also consider Niacin.	Fibrates. May combine with Statins if needed*. Could also consider Niacin.	Statins.	Statins. May be combined with Fibrates* (or niacin) if necessary	Fibrates. May be combined* with Statins if necessary.	

*with appropriate monitoring, especially liver function tests.

Secondary prevention and ischemia

Patients considered eligible for secondary prevention should be evaluated for ischemia and left ventricular (LV) dysfunction. Statin therapy has been shown to decrease ischemia, probably by improving endothelial function.[89,91] Revascularization should be considered for patients with severe symptoms, evidence of severe ischemia, especially when multi-vessel disease or LV dysfunction is evident. Those at highest risk are diabetic patients after an MI.[32,73] Asymptomatic patients, even after CABG, should still receive lipid therapy to prevent native and coronary graft atherosclerosis.[74,79] Again, this is especially important for patients with diabetes.[32,73,77,93]

Non-lipid drug therapy

Patients indicated for secondary prevention often have indications for non-lipid lowering drugs, including those in Figure 11.

Figure 11. Other Drug Considerations in Secondary Prevention.

- Aspirin 81 – 325 mg for all patients,
- Beta-blocker drugs for any patient with angina, hypertension and CAD, and all patients post-MI.
- Angiotensin converting enzyme inhibitors for patients post-MI, with significant LV dysfunction, or clinical congestive heart failure, and diabetic patients with hypertension and/or nephritis. The recent H.O.P.E. trial suggests most patients indicated for secondary prevention should be considered for ACE inhibitors.
- Antidiabetic drugs (metformin or thiazolidinedione intermediate preferred; sulfonylureas or insulin less favored) to achieve glycemic control. This may secondarily improve HDL cholesterol and triglyceride levels.

Cultural considerations

Coronary atherosclerosis and dyslipidemia are difficult concepts for physicians and others in the medical field to master; Native American patients may also have trouble with these clinical issues. Extensive time must be taken for discussion of the clinical concepts and should include the rationale for treatment and therapy goals, in understandable terms. Native-speaking health educators, dietitians, pharmacists and other professionals, as well as key family members, should always be included when possible. Diet and lifestyle advice is much more effective when concepts are carefully explained, especially by native speakers. Describing the goal of dietary, physical and drug therapy to return one's bodily function to normal and emphasizing the positive and hopeful results cannot be overemphasized, especially in asymptomatic individuals. For instance, many individuals may not be particularly willing to "exercise," but are very willing to daily herd sheep, or daily walk to a relative's house or to the post office. Adherence to drug therapy often wanes over time and may be affected by any number of patient issues. A discussion of medication side effects and adherence as well as potential drug-drug interactions (especially use of macrolide antibiotics) should accompany each clinic visit. The development of a warm, caring relationship based on respect for the patient and his or her cultural milieu may in the end be as important as designing optimal drug therapy and achieving optimal goal lipids.

VIII. Compliance Development and Recommendations for Counseling

Introduction and rationale

Successful treatment of dyslipidemia in Native American individuals requires the development of an interpersonal trust between the provider and the patient as well as similar beliefs related to the importance and effect of the goal. Successful outcomes will result if a variety of methods are used to enhance patient adherence, tailored to the individual. Specific recommendations for individuals should be developed as a provider-patient team, paying particular heed to their beliefs, values and culture.

These guidelines are meant to serve as a framework for a consistent set of standards and an approach to the management of dyslipidemia in local Indian Health facilities, but efforts should be undertaken by local providers to tailor these recommendations according to the local culture and belief systems as well as the availability of resources and the needs of the community.

Recommendations

Treating patients with dyslipidemia should involve a holistic approach. Providers need to treat the whole patient with attention to physical, mental, cultural, and spiritual dimensions. Patient education and treatment strategies should be developed which take in to account patients learning styles, traditions, values and personal goals. Efforts should be made to empower patients and encourage self-management. Goals for lifestyle change should be developed with the patient. Providers should be attentive to cultural, psychosocial and socioeconomic issues that may present barriers to achieving these goals.

Any approach to treating dyslipidemia should be undertaken with compassion, respect, understanding and hope. Successful management of dyslipidemia in AI/AN individuals has the potential to help prevent tremendous morbidity and mortality from cardiovascular disease in AI/AN communities. However, no intervention or lifestyle change has a chance of succeeding without the active participation of the patient in a plan that fits his or her beliefs and goals.

IX. Hypertensive Therapeutic Interventions

Introduction and rationale[94,95,96,97,98,99,100,101]

The importance of hypertension control can not be overstated, especially in those with other cardiac risk factors, most notably diabetes mellitus. Progression of diabetic renal disease and cardiovascular disease are inextricably linked with blood pressure. Microalbuminuria is an early predictor of both progressive renal injury and cardiovascular disease. Elevations in blood pressure, though not necessarily to hypertensive levels, are detectable along with a drop in glomerular filtration rate well before the serum creatinine changes. "Normal" blood pressure can be associated with progression of renal disease. Deaths of ESRD patients are attributed predominantly to cardiovascular complications. Results from the UKPDS show that “tight” blood pressure control reduces cardiovascular risk to a greater degree than “tight” glucose control.

Several long-term studies have demonstrated that anti-hypertensive therapy is beneficial in early and late stages of diabetic nephropathy. In untreated hypertensives GFR declines approximately 1 ml/min/month; anti-hypertensive treatment slows the rate of decline by about two-thirds. Anti-hypertensive therapy reduces proteinuria, presumably by lowering glomerular capillary pressure. Angiotensin converting enzyme inhibitors lower glomerular capillary pressure by dilation of the efferent arteriole. These agents have been shown to ameliorate the renal injury even when systemic blood pressure is not effected. In hypertensives, ACE inhibitors provide a significant additional benefit when compared to other anti-hypertensives with the same level of blood pressure control. A recent NIH-sponsored management conference recommended that ACE inhibitors be initiated in diabetic patients with any one of the following: hypertension (>140/90), creatinine>1.5, or proteinuria > 300 mg/day. There is

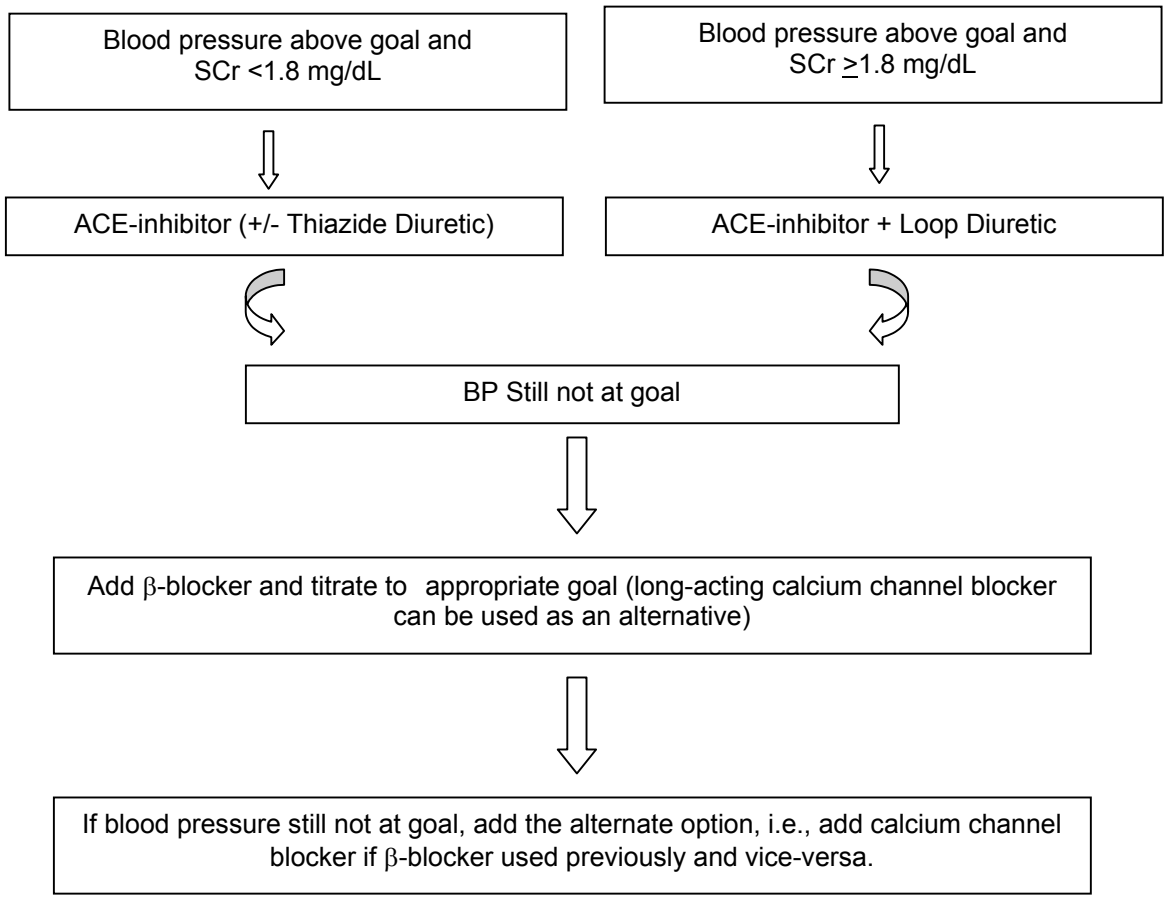
evidence that treatment of normotensive Type II patients with microalbuminuria may benefit from treatment with ACE inhibitors.

Not only are conventional drugs being replaced with ACE inhibitors, but recently published studies justify a lower therapeutic goal for blood pressure than the traditional 140/90. The MDRD (Modification of Diet in Renal Disease) study showed that maintaining a mean arterial pressure of 90 mm (equivalent to 125/75) slows progression of renal disease to a greater degree than higher BP levels in persons with more than 1g/day of proteinuria. Benefit is greatest in patients with more severe disease. A recent National Kidney Foundation consensus statement describes an approach to controlling blood pressure in patients with diabetes and kidney disease with the goal of reducing progression of blood kidney disease and cardiovascular disease.

Recommendations

The consensus statement synthesizes evidence in the literature into a cost-effective algorithm, which provides maximum renal and cardiovascular protection to the diabetic patient. Key elements are: 1) Blood pressure goal of <130/80 in diabetics and 140/90 for non-diabetics, 2) Use of ACE inhibitor as initial drug (with a diuretic if renal dysfunction), with a beta-blocker generally as second line if without contraindication or specific indications for another agent, 3) Necessity to use multiple drugs (including diuretics early) in diabetics if initial blood pressure is >15/10 mm Hg above goal.

Figure 12. Blood Pressure Goals and Treatment Regimen



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