Task Force on Research in Epidemiology and Prevention of Cardiovascular Diseases

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Over the past two decades, the United States has witnessed noteworthy increases in life expectancy and major decreases in the death toll attributed to cardiovascular diseases (CVD). Age-adjusted death rates from coronary heart disease (CHD) are now half what they were 20 years ago, and death rates from stroke have declined even more sharply. It is well recognized that research in epidemiology and prevention of CVD has made major contributions to these favorable trends.

Nonetheless, the public health and economic burden of CVD is still considerable, and much remains to be discovered if we are to achieve effective disease control and prevention. To identify new opportunities and chart a course for future research efforts, the National Heart, Lung, and Blood Institute (NHLBI) in 1992 convened a Task Force on Research in Epidemiology and Prevention of Cardiovascular Diseases. Composed of national experts, the task force was charged to review the state of knowledge in epidemiology and prevention of CVD over the past 5 years and develop a comprehensive plan, including scientific priorities, for NHLBI support of research in this area over the next several years.

During a series of meetings that spanned nearly 2 years, the task force members worked to develop a detailed report of its findings and conclusions. The full report is available on the NHLBI Gopher (accessible through the Internet Gopher client-Server: gopher.nhlbi.nih.gov, Port: 70). A printed copy can be obtained from Charlene French, NHLBI, Building 31, Room 5A03, National Institutes of Health, 31 Center Dr, MSC 2482, Bethesda, MD 20892-2482.

The summary that follows was prepared by the task force to highlight its overall findings. It conveys an appreciation of how far we have come and a vision of what the future holds.

The Institute is very pleased to have this report to guide its activities with respect to CVD epidemiology and prevention. We are grateful to the task force chair, Dr. Albert Oberman; the subgroup chairs, Drs. Lewis H. Kuller and Richard A. Carleton; and the members for their valuable contribution to this important and timely endeavor.

Report of the Task Force

In the 1990s, adult Americans are experiencing the longest life expectancy ever. This extended life span results primarily from a marked decline in death rates from major categories of CVD—a decline that results from the application of new knowledge on the prevention and treatment of CVD, amassed through the combined efforts of biomedical scientists conducting clinical and pathological investigations, laboratory experiments, and epidemiological research. Studies of populations nationally and internationally and trials of preventive measures have contributed information indispensable for preventing CVD in the United States and elsewhere.

Despite major progress, however, almost one in four deaths in the United States is from CHD, totaling about 500,000 deaths per year. During the coming years, CHD, a major component of CVD, will continue to be the main cause of sudden and premature deaths. Even if the most dire predictions are realized for acquired immunodeficiency syndrome or cancer, the number of deaths from those two conditions will not approach the number from CVD, which accounts for the greatest percentage by far of deaths in the United States today (42% of all deaths).

Prevention of CVD and promotion of cardiovascular health have been major contributions of biomedical research to the health of the American people. CVD (as used here) refers to the major disorders of the heart and blood vessels and includes heart disease, cerebrovascular disease, congenital anomalies of the cardiovascular system, and peripheral vascular disease. Of all cardiovascular deaths, more than 50% are due to CHD and nearly 16% are due to stroke.

Cardiovascular diseases also continue to account for sickness and disability in millions of Americans, resulting from heart attack, angina pectoris, cardiac dysrhythmias, heart failure, and strokes. Other important categories of CVD include hypertensive disease, cardiomyopathies, renal vascular disease, and rheumatic heart disease. About 70% of all CVD deaths are related to severe atherosclerosis, a lipid disorder involving the arteries.

Of the decline in total mortality since 1963, more than 80% is from the decline in CVD, especially CHD and stroke. The average annual percent decline in age-adjusted CHD mortality between 1981 and 1991 was 3.8% overall: 4.1% in white men, 3.5% in white women, 2.6% in black men, and 2.3% in black women. The task force notes that it is both possible and desirable to accelerate the rates of decline in CHD mortality in all ethnic and socioeconomic groups in the United States and, in accordance with the nation's health goals for the year 2000, reduce the differences in these rates of decline by enhancing them in socioeconomic, ethnic, and geographic strata that now have the higher rates.
By effectively applying available scientific knowledge, it would be possible to accelerate the rate of decline in CHD mortality to about 6% per year, yielding an overall reduction in CHD mortality of almost 50% in 10 years. Indeed, CHD mortality rates throughout the United States could be reduced to the level of states that have the lowest rates or even to that of Japan, which has the lowest rate of all industrialized countries. Such a reduction is possible because the higher CHD rates are due primarily to variations in lifestyles and lifestyle-related risk factors, which are amenable to change. Thus, every effort must be made to advance population-based research on the epidemiology and prevention of CVD.

**Two Prevention Approaches**

Achievements in reducing CVD rates in the United States during the past 30 years have resulted from two complementary strategies: a population-based approach and a medical approach targeted to individuals at high risk of CVD. The first approach is characterized by community-wide efforts to prevent and modify unfavorable lifestyles and related risk factors that have resulted in the current CVD epidemic in the United States. It is based on the recognition that most new cases of CHD, the major component of CVD, actually arise in the large number of Americans who have "high normal" or borderline levels of multiple risk factors rather than in individuals who have a single, excessively high factor. The second approach, the high-risk or medical approach, targets individuals who are recognized to be at higher risk of CVD because they have unfavorable levels of risk factors or clinically manifest CVD.

The population approach is central to prevention because, for many individuals, advanced disease or death from CVD often occurs before CVD is detected or any intervention has been applied. Even small changes in the mean level and distribution of risk factors, which are achievable in the total US population, can have enormously favorable effects on public health.

Two key underlying issues in CVD prevention are (1) the determinants of population risk-adverse dietary patterns, mean blood pressure and blood cholesterol level, smoking, and physical activity and (2) how these determinants can be modified. Intensified research efforts and innovative preventive approaches are needed to correct these factors underlying the CVD epidemic.

**Prevention: A Continuum**

Prevention can be viewed as addressing a series of stages: from risky behaviors and elevated risk factors to the onset and progression of disease to acute events and premature death. Primary prevention refers to the prevention of first episodes of clinical CVD; secondary prevention refers to the prevention of symptoms or additional cardiovascular events or complications in individuals who already have manifest CVD.

The earliest stage of disease (ie, elevation of risk factors) can be prevented through avoidance or early modification of risky behaviors and exposures. Although disease prevention at this stage is called "primordial prevention" by the World Health Organization, no term for prevention of risky behavior or early prevention of elevated risk factors has been widely accepted. The widest benefit to the health of a population is derived from intervention at the earliest possible stage. To achieve the highest reductions in CHD mortality rates, emphasis must be placed on primary prevention, ie, preventing first episodes of CVD (first heart attacks, strokes, etc) by controlling or eliminating major CVD risk factors.

Once CVD is manifest, further risk is only partly reducible. Indeed, the prospect of a growing population of older persons who have accumulated disabilities because of lack of early prevention is sobering, as are the social costs associated with them. Nevertheless, secondary prevention can reduce morbidity and disability, as well as the risk of CVD mortality. As such, it must be an integral part of patient management. All patients at high risk for CVD or with overt CVD should be treated effectively to reduce their risk factor levels and their risk of future CVD events.

It is now possible not only to prevent the progression of CHD and its associated complications and disability but also to achieve regression of atherosclerosis. Because atherosclerosis progresses in distinct phases well before it is clinically manifest and because it probably begins in childhood, each phase is an appropriate target for prevention research and practice.

During the three decades since the launching of a population-wide effort to prevent CVD in the United States, substantial improvements have been made in lifestyle patterns and in the pharmacological control of risk factors. However, these positive changes still fall short of the national goals set forth in Healthy People 2000: National Health Promotion and Disease Prevention Objectives, and they are distributed unevenly in the population. Prevention efforts must reach all segments of American society to have a significant impact nationwide. Therapeutic advances for high-risk patients can play an important role in preventing both first and recurrent cardiac events.

**Contributions of Epidemiology**

Epidemiology is the basic science of preventive medicine, health maintenance, and health promotion. It is concerned with the distributions and determinants of disease in populations, particularly common diseases affecting large numbers of people. Key questions in epidemiology are: Who gets a disease and why? Why are disease rates high in some populations and low in others? What is the usual course of disease over time? What individual and group characteristics contribute to the disease? How common are they? How much can they be modified and to what effect?

The knowledge established through epidemiological studies provides a sound basis for intervention and prevention of widespread diseases, such as CVD, at both population and individual levels. The CVD epidemic, like other epidemics (ie, unusually frequent occurrences of disease), arises from the interaction between a widespread individual susceptibility to disease (heredity) and specific, powerful environmental factors, such as diet and cigarette smoking. Genetic abnormalities alone, without these environmental components, usually do not lead to a common expression of disease, and the environmental factors do not produce disease in all those exposures. A major focus of research on the epidemiology and prevention of CVD is, thus,
the clarification of interactions of genes and environment in CVD.

Progress in epidemiological and prevention research has been fostered by parallel laboratory, clinical, and epidemiological studies through which new knowledge has been uncovered and transferred into practice. Epidemiological findings have stimulated major questions for laboratory and clinical research, and laboratory and clinical research has stimulated questions for epidemiology. Clues derived from epidemiological studies have opened up entire new fields of inquiry on biological mechanisms and have led to valuable clinical investigations. By corroborating or clarifying previously noted associations in CVD, population studies have contributed significantly to elucidating the causes of the current CVD epidemic.

Based on an enhanced knowledge of the causes and mechanisms of disease, randomized, controlled trials and community demonstration projects have been undertaken to test the possibility of breaking the links in disease causation and, thereby, preventing and controlling CVD. These methods will be especially useful in evaluating interventions based on emerging genetic techniques and enhancing understanding of the relation between genetic susceptibility and environmental exposures.

Finally, as new knowledge is transferred into preventive practice in public health and medical care, epidemiologists monitor the effects in samples of the general population. The information gained from surveillance research serves as a basis for subsequent approaches for achieving optimal prevention and control of CVD.

Promises for the Future
Opportunities for Epidemiological Research

Over the next period, epidemiological studies will benefit from the availability of new methods for assessing atherosclerosis in the population; improved techniques for quantifying thrombosis, measures of inflammation, and lipoproteins; and advanced approaches for quantifying genetic polymorphisms and host susceptibility. With these new tools, epidemiological studies will probably lead to much more accurate definition of disease risk for individuals. Improved definitions, in turn, will lead to substantially improved approaches for preventive practice. Enhanced understanding of the acute precipitants of a heart attack, and especially sudden death, for example, should result in both earlier detection and treatment of heart disease in the community and better pharmacological and nonpharmacological therapies for individuals. Epidemiological studies will provide a better understanding of why risk factors increase with age and how age-related changes in risk factors affect the progression of atherosclerosis. This new understanding can be expected to lead to more successful efforts in preventing elevation of risk factors, development of atherosclerosis, and subsequent morbidity and mortality from CVD. Genetic and environmental determinants of differences in risk factors and CVD among racial, ethnic, and socioeconomic groups can be evaluated in epidemiological studies using new laboratory methods. The reasons for these differences, such as the apparent lower rates of heart disease among some Native American and Asian Pacific populations and the higher rates of heart disease among black Americans compared with whites, may be important links in understanding the determinants of risk factors, atherosclerosis, and clinical disease in populations.

The next generation of epidemiological studies is also expected to improve understanding of the role, in CVD, of lipoprotein subgroups and oxidation of lipoproteins; homocysteine and vitamin metabolism; infection and injury to the arterial wall; macronutrients and micronutrients in the diet and risk of hypertension; physical activity and psychosocial factors; and sex-steroid hormone metabolism and risk of disease, especially among women. An understanding of the relation of various measures of obesity to insulin resistance and associated risk factors should make it possible to elucidate the role of obesity in CVD and to clarify the relation of diabetes and glucose metabolism to CVD in populations. Enhanced knowledge of the distribution, trends, and determinants of CVD offers the potential for new approaches to promoting cardiovascular health.

Opportunities in Primary Prevention

As noted above, additional advances in primary prevention are essential to realizing further reductions in the overall burden of CVD. Disease prevention not only postpones morbidity and mortality but also allows for a maximum number of healthy years before death. Atherosclerosis is not an inevitable consequence of aging; factors predictive of CVD in younger individuals are also predictive of CVD risk in older persons. The ability to prevent CVD is particularly relevant today because of the increased number of elderly persons in the population, improved survival rates after initial myocardial infarction (MI), and rapid development of new technologies for treating CVD, all of which translate into substantial increases in demand for medical care. Much greater emphasis should be placed on primary prevention of CVD and its risk factors, with the goal of achieving further marked reductions in the total incidence of CVD in the population and in differences in CVD according to socioeconomic status, ethnicity, and sex.

Major Research Advances During the Past 5 Years

Major research accomplishments in CVD epidemiology and prevention have been made over the past 5 years in the following areas: understanding CVD risk factors, identifying CVD risk in specific populations, demonstrating benefits of secondary prevention of CVD, improving research methodologies, and developing effective community surveillance and prevention strategies. Advances in each of these areas are summarized below.

Risk Factors

Key contributions of epidemiological research in the past 5 years include elucidation of the long-term impact of established major risk factors and discovery of new CVD risk factors. For example, with the availability of almost 20 years of follow-up data on large cohorts, it has been possible to establish CVD incidence rates for middle-aged and older US men and women having desirable values for each of the major CVD risk factors.
These “low-risk” cohorts (which comprised ≤3% of all persons in the population samples studied) have very low CHD and CVD death rates and low death rates from all causes. These findings point to the great potential for prevention strategies in this country.

Recent data on US men and women of different ages, ethnicity (black, Native American, Asian, Hispanic, white), socioeconomic status, and geographic residence show that the major CVD risk factors strongly influence CHD and CVD risk throughout the US population. Findings from NHLBI-supported and other studies in Europe and Asia, including countries that have rising CHD and CVD rates (eg, Poland) as well as those that have low CHD and CVD rates (eg, China), also show the universal effects of major risk factors for CHD and CVD.

These and related findings not only confirm the soundness of population-wide approaches for improving CVD risk factor status of virtually all Americans but also underscore the very large potential for preventing CVD by controlling major CVD risk factors among all ethnic groups, in both sexes, and throughout the age span. The major risk factors include adverse dietary patterns, blood lipid and lipoprotein abnormalities, blood pressure elevation, smoking, physical inactivity, obesity, diabetes mellitus, and psychosocial factors. Current understanding of each of these risk factors is summarized below. Other CVD risk factors are also noted.

**Adverse Dietary Patterns**

Recent epidemiological studies and trials have extended and refined knowledge of the pivotal role of adverse dietary patterns—long-term dietary excesses and deficiencies—as essential causes of epidemic CVD. Valuable new data reveal that dietary intake of specific fatty acids and cholesterol, caloric balance (gain or loss of weight), and types of dietary fiber have interactive effects on serum cholesterol and its fractions. Studies also suggest that the intake of antioxidants is inversely related to risk of CVD and arterial thickness. New data on the intake of dietary cholesterol show that it is associated with CVD risk independent of blood cholesterol and blood pressure levels. Other data indicate that the fatty acid composition of dietary intake may similarly relate to risk.

Recent studies and trials indicate that nutritional components that reduce CVD risk also have favorable effects on diabetes and various cancers. The inverse association between marine foods and frequency of atherosclerotic disease poses important questions for further research on the pathogenetic significance and possible mechanisms of disease (eg, the fatty acid-prostacyclin cycle and platelet activity) and suggests new hypotheses regarding the preventive and therapeutic role of fish oils, aspirin, and anticoagulants.

**Blood Lipid and Lipoprotein Abnormalities**

Population comparisons demonstrate that high blood cholesterol—with its main cause, an adverse dietary pattern—is a necessary condition for the common occurrence of severe atherosclerosis and its clinical sequelae. CHD rates in populations can be predicted from average levels of total blood cholesterol and from changes in these levels.

In large, long-term, prospective investigations of individual men and women, the relation of serum cholesterol to CHD risk has been found to be strong, to be graded over a wide range of levels, to be consistent in multiple studies, and to manifest for both nonsmokers and smokers, persons with blood pressures at all levels, nondiabetic and diabetic persons, and persons with and without a history of heart attack. Serum cholesterol relates similarly to CHD risk in adults living in diverse geographic areas; in persons of African, Asian, European, Hispanic, and Native American backgrounds; in individuals at all socioeconomic levels; and in both middle-aged and older men and women. Moreover, recent data on men 18 through 39 years old show that the long-term risks of developing CHD and CVD are especially high for young adult men who have high serum cholesterol levels.

Major clinical trials completed recently confirm that reduction of coronary events is proportional to the duration and extent of lowered levels of total cholesterol and/or LDLs. In three multifactorial, primary prevention trials that made dietary recommendations similar to those of the American Heart Association and the NHLBI National Cholesterol Education Program, long-term reductions were obtained not only in the incidence rates of CHD and CVD but also in the death rates from other diseases. These favorable outcomes were proportional to the serum cholesterol reductions achieved in the treatment groups during intervention compared with those of the control groups.

Research has been stimulated by epidemiological observations in some population studies that indicate an association between very low blood cholesterol levels and cholesterol lowering by drugs and excess non-CVD mortality. The principal confounders of this relation appear to be heavy smoking and alcohol consumption, as well as subclinical neoplasms and other disorders that can also produce low blood cholesterol. These confounders account for much of the excess mortality, but explanations are being sought for persistent associations, including the one between hemorrhagic stroke and hypertensive individuals who have very low cholesterol levels.

Arteriographic studies of the progression and regression of atherosclerotic lesions have shown the benefit of lipid lowering by diet and/or drugs and by ileal bypass surgery. Many epidemiological studies have shown that HDL levels, especially among women, are inversely correlated with CHD incidence rates. Advances have been made in understanding the role of thrombosis in acute coronary events and its possible role in the progression of atherosclerosis. High intakes of saturated fatty acids and cholesterol have been shown to influence thrombogenic factors adversely.

At both the epidemiological and clinical levels, risk discrimination has been improved by partitioning cholesterol into its lipid and lipoprotein components. Qualitative differences in lipoprotein patterns further clarify the associations between lipids and CHD.

**Blood Pressure Elevation**

New evidence has been obtained on the relation of high salt and low potassium intake, high body mass, and heavy alcohol intake to blood pressure and the age-related increase in blood pressure. Dietary salt appears...
to influence systolic blood pressure in most people and not only in a minority of “salt-sensitive” individuals. The higher blood pressure levels found in the less-educated strata of the population are due, in part, to more adverse patterns of salt and potassium intake, a greater prevalence of overweight, and higher alcohol intake among these strata compared with more educated persons. In addition, the amount and type of dietary protein and lipid, as well as antioxidant vitamins, fibers, and magnesium, influence blood pressure.

New data from large, long-term, prospective studies clearly show that, in middle-aged adults, systolic blood pressure is consistently a stronger predictor of CHD, stroke, CVD, and total mortality than diastolic blood pressure. At every level of diastolic blood pressure, CVD risk increases directly with systolic blood pressure. Isolated systolic hypertension is associated with increased CVD risk in middle-aged and older persons.

New methods allow better characterization of blood pressure throughout the day and evaluation of left ventricular enlargement. Left ventricular hypertrophy is a powerful predictor of subsequent cardiac events. In addition, accumulating data on blood pressure variation indicate that this blood pressure parameter may relate to CVD risk. These advances permit better assessment of CVD risk.

Recent results from randomized, controlled trials demonstrate that weight reduction, reduction of salt intake, and increased physical activity are effective, separately and in combination, in reducing blood pressure levels and the age-related rise in blood pressure. These findings have been observed not only in persons with documented high blood pressure but also in individuals with high-normal blood pressure levels. The latter data are important evidence of the ability to prevent hypertension by improving lifestyles.

Data from clinical trials show that in persons with high blood pressure, long-term intervention combining low-dose antihypertensive drugs with sustained counseling is effective in reducing overweight and improving diet composition, alcohol drinking patterns, and leisure-time exercise habits. They also show that effective reduction of CVD rates can be achieved through antihypertensive drug treatment in older individuals who have isolated systolic hypertension.

Smoking

Follow-up data from large, long-term cohort studies of Americans demonstrate that cigarette smoking increases the risk of CHD, stroke, CVD, and all-cause mortality for adult men and women 18 through 74 years old, at every level of serum cholesterol and blood pressure, in nondiabetic and diabetic persons, and in persons without and with a history of MI, irrespective of ethnicity and socioeconomic status. Other studies indicate that smoking cessation has a beneficial effect on symptoms and event rates in peripheral arterial disease as well as other CVD. Available data on the effects of secondhand smoke, or passive smoking, suggest harmful cardiovascular effects.

School-based and community-wide strategies of smoking cessation appear to achieve a wider and more sustained effect on smoking cessation than do medical and clinic-based approaches.

Physical Inactivity

Observational studies and recent meta-analyses of them generally support the evidence that physical inactivity is an independent risk factor for CHD. Recent studies also demonstrate that levels of fitness are strongly and inversely associated with long-term CVD mortality and all-cause mortality. Regular exercise and a high level of cardiorespiratory fitness appear to protect against the triggering of MI by strenuous exercise.

How much exercise and what kinds of physical activity are best for achieving optimal cardiovascular health are not known. Longitudinal data from US college alumni, British civil servants, and a Norwegian cohort strongly indicate that there is a threshold for vigorous exercise (4.5 to 6 metabolic equivalents) in reducing heart attack rates and deaths from CHD. One metabolic equivalent is the amount of oxygen required per minute at rest; it equals 3.5 mL of oxygen consumed per kilogram of body weight per minute (3.5 mL·kg\(^{-1}\)·min\(^{-1}\)). Nevertheless, increasing evidence suggests that moderate physical activity (less than the level required for cardiorespiratory fitness) can significantly reduce the risk of CHD. Study results support the concept that moderate levels of physical activity and cardiorespiratory fitness suffice to reduce the risk of CHD in men. Further data are necessary to establish the link between physical activity and fitness in women and other population subgroups for whom few data are available.

Favorable influences of physical activity on weight control, glucose tolerance, insulin sensitivity, blood pressure, and lipid levels are also established. Studies show that diet and exercise, in combination, are more effective in reducing CHD risk factors than either diet or exercise alone. Trials of prescribed physical activity have demonstrated decreases in blood pressure; increases in HDL; and decreases in triglycerides, the ratio of total cholesterol to HDL cholesterol, and body mass index in both women and men. Physical activity and rehabilitation programs after MI appear to reduce mortality and fatal recurrent MI by about 25% over a 3-year period, but they apparently have no effect on the rate of recurrent nonfatal MI.

Obesity

The distribution of body fat appears to have a greater influence on CVD risk factors and CVD rates than does body mass. Distribution of intra-abdominal fat may be particularly significant, and improved methods are available to measure it. The benefits of weight loss in reducing CVD risk factor levels have been well documented.

Diabetes Mellitus

Prevalence rates of diabetes are about twice as high among black and Hispanic Americans as among whites, and they are generally higher among persons of lower socioeconomic status. Native Americans, particularly the Pima and Zuni tribes, have prevalence rates among the highest in the world. This high prevalence of diabetes, exceeding 40% in adults, appears to be related to the increasing obesity among the tribes.

Long-term data on large cohorts show that diabetic persons are at much higher risk of CVD and death at any level of the major CVD risk factors compared with
nondiabetic persons. Unfavorable patterns of the major CVD risk factors are common among diabetic men and women in the United States. The relative risk of CVD among persons with diabetes is higher for women than for men, but this differential diminishes after age 65. Diabetic dyslipidemia, with low HDL and high triglycerides, is a strong predictor of CVD in persons with non-insulin-dependent diabetes mellitus (NIDDM). These data indicate that there is considerable potential for preventing CVD and death by controlling the major risk factors in persons with diabetes, especially women.

Insulin resistance is highly prevalent in obese people and in lean or obese persons with NIDDM. Intra-abdominal fat is more closely associated with blood glucose and insulin concentrations than is total body fat. Insulin resistance syndromes have been described. Impaired tissue sensitivity to insulin and the resulting hyperinsulinemia are found to be related to obesity, hypertension, atherosclerosis, and risk of CVD complications. New evidence from major trials indicates that close control of blood sugar by insulin therapy has a favorable effect in individuals with insulin-dependent diabetes mellitus, substantially reducing the risk of neuropathy as well as kidney and eye disease from microvascular pathology.

**Psychosocial Factors**

Degree of social support has been reported to be a strong predictor of long-term survival after MI. Hostility, anger, and depression have been related to CHD risk, and anxiety has been related to blood pressure. The demand and control characteristics of the work environment have also been reported to relate to hypertension and CVD risk.

Cardiovascular reactivity has been found to be related to psychosocial stress in both sexes, and ethnic differences in hemodynamic responses to experimental psychosocial stress have been found among women at different reproductive stages. Both mental stress and exercise stress produce silent myocardial ischemia; however, mental stress induces ischemia with smaller increases in heart rate.

**Other CVD Risk Factors**

Serum uric acid is independently related to blood pressure and to risk of CVD, but its role in atherosclerosis remains to be elucidated. New risk factors for CHD have been found, including elevated plasminogen activator inhibitor I, increased fibrinogen, elevated lipoprotein (a), and increased blood homocysteine. A low ankle-arm pressure index (ie, the ratio of systolic blood pressure in the ankle to that in the arm) has been noted to be a reliable measure of peripheral arterial disease and a predictor of CVD risk. Ultrasound studies of carotid and other arteries provide an opportunity for limited but reliable testing of associations between arterial wall characteristics and the effects of CVD prevention on atherosclerosis. Evidence suggests that impaired sodium-coupled cell membrane transport mechanisms are involved in the pathogenesis of hypertension.

**Specific Populations**

Comparative epidemiological data are available for persons of lower socioeconomic status; minorities; older persons; women; and infants, children, adolescents, and young adults. Current understanding of CVD in each of these groups is summarized below.

**Lower Socioeconomic Groups**

Educational status is strongly and inversely associated with CVD risk factor levels and CVD death rates. The decline in CVD mortality since the 1960s has been much smaller among groups with lower socioeconomic status than among those with higher socioeconomic status. This disparity is due largely to group differences in CVD risk factors and risk factor trends over the past three decades.

**Minorities**

Age-specific CHD mortality rates are similar in black and white men until age 70, then higher in white men; they are higher in black women than in white women until age 85. The recent decline in CHD mortality has been less in blacks than in whites and least among black women, possibly related to socioeconomic status. Black Americans are at higher risk for sudden cardiac arrest than whites. Recent studies show that the major CVD risk factors are as strongly related to CVD risk in black Americans as in whites.

The major CVD risk factors affect US Hispanics as they do blacks, whites, and Asian Americans. However, Mexican Americans have higher hospitalization rates for CHD and greater in-hospital and later CHD mortality than non-Hispanic whites in the same communities. Diabetes and other risk factors develop early in Mexican Americans, possibly due to a higher incidence and prevalence of obesity.

Age-adjusted death rates for major CVD among older Native Americans and persons of Hispanic origin are lower than for older blacks and whites but greater than for older Asian and Pacific Islanders in the United States. The lower rates among Native Americans have been attributed in part to higher death rates among young adults, so that the contribution of chronic diseases to mortality rates tends to be less marked in this population group.

**Older Persons**

New analyses indicate that the influence of CVD risk factors is important in older as well as younger individuals. The major risk factors for CHD continue to be independent predictors of CHD in men and women 65 to 74 years old. Contrary to previous impressions, older persons can benefit greatly from prevention strategies because of their high absolute risk of a CVD event.

**Women**

Recent studies show that the major CVD risk factors increase CVD risk in middle-aged and older American women. Findings from epidemiological studies also indicate that hormone replacement therapy after menopause has beneficial effects on blood lipid levels and vasoregulation, may favorably influence the progression of atherosclerosis, and may reduce CVD death rates. Estrogen replacement therapy reduces LDL levels by about 15% and increases HDL levels similarly. Estrogen use is also associated with less thick carotid artery walls in older women. Overall, the risk of CHD in women...
receiving estrogen replacement therapy is about 50% lower than that in women who are not.

**Infants, Children, Adolescents, and Young Adults**

Early atherosclerotic lesions in youth are strongly related to postmortem measures of LDL and very-low-density lipoprotein and to thiocyanate levels (which indicate smoking exposure). Further refinement of ultrasound, fast computerized tomography, and magnetic resonance imaging offer potential for assessing premature atherosclerosis.

Epidemiological studies show that blood cholesterol and blood pressure levels and obesity "track" from childhood into adulthood and that the rank order of individuals according to these factors is generally maintained over time. A relation has been found between premature CVD mortality and risk factor levels in offspring. This is accounted for, to some degree, by body mass index and genetically determined factors. During the rapid growth phases of childhood, body size, maturation, obesity, and dietary and exercise habits all interact in girls and boys to influence blood pressure levels. New findings indicate that the nutritional status of mothers and the intrauterine and early postnatal environments may be important determinants for subsequent CVD risk.

**Secondary Prevention of CVD**

Secondary CVD prevention trials demonstrate that lowering blood cholesterol has beneficial effects both in slowing or reversing coronary atherosclerosis and in preventing recurrent CHD events. They also show that cigarette smoking cessation, exercise, and aspirin and clot lysis therapies have favorable effects on CVD. Other trials show that it is possible to prevent stroke in most patients with atrial fibrillation by anticoagulant therapy. Trials of angiotensin-converting enzyme inhibitors demonstrate that their use improves survival in patients with ventricular dysfunction and has potential for preventing heart failure.

**Research Methodology**

During the past 5 years, many advances have been made in the methodology of epidemiological and prevention research. They include development of noninvasive techniques for visualizing early atherosclerosis in major arteries and improved methods of biochemical measurement (eg, of serum lipids and thrombogenic factors); enhanced understanding of the relations between sample size, measurement precision, and the ability to quantify risk factor impact; adoption of statistical techniques for multivariate analyses, sequential analyses, and longitudinal analyses and correction for imprecise measurements; use of meta-analyses; and novel applications of computers at multiple levels of epidemiological and prevention research.

**Community Surveillance and Prevention Strategies**

Recent population-based surveillance studies reveal that much of the decline in CVD deaths can be attributed to a decline in sudden and out-of-hospital deaths, the most severe expression of CHD. NHLBI-supported, community-wide studies have demonstrated that population-wide strategies of disease prevention and health promotion are feasible, that environmental change pro-
The first three priority areas represent a progression across the prevention spectrum, from enhancement of basic knowledge relating to prevention of adverse lifestyles and elevated risk factors (i.e., prevention of CVD risk itself, or “primordial prevention”) to control of existing high blood pressure levels or other major risk factors and, finally, to reduction of CVD morbidity, disability, and mortality in diverse populations. The next two focus on elucidating fundamental aspects of CVD significant to prevention; they address prevention of risk factors and atherosclerosis beginning in youth and development and demonstration of improved, population-wide prevention strategies. The nature and contributions of familial risk factors should be determined and their interaction with other determinants assessed. Preventive interventions could then be targeted to those at high risk.

The sixth priority concerns the clustering of multiple CVD risk factors (obesity, insulin resistance, atherosclerosis) and their determinants. The last two priorities are important for all epidemiological and prevention research, reflecting a continued need for development of technical resources and expansion of effective research training programs. The research needs in each priority area are summarized below.

**Prevention of Adverse Lifestyles and Related Risk Factors**

Studies are needed to advance understanding of the key determinants of elevated CVD risk factors, including the rise in risk factor levels with age, particularly in societies that have a high prevalence of CVD, and to strengthen our ability to influence them. Such studies are essential for achieving the task force’s highest priority: primary prevention of elevated CVD risk.

The major risk factors are partially under genetic control. Interactions between genetic susceptibility and adverse lifestyles merit further study using recent advances in genetic epidemiology and molecular genetics.

The task force recommends epidemiological studies of the disease-causing and disease-protecting effects of lifestyles, especially nutrition. Multiple dietary components need to be assessed concurrently in population samples as they relate to blood pressure and blood lipids, as well as blood glucose and body mass. To resolve many key issues, both cross-sectional and prospective measurements, which use high-quality dietary methods and samples of adequate size and composition, are essential.

The task force also recommends trials of the effects on blood pressure and lipid-lipoprotein profiles of specific dietary patterns in conjunction with other lifestyle changes, including smoking and physical activity changes. Community-wide demonstration programs are recommended for identifying optimal strategies for the primary prevention of elevated risk factors.

**Control of High Blood Pressure and Other Established CVD Risk Factors**

Control of high blood pressure, adverse blood lipids and lipoprotein patterns, and smoking, which are still widely prevalent in the United States, is an essential complement to preventing CVD. Improved and intensified prevention measures for individuals and populations are needed to attain the public health goal of eradicating CVD risk factors in the population.

The task force recommends epidemiological studies of the relations among levels and variations in blood pressure, left ventricular hypertrophy and dysfunction, evolution and prognosis of high blood pressure, and development of CVD. Distributions and trends in the prevalence of major risk factors must be monitored in parallel with disease rates and in research settings that allow their continued evaluation and investigation.

The task force also recommends trials to determine optimal initial and long-term combinations of lifestyle and drug therapy to reduce high blood pressure, modify lipoprotein patterns, and prevent CVD complications. Such trials are now needed among segments of the population that have lower levels of elevated blood pressure (“high normal”), especially systolic blood pressure; moderately high (borderline) total cholesterol levels; or low HDL levels.

**Reduction of CVD Events, Disability, and Death Associated With Socioeconomic Differences**

Large differences in CVD death rates and other measures of CVD burden across population strata classified by socioeconomic level, ethnicity, and geography need to be better understood. Improved intervention strategies could potentially reduce or eliminate these differences. The goal, for all segments of the US population, is to reduce CVD morbidity, disability, and mortality to the lowest attainable levels and thereby eliminate, if possible, the excess burden of CVD that still persists in most segments of American society.

The task force recommends epidemiological studies to clarify the roles of adverse lifestyles, elevated risk factors, and diminished access to health care in causing higher CVD rates and less favorable trends in these rates among more vulnerable segments of the population. The task force also recommends trials and demonstration projects to determine the most effective interventions for preventing CVD risk in families and communities in all population strata.

**Prevention of Hypertension, Dyslipidemia, Smoking, and Atherosclerosis Beginning in Youth**

A strong and compelling rationale for studies early in life is that unfavorable patterns of eating, blood lipids and blood pressure, smoking, and physical inactivity, as well as atherosclerosis itself, all begin in childhood. A much fuller understanding is needed of the causes of population and individual differences in the early onset and progression through adolescence of risk factors and atherosclerosis, including interactions of genes and environment.

Especially important are epidemiological studies of specific environmental, behavioral, nutritional, and heritable influences on the onset and early progression of atherosclerosis in youth. Also needed during early periods of life are trials and demonstration projects focused on the prevention of risky behaviors and elevated risk in individuals, families, and populations.

**Improvement of Population-Wide Prevention Strategies**

Research findings on the beneficial effects of lifestyle and behavioral modification need to be translated into population-wide strategies to prevent and control the
The advances in epidemiology and prevention research proposed by the task force depend on better techniques for achieving more comprehensive, population-based dietary assessments and more precise non-invasive estimates of the extent of atherosclerosis from the earliest to the latest stages of the disease process. Further research on methods to characterize and quantify lifestyles, genetic susceptibility, risk factors, and stages of CVD could enhance the effectiveness of epidemiological research and prevention trials.

New mechanisms are needed to facilitate the maintenance and utilization of research archives and specimen banks. Collaborative research involving epidemiologists, population geneticists, laboratory scientists, molecular geneticists, and clinical investigators is needed to elucidate relations between genetic susceptibility and behavioral and environmental determinants of CVD.

Expansion of Research Training Programs

Critical shortages persist in the number of clinical subspecialists, epidemiologists, and other health professionals available to conduct research and practice in CVD epidemiology and prevention. National goals for controlling CVD can be attained only if adequate numbers of trained health professionals are available to conduct the research needed and to apply research findings through prevention strategies.

The task force recommends expanded programs for training new investigators in epidemiology and in approaches to individual and population-wide prevention and their evaluation. Training should emphasize current public health priorities and greater development of cross-disciplinary skills and interdisciplinary exchange and collaboration. For established health professionals, enhanced support is needed for specialized training, ranging from intensive, short-term seminars to formal degree programs. Continued and increased emphasis should be given to the development of epidemiological and prevention skills in clinical training programs at all levels. Only in this way can continued progress be made in preventive cardiology.
Task force on Research in Epidemiology and Prevention of Cardiovascular Diseases.

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