National Heart,

Lung, and

Blood Institute

Report

of the

Task Force on

# Behavioral Research in Cardiovascular, Lung, and Blood Health and Disease

U.S. DEPARTMENT OF
HEALTH AND
HUMAN SERVICES

Public Health Service
National Institutes of Health

National Heart,

Lung, and

Blood Institute

Report

of the

Task Force on

# Behavioral Research in Cardiovascular, Lung, and Blood Health and Disease

The National Heart, Lung, and Blood Institute (NHLBI) provides leadership for a national program in diseases of the heart, blood vessels, lungs, and blood; sleep disorders; and blood resources. It plans, conducts, fosters, and supports an integrated and coordinated program of research that includes basic investigations, clinical trials, observational studies, and demonstration and education projects related to the causes, prevention, diagnosis, and treatment (including emergency medical treatment) of heart, blood vessel, lung, and blood diseases, sleep disorders, and the management of blood resources, through research performed in its own laboratories and through research grants and contracts to scientific institutions and to individuals. The Institute also supports research training and career development for new and established researchers in basic and clinical research relating to these topics.

U.S. DEPARTMENT OF
HEALTH AND
HUMAN SERVICES

For Administrative Use
February 1998

Public Health Service
National Institutes of Health

# Foreword

I am pleased to present this report of the National Heart, Lung, and Blood Institute (NHLBI) Task Force on Behavioral Research in Cardiovascular, Lung, and Blood Health and Disease. It is an important document that addresses a topic of great timeliness and interest to those of us who are concerned with the public health of the United States.

The NHLBI has a longstanding appreciation of the value of behavioral research. From the earliest days, when the concept of "coronary prone" behavior was introduced, to the growing recognition of the need for strategies to encourage health-promoting behaviors and lifestyles, to more recent efforts to incorporate health-related quality of life measures into our clinical studies—behavioral research has contributed much to our understanding of cardiovascular disease. Although still in its infancy, the application of this discipline to lung and blood diseases, sleep disorders, and transfusion medicine issues clearly offers much promise for advances in treatment and prevention.

Acknowledging that many opportunities lie in biobehavioral research, the NHLBI convened this Task Force in November 1995 to chart a course for future research efforts. Composed of national experts, it was charged to:

- Review the state of knowledge in biobehavioral research in cardiovascular, lung, and blood diseases and sleep disorders over the past 5 years
- Identify research opportunities
- Develop a comprehensive plan, including scientific priorities, for NHLBI support of research on health and behavior for the next several years.

During a series of meetings that spanned nearly 2 years, the Task Force members worked to develop the report published herein. Organized into two major divisions—*Behavioral Antecedents of Disease* and *Behavioral Interventions: Prevention and Management of Disease*—it provides a detailed summary of accomplishments to date, highlights new scientific opportunities, and identifies specific recommendations for future research. Throughout the report, there is ample evidence of past progress and a compelling vision of the challenges that lie ahead.

The Institute is very pleased to have this report to guide its future activities with respect to behavioral research in cardiovascular, lung, and blood diseases and sleep disorders. We are grateful to the Task Force members for their valuable contribution to this important and timely endeavor.

CLAUDE LENFANT, M.D.
Director

# Contents

National Heart,
Lung, and
Blood Institute
Report
of the
Task Force on
Behavioral Research in
Cardiovascular, Lung,
and Blood Health and Disease

# Executive Summary

# Executive Summary

Behavior contributes significantly to health, well-being, and longevity. Indeed, clinical and epidemiological research supports numerous behavioral guidelines for the prevention of disease. These guidelines include regular physical activity and the maintenance of appropriate weight; avoidance of tobacco products; dietary intake of fruits, vegetables, and fiber, coupled with a low consumption of fat; moderate use of alcohol; and the ability to cope effectively with stress. Among persons who suffer from disease, behavior also is often critical to achieving treatment objectives. For example, patients must frequently comply with complex and lengthy treatment regimens, as well as assume significant personal responsibility for managing their symptoms and monitoring their health status.

Although we may aspire to greater health through prudent behavior, reality reflects abundantly our frequent failure to do so. Many examples may be cited. Cigarette smoking remains prevalent in American society and is currently increasing in some segments of the teenaged population. Only a quarter of Americans engage in regular physical exercise, and although fat consumption has decreased somewhat in recent years, rates of obesity have risen appreciably over the same period. It is also estimated that five of every ten patients fail to adhere fully to prescribed therapies.

Hence, behavior's role in health and disease encompasses both promise and challenge—the promise of a reduced risk for illness and better disease management, and the challenge of promoting actions that will contribute significantly to this goal. Behavioral research seeks to inform both of these objectives. Two of its primary aims are to:

- Elucidate the nature, origins, and effects of health-related behaviors

- Apply behavioral principles to modify individuals' health-impairing behaviors and lifestyles.

In this report, the Task Force on Behavioral Research in Cardiovascular, Lung, and Blood Health and Disease reviews the current status and prospects for behavioral research into disease risk, risk reduction, and treatment, as related to diseases of the heart, vasculature, lungs, and blood, and to sleep disorders.

For many decades, clinicians and scientists have also speculated on the role that emotional stress and personality traits play in the pathogenesis and clinical expression of various disorders, including coronary heart disease (CHD), essential hypertension, and asthma. The rigorous study of such concepts was long hampered by imprecise definitions of stress and personality and by the absence of reliable methods of assessing these variables. In recent years, however, this research has progressed significantly because of the availability of new measurement techniques and advances in behavioral science methodologies. Consequently, the increased risk for disease conferred by psychosocial factors and, with respect to cardiovascular diseases (CVD), the biological processes underlying these associations are much better understood than was the case a decade ago.

Beyond the causes and treatment of disease is the individual's experience of illness itself. Disease is often accompanied by pain, apprehension, restricted mobility and other functional

impairments, difficulties fulfilling personal, family, and financial responsibilities, and occasionally, impaired cognitive function. Diagnostic procedures and medical interventions may affect behavior in a variety of ways, sometimes eroding (and at other times enhancing) patients' overall quality of life, even while improving medical outcomes. Behavioral scientists are currently studying these effects and defining the dimensions of quality of life for both ill and healthy individuals.

It is now widely acknowledged that medicine's concerns extend beyond the biological end points of disease to encompass a wider spectrum of patients' experiences, including their emotional, cognitive, and interpersonal functioning. Because heart, lung, and blood diseases are responsible for a substantial portion of all morbidity and mortality in the United States, the behavioral and social sequelae of these diseases and their treatments have become increasingly important areas of behavioral science research.

With an aging population in the United States, the prevention and management of chronic illnesses are becoming significant concerns. Here, behavioral research is enhancing understanding of the ways patients cope with serious illness and the efficacy of psychosocial and other environmental interventions to ease patients' adjustment to illness, promote their recovery, and prevent the recurrence of disease.

The scope of behavioral research is therefore wide-ranging. For cardiovascular, pulmonary, and blood diseases and sleep disorders, it includes three main areas:

- Effects of behaviors, stress, and psychosocial factors on individuals' risk for disease
- Behavioral aspects of illness and of treatments for disease
- Psychosocial and behavioral factors in the management of chronic disease.

Recent advances in each of these areas are reviewed in this report. In this executive summary, the Task Force describes the scope of the report; defines key terms; provides an overview of the report; summarizes research accomplishments and presents overall conclusions; and recommends several thematic objectives for future research.

## Scope and Organization of the Report

The National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) convened the Task Force on Behavioral Research in Cardiovascular, Lung, and Blood Health and Disease in November 1995. This Task Force was composed of national experts in basic and applied behavioral research on cardiovascular, pulmonary, and blood diseases and sleep disorders. Several additional scientific consultants assisted the Task Force.

The NHLBI charged the Task Force to review the state of the science of behavioral research on heart, lung, and blood diseases and sleep disorders; to identify key opportunities for behavioral investigation; and to make specific recommendations for future research. The Task Force focused its review on research accomplishments of the past 10 years and sought to identify priority areas of research for the decade ahead.

Although the scope of research pertinent to this review encompasses all diseases of heart, lung, and blood, and topics ranging from pathophysiology to clinical management, the Task Force was necessarily constrained by the breadth of its members' expertise. Addressing every topic of potential interest to behavioral research was not possible, but the general strategies of research and research recommendations presented in this report are also applicable to currently understudied areas and areas not explicitly covered in the report. Research on sleep was included within the charge of this review because of the relevance of sleep disturbances to behavior and to heart and lung

diseases and because the NHLBI houses the National Center on Sleep Disorders Research.

The Task Force also notes that behavioral research has not progressed equally for cardiovascular, pulmonary, and blood diseases. Because the preponderance of existing work is in the cardiovascular area, most of the scientific accomplishments reported by the Task Force also pertain to CVD. However, the diseases of lung and blood, as well as sleep disorders, are areas of rich opportunity for future behavioral research. The Task Force therefore attempted to identify major questions to be addressed in these currently less-established areas, particularly as they relate to the expression of symptoms and the management of disease. It is hoped that the report will stimulate such work.

## Definitions and Terms

The term "behavior" is used here in its broadest sense. In this report, behavior denotes both the external actions of individuals and the more subjective qualities of individuals' experiences. These subjective experiences are represented "internally" by feelings, moods, attitudes, perceptions, and psychological dispositions (e.g., personality traits).

The term "environment" also is defined broadly and includes both psychosocial and physical environments. Psychosocial environmental factors, such as socioeconomic status, social isolation, and networks of social affiliation and support, figure prominently in behavioral research. Other pertinent psychosocial factors include ethnicity, culture, and occupational and social stress. Physical environmental factors include geographic areas of residence, quality of habitat, and substances (e.g., allergens) to which individuals may be exposed in occupational and residential settings.

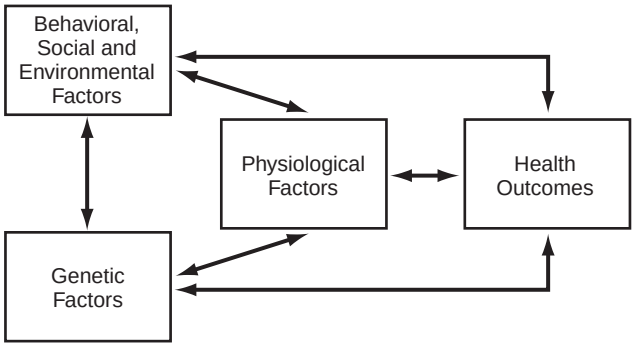


**Figure 1.** Factors affecting health. Adapted and reprinted from A Strategic Plan for the Office of Behavioral and Social Sciences Research at the National Institutes of Health. NIH Publication No. 97-4237.

Behavioral variables affect disease in the context of genetic and biological predispositions. Thus, genetic variability among individuals, often in interaction with environmental variables, can affect both behavior and disease-relevant physiology. Figure 1 depicts the various relationships among variables that define the domain of behavioral research in health and disease, as formulated recently by the NIH Office of Behavioral and Social Sciences Research.

To the extent that some of these behavioral factors conspire to increase risk for disease, it also follows that their modification might diminish risk or aid in the management of disease. Psychological interventions therefore seek to alter the behaviors of individuals in beneficial ways, by changing certain aspects of the environment, reinforcing preferred behaviors, or modifying patients' motivational states, thoughts, or feelings.

## Two Broad Conclusions

The Task Force reached two broad conclusions based on its review of the state of the science of behavioral research on heart, lung, and blood diseases and sleep disorders:

- Behavioral research has contributed significantly to the understanding of disease risk and the progression and clinical manifestations of disease.

- Effective modification of individuals' behavior and/or psychosocial environments can potentially reduce disease risk, ameliorate the burdens of illness, and promote recovery and rehabilitation.

The Task Force report is organized in relation to these two conclusions or themes. Part I focuses on associations between behavior and disease, and Part II addresses the behavioral aspects of managing disease.

## Overview of the Report

In Part I, *Behavioral Antecedents of Disease*, the Task Force addresses two main topics: the extent to which behavioral factors increase risk for cardiovascular and lung diseases, and the influences of these factors on the pathophysiology of disease and the expression of symptoms. Three types of behavioral variables are implicated in individuals' risk for disease:

Lifestyle factors, such as cigarette smoking, physical inactivity, adverse diet, obesity, and consumption of alcohol

Individual characteristics, including psychological traits (e.g., anger, hostility, depression), personality, and physiological responsiveness to stress

Social and environmental variables, such as socioeconomic status, ethnicity, lack of social support, and occupational stress.

Some of the lifestyle factors addressed in this report also were considered in the NHLBI Report of the Task Force on Research in Epidemiology and Prevention of Cardiovascular Diseases, published in August 1994. These reports are complementary, with the former report emphasizing the links between lifestyle and disease and the present report emphasizing advances in behavioral research on the development, maintenance, and modification of health-impairing habits.

In addition to its emphasis on behavioral factors, Part I also includes a review of experimental and clinical research on physiological processes that link behavior with disease. For example, there is increasing evidence that behavioral factors exacerbate atherosclerosis, promote hypertension and related alterations in cardiac structure and function, induce myocardial ischemia in persons with coronary artery disease (CAD), affect processes involved in hemostasis and thrombosis, and trigger cardiac arrhythmias.

Many of the lifestyle factors that increase risk for CVD also appear to aggregate in relation to abnormalities of insulin and glucose metabolism. In addition, sleep disorders can profoundly affect cardiovascular and pulmonary conditions. Studies of individuals with asthma indicate that psychological factors may also affect airway obstruction and that individual differences in the ability to perceive diminished airflow in asthma may be related to the exacerbation of symptoms.

In Part II, *Behavioral Interventions: Prevention and Management of Disease*, this report focuses on applied behavioral research. Interventions to reduce the risk of disease or improve disease management may be targeted to individuals, groups, or communities and may range from health education to behavior-modification programs, "skills" training, and some forms of psychotherapy.

The objectives of interventions to modify risk factors for disease include prevention and cessation of smoking, promotion of regular exercise and increased physical activity (including physical rehabilitation of cardiac patients), dietary modification, weight loss, and control of alcohol use and abuse.

Addressing the behavioral aspects of disease management, the Task Force focuses on chronic

diseases. Topics include prevention of the progression or recurrence of CVD; behavioral management of chronic lung diseases (asthma, chronic obstructive pulmonary disease [COPD], cystic fibrosis [CF], and tuberculosis); treatment of sleep disorders; adjustment to the debilitating symptoms of sickle cell disease, thalassemia disorders, and hemophilia; and behavioral aspects of blood donation and transfusion medicine.

Concluding this part of the report is a discussion of two key issues for improving health outcomes: ensuring adequate adherence to treatment regimens that frequently are complex, inconvenient, or painful; and evaluating the effect of disease and medical treatments on patients' quality of life. These cross-cutting issues are highly pertinent to the management of all cardiovascular, pulmonary, and blood diseases and to sleep disorders.

## Summary of Research Accomplishments

The accomplishments of behavioral research on heart, lung, and blood diseases and sleep disorders are summarized below under six major topics. The Task Force provides a more detailed discussion of these accomplishments in Parts I and II of its report. The major topics for organizing this summary are:

- Lifestyle risk factors
- Psychosocial risk factors
- Behavior, pathophysiology, and symptom expression
- Modification of risk factors
- Behavioral aspects of disease management and adherence to treatment
- Quality of life.

### Lifestyle Risk Factors

Behavioral scientists have made significant progress in understanding the initiation and maintenance of health-damaging behaviors that are risk factors for cardiovascular and pulmonary diseases. The most prominent of these risk factors are cigarette smoking, adverse diet, obesity, excess consumption of alcohol, and physical inactivity.

Smoking accounts for more than 400,000 deaths each year in the United States. It is a major risk factor for CHD and is the primary cause of COPD. Coronary disease risk is also elevated in sedentary individuals, as it is among persons whose serum cholesterol levels are increased due to consumption of a high-fat diet.

Diet also can protect against CVD. For example, diets abundant in fruits and vegetables appear to reduce risk for hypertension and stroke. Obesity, on the other hand, is associated with an increased risk for hypertension, diabetes, CHD, and altered respiratory function, which is associated with sleep apnea. Excessive consumption of alcohol is a risk factor for cardiomyopathy, cardiac arrhythmias, CHD, sudden cardiac death, and stroke.

The prevalence of these lifestyle risk factors varies substantially among different segments of the population and is disproportionately high among persons of lower socioeconomic status. Cigarette smoking, for example, has declined overall in the United States over the past several decades, but the prevalence of smoking among teenagers remains unacceptably high and has increased recently among young women, Asian Americans, and possibly black men.

In addition, only one-fourth of Americans exercise regularly, and women, especially black women, and elderly persons exercise the least. Because a sedentary lifestyle is conducive to gaining weight, it is not surprising that obesity also is highly prevalent. Indeed, it is estimated

that one-third of adults and one-fourth of children and adolescents are currently overweight—a dramatic increase over the number of Americans who were overweight just a decade ago. Being overweight is especially prevalent among black women and Mexican American and Native American women, 50 percent of whom may be considered obese.

Americans' intake of dietary fat has decreased somewhat in recent years, but no more than 25 percent of persons in any age category consume 30 percent or less fat in their diets, and only a third of the population eats the recommended daily servings of fruits and vegetables. Unlike smokers, among whom nicotine-dependence is the norm, most people who drink do so in moderation. Nonetheless, the lifetime prevalence of alcohol dependence is 14 percent in the United States and approximately 20 percent among men.

## *Antecedents of Risk Factors*

Most behaviors that constitute risk factors for cardiovascular and pulmonary diseases emerge early in life and reflect genetic and environmental influences. For example, genetic factors affect the onset and persistence of tobacco dependence, just as there is significant genetic predisposition to alcohol dependence. The reinforcing effects of alcohol also appear to be greater among alcoholics who have a family history of alcoholism than among offspring of nonalcoholics.

The age of onset is similar for cigarette smoking and alcohol consumption. Use of alcohol is initiated usually during adolescence, and nearly all dependent smokers begin to smoke by age 19. A few years of experimentation with smoking usually precedes an addiction to smoking.

Several other risk factors also exhibit significant heritability—body weight, obesity, and the amount of weight gained when consuming a high-calorie diet. Underscoring these observations is the recent identification of an obesity-promoting gene and its protein product, leptin. Other evidence shows that dietary preferences generally are established during childhood, whereas large weight gains that result in obesity often occur during the third and fourth decades of life, for both men and women.

Psychosocial and environmental factors also are important determinants of lifestyle risk factors. For example, peer pressure, family problems, depressed mood, failure in school, antisocial behavior, and use of other drugs all increase the risk for smoking among teenagers. In addition, smoking may be reinforced by somewhat different factors in men and women, with the effects of nicotine playing a greater role among men and social factors, such as concerns relating to weight control, predicting initiation of smoking among young women.

The behavioral predictors of alcohol use are similar to many of the predictors of smoking. These include antisocial characteristics, emotional problems, attention disorders, and high activity levels. Alcohol reduces tension, and individuals' expectations of this effect are related to both their initial and their later use of alcohol. Over time, situations that are associated with alcohol use (such as stress or socializing with peers) also elicit urges to drink. In addition, an individual's tolerance for alcohol increases over time, and greater quantities must be consumed to maintain the same effects.

Researchers are only now beginning to focus on the development of dietary preferences. With the introduction of fat-reduced foods, it has become apparent that individuals vary markedly in the degree to which they will adopt modified food items as calorie substitutes, or alternatively, increase their overall consumption. The determinants of this variability among individuals are not yet understood.

Obesity has multiple determinants. Low levels of physical activity predispose individuals to gaining weight, as does consumption of excess

calories. Other factors include low metabolic rate, a high intake of dietary fat, the tendency to utilize carbohydrates instead of fat for fuel, higher insulin sensitivity, and stress. Interestingly, some evidence indicates that obese persons often may consume foods that are higher in fat but equal in calories to the diets of leaner individuals.

Little is yet known regarding the determinants of an active or sedentary lifestyle, although several factors are associated with individuals' participation in structured exercise programs. These factors include convenience, cost, perceived benefits of exercise, enjoyment of the activity, and involvement of family and other forms of social support.

## Psychosocial Risk Factors

Behavioral characteristics of individuals and adverse social environments increase risk for CVD. Psychological variables associated with risk include traits of personality, mood disturbances, and physiological responses to stress. The social risk variables include low socioeconomic status, life stress, work environment characteristics, and lack of social resources.

### *Psychological Traits*

Extensive research on the various components of the Type A behavior pattern—a constellation of traits involving competitiveness, time urgency, and hostility—has identified hostile attitudes of cynicism and mistrust toward others as a robust risk factor for all-cause mortality, and to a somewhat lesser extent for the development of CHD.

Depression is another significant disease risk factor. Clinical depression is highly prevalent among persons surviving a myocardial infarction (MI)—heart attack—and, independently of disease severity, predicts later clinical events, including reinfarction, cardiac arrest, and mortality. Risk for stroke is also elevated in depressed individuals, as is the incidence of sudden death among women with a history of mental health disorder, principally depression.

In addition, symptoms of lesser severity, such as pessimistic attitudes toward the future and "vital exhaustion" (a combination of traits characterized by fatigue, dejection, and irritability), are associated with a poor prognosis for CHD patients. Vital exhaustion is associated with restenosis of the coronary arteries after angioplasty and with the 4-year incidence of angina and nonfatal heart attack. Individuals' levels of anxiety following an MI also predict subsequent arrhythmia and ischemic events, reinfarction, and sudden death.

### *Hemodynamic Responses to Stress*

People vary not only in personality traits and mood, but also in their cardiovascular responses to the events of daily life. Researchers have long hypothesized that exaggerated hemodynamic (blood pressure and heart rate) responses to stress, as seen in certain "hyperreactive" individuals, contribute to risk for CVD. Some evidence now indicates that this reactivity (heightened hemodynamic responses to stress) predicts the development of hypertension over intervals of 3 and 4 decades, as well as relative increases in blood pressure among normotensive individuals over periods of shorter duration.

In some studies, stress-induced blood pressure reactivity also is found to correlate with measures of left ventricular (LV) mass, and among CHD patients, with episodes of myocardial ischemia. Moreover, recent studies suggest that blood pressure reactivity elicited by mental stress is associated with the extent and progression of atherosclerosis in the carotid arteries, as measured by ultrasonography, and may increase risk for later clinical events among individuals who survive an acute MI.

### *Socioeconomic Status and Health*

There is now abundant evidence that individuals of lower socioeconomic status experience earlier mortality, as well as higher rates of heart disease, diabetes, hypertension, chronic bronchitis, emphysema, and tuberculosis, compared with persons occupying more advantaged positions in society. The socioeconomic status "gradient" for health outcomes extends across the entire continuum of socioeconomic stratification, and therefore is not attributable to poverty alone or to poor nutrition, inadequate hygiene, or restricted access to medical care services (factors that differ little between the middle and upper strata of society, particularly in countries having universal health care). Lifestyle risk factors for disease, such as smoking, inactivity, obesity, and alcohol abuse, also correlate inversely with socioeconomic status, yet these factors too do not fully explain the increased morbidity and mortality associated with lower socioeconomic status.

In the United States, race and ethnicity are strongly related to disease risk as well; for example, blacks experience higher rates of stroke, hypertension, LV hypertrophy, diabetes, obesity, and mortality from asthma, compared with their white counterparts. However, the socioeconomic status–health gradient cannot be explained solely by the lower occupational prestige, income, and educational attainment of minority racial and ethnic groups in American society. On the other hand, it remains unclear to what extent the poorer health outcomes of black, Hispanic, and Native American populations may be explained by socioeconomic status effects.

### *Other Social Stressors and Health*

A number of social variables also vary inversely with socioeconomic status. These include exposure to stressful life events, characteristics of the work environment, and social resources. Much recent research indicates that stress and an individual's social environment can affect health. Especially traumatic events (e.g., earthquakes) can trigger MI and sudden cardiac death in susceptible individuals. In addition, long-term occupational stress, such as the strain of a demanding job that affords little opportunity for decision-making, increases risk for CHD, hypertension, and stroke.

Most of the evidence accumulated on these stressors comes from studies of men. Additional studies are needed of women to determine whether the salient features of work-related stress are the same as in men and whether they are complicated by the multiple work, home, and family roles and responsibilities frequently faced by women.

Limited access to important social resources, such as intimate relationships, marriage, social contacts, and participation in community organizations, and the lack of tangible or emotional sources of support, also increase individuals' risk for disease. Compared with persons having many social contacts, socially isolated individuals experience a twofold increased risk for premature mortality from all causes and, especially in men, death attributable to CVD. The same social factors are also important for persons with existing CHD, in whom social isolation (e.g., living alone) or an absence of social support predict shortened survival, recurrent MI, and other clinical events.

## Behavior, Pathophysiology, and Symptom Expression

Behavior influences individuals' risk for disease by affecting important pathophysiological processes and the expression of symptoms. Significant advances have been made in understanding these processes in CHD, hypertension, insulin metabolic abnormalities, asthma, and sleep disorders. Recent accomplishments in each of these areas are summarized below.

## *Coronary Heart Disease*

For CHD, the Task Force highlights behavioral research relevant to three disease processes: atherosclerosis, acute cardiac events (myocardial ischemia [a deficiency of blood supplied to cardiac tissue via the coronary arteries], MI, and sudden cardiac death), and hemostasis and thrombosis. The protective effect of activity of the parasympathetic nervous system is also considered.

*Atherosclerosis*. Experimental research on animals has greatly enhanced understanding of the role that behavior plays in promoting the underlying lesions of CAD. For example, studies of monkeys show that certain behaviors exacerbate atherosclerosis. Among monkeys that live in social groups characterized by hierarchies of social status, subordinate females develop greater atherosclerosis than dominant females. Among males, however, dominant monkeys develop greater atherosclerosis, but only when housed in stressed, or unstable, social groups. This exacerbation of atherosclerosis is partly caused by suppression of normal ovarian function in subordinate female monkeys and, among males, by an activation of the sympathetic nervous system that accompanies the dominant animal's struggle to retain elevated status in an unstable social environment.

*Myocardial ischemia, infarction, and sudden cardiac death*. The development of atherosclerosis in humans is a lengthy process that ordinarily spans decades of life. The events that constitute clinical manifestations of CHD, by contrast, often occur acutely and without warning.

Many of the 1.5 million heart attacks that occur annually in the United States are experienced without prior symptoms, and about one-third culminate in sudden death. In hearts that are rendered intrinsically unstable by atherosclerotic disease, acute emotional stress may precipitate an MI and/or sudden cardiac death by causing an inappropriate constriction of the coronary arteries, promoting the rupture of atherosclerotic plaques and the subsequent formation of blood clots (thrombi) within the artery, and by disrupting the heart's normal electrical activity, resulting in lethal cardiac arrhythmias.

Recent laboratory studies show that acute psychological stress induces myocardial ischemia in about half of patients with CAD. Observations on CAD patients during their normal activities also show that mental stress can provoke episodes of myocardial ischemia similar to those elicited by strenuous physical exercise. Moreover, some evidence indicates that in patients who experience ischemia during exercise, mental stress-induced myocardial ischemia, if present, may add important prognostic information in the prediction of clinical events.

The pathophysiology of mental stress-induced ischemia is being clarified. This ischemia appears to involve two processes—the constriction of diseased epicardial coronary arteries and the failure of smaller resistance vessels in the heart to dilate normally. These processes act to decrease blood supply to the heart muscle during periods of stress. In addition, studies in monkeys show that long-term social stress also impairs the normal vasomotor function of the coronary arteries and that this impairment occurs somewhat independently of the extent of atherosclerosis present in the arteries.

*Hemostasis and thrombosis.* Hemostasis and thrombosis relate to the clotting of blood and are important processes involved in MI and other acute coronary events. Arousal of the sympathetic nervous system and alterations in blood flow in response to stress activate blood platelets, a central event in the formation of thrombi in the coronary arteries. Activation of the sympathetic nervous system in response to intense emotional arousal also increases the heart's vulnerability to ventricular arrhythmias.

Considerable progress has been made recently in identifying the cardiovascular effects of intense emotional states. Using sophisticated neurobiological techniques, investigators have mapped brain areas and neurochemical pathways (e.g., those involving the neurotransmitter serotonin) that mediate emotional influences on the heart.

*The role of the parasympathetic nervous system.* In contrast to the deleterious effects of arousal of the sympathetic nervous system, enhanced activity of the parasympathetic nervous system exerts a protective, or antifibrillatory, effect on the electrical activity of the heart. Recent studies show that an index of parasympathetic tone derived from the quantification of heart rate variability is useful for stratifying patients who have suffered an MI in relation to their risk for future events.

Positive behavioral influences such as exercise conditioning can promote a beneficial pattern of autonomic function—enhanced parasympathetic tone, increased heart rate variability, reduced activity of the sympathetic nervous system, and decreased susceptibility to arrhythmias. In general, the triggering of clinical events in patients with symptomatic CHD appears to involve multiple, complex mechanisms—electrochemical processes in the heart, alterations in myocardial perfusion associated with abnormalities of coronary vasomotion and, possibly, increased aggregability of platelets. All these processes can be influenced by the behavioral and emotional states of individuals.

## Hypertension

As noted previously, various behavioral factors (e.g., overweight, high intake of salt, consumption of alcohol, stress, job strain) increase an individual's risk for hypertension. Animal experiments demonstrate that chronic exposure to aversive stimuli promotes sustained hypertension, as does electrical stimulation of brain areas involved in emotional behavior.

In addition to the prominent role that sympathetic nervous system arousal may play in the development of hypertension, a high dietary intake of salt appears to augment blood pressure elevations due to stress in some animal models. This effect is associated with slower elimination of excess sodium and water by the kidney.

Studies of humans show that stress also may result in a slow elimination of sodium in persons who are particularly susceptible to hypertension, such as blacks and persons who have a family history of hypertension or marginal elevations in blood pressure levels. By using portable, automated monitors to measure blood pressure levels in ambulatory conditions, researchers also have been able to document the effects of naturally occurring (daily) stressors on the levels and variability of individuals' blood pressure.

Ambulatory monitoring also has been used to identify groups of hypertensive individuals who may differ in prognosis. For example, some patients, known as "white-coat" hypertensives, have elevated blood pressure levels in clinical settings, but not during normal daily activities. Compared with hypertensives whose blood pressures are elevated in both clinic and ambulatory environments, these patients are more likely to show normal cardiac structure and function and an absence of increased risk for coronary morbidity and mortality.

Increased LV mass and wall thickness, which often accompany hypertension, are important predictors of risk for death from CVD. Although blood pressure level is a major determinant of LV mass, other factors associated with ventricular enlargement include job strain, dietary salt intake, and activity of the renin-angiotensin and sympathetic nervous systems.

## Insulin Metabolic Syndrome

Several prominent risk factors for CVD tend to aggregate within individuals. These risk factors

include abdominal obesity, hypertension, glucose intolerance, and dyslipidemia. This constellation of correlated risk factors, among which abnormalities of glucose metabolism are thought to play a central role, may also have important origins in behavior and lifestyle. Smoking, overeating, physical inactivity, and psychological stress all appear to increase insulin resistance, whereas "heart-healthy" behaviors (e.g., appropriate diet, exercise) enhance insulin sensitivity.

The biological mechanisms linking each of these behaviors to the various components of the syndrome are not yet fully understood. One possibility is that insulin resistance interacts with activation of the sympathetic nervous system in an expanding circle of reciprocal influence. These factors may each be fueled partly by behavior (e.g., stress, smoking, physical inactivity, adverse diet) and, together, may culminate in elevated blood pressure, dyslipidemia, obesity, glucose intolerance, and atherosclerosis, thereby increasing risk for CHD.

## *Asthma*

Unlike much of CVD, many pulmonary and blood disorders such as CF, sickle cell disease, thalassemia disorders, and hemophilia stem from genetic abnormalities. Behavioral factors are rarely, if ever, involved in the cause or course of these diseases. In other disorders, environmental or occupational exposures may be causative, as in black lung or asbestosis. Another lung disorder, COPD, may be attributed to a single aspect of lifestyle, cigarette smoking, which accounts for almost 90 percent of cases of this disease.

Asthma poses a somewhat different problem, as it is influenced by both genetic and environmental variables. The latter include a host of factors that may precipitate asthma attacks, including allergens, air pollution, chemicals, food additives, exercise, and exposure to cold. There is now some evidence that central nervous system processes involving emotion, reactions to stress, or conditioning can cause constriction of the airways in susceptible individuals and, consequently, may play a role in the expression of asthma symptoms.

Recent studies also show that emotional states can alter the function of T-lymphocytes, including the production of cytokines, which suggests a possible link between emotional experiences and the body's regulation of inflammation. Obtaining direct evidence of an association between stress or emotional responses and inflammatory processes in the lung is an important goal for future research.

## *Perception of Symptoms*

Another important area of investigation is patients' perceptions of their physical symptoms. Among CHD patients, for example, both biological and behavioral factors determine whether a patient experiences anginal pain during myocardial ischemia. Anxious and depressed individuals report more anginal pain than nonanxious and nondepressed patients during episodes of ischemia. Depression in these patients may be related to both a diminished beta-endorphin responsiveness to exercise and an earlier onset of exercise-induced anginal pain.

Patients with asthma also differ in their abilities to perceive varying levels of airflow obstruction. For these patients, a failure to perceive shortness of breath (dyspnea) can delay appropriate treatment seeking and thereby increase risk for more serious exacerbations of the disease.

## *Sleep Disorders*

Sleep disturbances have many behavioral and physiological consequences, and some of these can affect the clinical manifestations of cardiovascular and pulmonary diseases. Disrupted sleep contributes to the enhanced risk for sudden cardiac death among patients with heart failure and may similarly affect persons with CHD.

The profound surges in activity of the sympathetic nervous system that occur during sleep can trigger myocardial ischemia and potentially fatal cardiac arrhythmias. For example, increased activation of the sympathetic nervous system during rapid-eye-movement (REM) sleep may inappropriately reduce blood flow in the partially obstructed coronary circulation. Moreover, because parasympathetic nervous system activity is diminished during sleep among patients with a history of MI, vagal "protection" against ventricular fibrillation is also compromised in these individuals and may increase risk for sudden death.

Obstructive sleep apnea syndrome (OSAS) is a breathing disorder characterized by closure of the throat during sleep, resulting in obstructed airflow. The obstruction is alleviated only on arousal. OSAS affects perhaps 10 million Americans, mostly obese, and has many behavioral and health consequences. These include morbid sleepiness, depressed mood, cognitive impairment, and increased risk for accidents while driving. OSAS is associated with risk for arterial hypertension and stroke. In persons with CHD, OSAS is also associated with risk for cardiac arrhythmias (which occur frequently during arrested breathing), nocturnal ischemia, and MI. Indeed, the risk for heart attack may be increased more than 20-fold among cardiac patients who have severe apnea. Approximately 120,000 cardiovascular events and an estimated 20,000 deaths each year in the United States are associated with OSAS.

## Modification of Risk Factors

Most public health and clinical efforts to reduce risk of disease and to prevent disease recurrence are aimed at altering the risk-enhancing behaviors of individuals and populations. These efforts are based on an understanding of the development and progression of high-risk behaviors, as well as principles of behavior change and social influence.

### *Smoking*

The decades-long decline in smoking prevalence, from 42 to 26 percent of Americans, has been aided by research on smoking and nicotine dependence and by developing treatments for smoking cessation, school-based prevention, and mass-media communications. Yet, new and continuing challenges lie ahead. The decline in smoking is less steep now than in previous decades, and the prevalence of smoking is increasing in some segments of the population. These challenges may be met, in large part, by additional research on smoking-related behavioral interventions.

Because of the addictive quality of nicotine, primary prevention must continue to be the central concern of public health efforts. Teenagers, in particular, misunderstand the nature of nicotine dependence; one-half of all teenage smokers predict they will quit within 5 years, but most do not. The success of early interventions to enhance children's abilities to resist peer pressures to smoke has varied from modest to good, with better outcomes achieved when these programs are conducted within the context of broader community efforts to prevent smoking (e.g., public policy restricting access to cigarettes).

Smoking cessation continues to be a top priority in the modification of risk factors for cardiovascular and pulmonary diseases. Smokers who quit before age 50 halve their risk of dying within the next 15 years, and the relative risk for heart disease, stroke, and smoking-related cancers declines even among smokers who quit in their mid-60s.

Although most smokers who quit do so on their own, smokers who participate in intensive interventions to stop smoking have higher rates of success. Quit rates of 20 to 25 percent at a 1-year follow-up are common for multi-session,

multimodal smoking-cessation programs for groups. These rates compare favorably with the rates of 5 percent or less for smokers who receive no help.

The primary focus of smoking-cessation programs is prevention of relapse. Relapse may be associated with symptoms of nicotine withdrawal or with behavioral factors such as psychological stress, concerns about weight, and conditioned cues for smoking. Individuals who are most likely to succeed in quitting are older and have higher incomes and educations, a lower dependence on nicotine, other acute health problems, and confidence in their ability to succeed.

Nicotine replacement therapy (by gum or transdermal patch) has helped prevent individuals from relapsing and has nearly doubled the success rates for smoking cessation when used correctly. That nicotine gum as a sole intervention may be no better than placebo, however, highlights the importance of behavioral factors in tobacco dependence—factors left unaddressed when treating by medication alone.

Intensive interventions result in the best outcomes. However, public health programs that target smoking behavior (e.g., through mass-media messages, creation of smoking-restricted work and public areas) also have been shown to increase smoking cessation and reduce relapse. Even physicians' directives to patients that they quit smoking can increase quit rates by 5 percent or more, over that achieved in smokers not directed to quit.

## *Physical Inactivity*

Physical activity is important for preventing disease and for rehabilitation. Several community efforts to increase physical activity in the general population, such as initiation of worksite exercise programs and development of recreational environments for exercise, have had beneficial effects. Programs to increase activity levels in the elderly, particularly supervised home-based exercise, have also produced positive results.

In addition, school-based programs can increase children's levels of physical activity. Many of these programs, however, have been restricted to elementary school students and have not included long-term follow-up. Moreover, additional efforts are needed to promote exercise among adolescents, as levels of physical activity frequently decline during this developmental period, especially among girls.

For persons with CVD, exercise training is an important component of efforts to prevent recurrent or subsequent disease because it improves hemodynamic, metabolic, and respiratory function. Exercise training also improves symptoms of angina in CHD patients and decreases symptoms of heart failure among persons with LV dysfunction.

Randomized trials of exercise cardiac rehabilitation show a 15 to 25 percent decline in mortality after 3 years among the patients assigned to an exercise program. This effect may be attributed to improvements in blood pressure levels, lipid profiles, and other CVD risk factors and, possibly, to increased thresholds for acute precipitants of cardiac events (e.g., strenuous physical activity, psychological stress).

Unfortunately, even though the cardiovascular effects of training are apparent within 6 to 12 weeks, one-half of the people who begin an exercise program quit within the first 6 months. As in smoking-cessation efforts and other behavioral interventions, prevention of relapse is a major challenge when developing therapeutic exercise programs.

## *Diet*

Research on dietary interventions to reduce the risk for CVD has focused largely on lowering individuals' cholesterol levels and reducing their

intake of saturated fat. Intensive, individualized approaches to modifying a person's diet are most effective, but also most costly. These interventions can reduce serum cholesterol levels by 5 to 17 percent and, in some cases, the outcomes mirror the effects of controlled studies conducted in hospital metabolic wards.

Dietary interventions also are most effective when combined with a loss of weight. For example, individuals' levels of high density lipoprotein (HDL) cholesterol (for which higher values are better) typically decline when a dietary intervention is used alone. These levels, however, can be maintained when the individual also loses weight and increases exercise.

Not surprisingly, the main obstacle to obtaining a long-term benefit from a dietary intervention is the failure to sustain the recommended changes in dietary habits. Highly prescriptive, structured diet regimens, as well as frequent contact with patients and the active support of spouses, maximize individuals' adherence to an intervention. Because patients often show diminished adherence to diet plans when beginning drug therapies for hyperlipidemia, treatment should ideally emphasize the advantages of a combination of pharmacotherapy and active dietary intervention.

In contrast to the success of individualized treatments, population-based programs have been less effective in reducing serum cholesterol levels. Recent research suggests that certain environmental manipulations, such as reducing the cost of healthful foods and increasing their variety, may be more effective than educational interventions alone in altering a population's dietary preferences and eating behavior.

## *Obesity*

Prevention of obesity is one of this country's greatest public health challenges. One-third of the U.S. adult population is currently overweight. This proportion continues to increase even though Americans are spending more than $30 billion a year on weight-reduction programs and products. Prevention efforts in communities, worksites, and schools have had little effect on individuals' body weights, and no major studies have been conducted to test strategies for preventing excess weight gains among persons at high risk for obesity.

Some success has been reported, however, in treating weight problems in children 8 to 12 years old. When the intervention includes diet, exercise, behavior modification, and parental involvement, these children can achieve and maintain significant decreases in their degree of overweight for at least 10 years.

Treating obesity among adults has been less successful. Typical programs, which combine diet, exercise, and behavioral training to manage eating behavior, result in an average weight loss of about 9 kg over 20 weeks. Studies show that about two-thirds of this initial loss is maintained for 1 year, but little is known about the longer-term outcomes of standard weight-loss treatments.

The success of these efforts is enhanced by greater patient contact, emphasis on both diet and exercise, use of certain behavioral strategies such as self-monitoring of eating behavior, and structured efforts to prevent relapse. Although modest, the amount of weight that individuals lose in these programs does beneficially affect their blood pressure levels and other CVD risk factors, and these changes persist for as long as the weight loss is maintained.

Previous concerns about the potentially deleterious effects of weight cycling (repeated weight loss and weight gain) among overweight individuals appear to have been overstated. Most studies now show that weight cycling *per se* does not have a negative impact on these individuals' metabolic or other physiological variables.

The introduction of new drug therapies has attracted a great deal of popular attention as a potential solution to the problems of overweight. However, increasing recognition that some drugs may have serious adverse side effects has curtailed initial enthusiasm for such treatments and led to recommendations that these drugs be used primarily in the very obese. In addition, current evidence suggests that pharmacological interventions, used alone, enhance weight loss only marginally, compared with interventions that do not include medication, and that drugs may be most effective when combined with diet, exercise, and behavior modification.

### *Alcohol Abuse*

NHLBI's prevention programs have not targeted primary prevention of alcoholism, nor have the cardiovascular effects of treatments to control individuals' intake of alcohol been evaluated extensively in well-controlled clinical studies or trials. Research indicates, however, that many of the detrimental cardiovascular effects of alcohol abuse can be reversed or ameliorated if individuals stop consuming alcohol.

These cardiovascular effects include disturbances of cardiac rhythm resulting from heavy consumption of ethanol, alcoholic cardiomyopathy, and risk of sudden cardiac death among patients with cardiomyopathies. Abstinence after long-term, heavy use of alcohol has also been reported to reduce blood pressure levels significantly in hypertensive and normotensive individuals.

Effective behavioral interventions are now available for alcoholics and problem drinkers. However, maintaining abstinence after achieving initial cessation is the greatest challenge for individuals seeking successful treatment. Additional, intensive studies of both the prevention and the treatment of alcohol abuse would be beneficial because of the probable reductions that could be gained in cardiovascular morbidity and mortality.

## Behavioral Aspects of Disease Management and Adherence to Treatment

Much of current applied research involves the development and evaluation of interventions to promote risk factor modification. Equally important, although less extensively studied, are the behavioral aspects of disease management, recovery, and rehabilitation. Such research seeks to elucidate the ways in which patients cope with their illnesses and the behavioral demands imposed by prescribed therapies and rehabilitation regimens. Behavioral interventions to improve the management of heart, lung, and blood conditions are now also being developed. These efforts are aimed at reducing the exacerbation of symptoms or recurrence of disease and at promoting effective coping, adherence to treatment, and adjustment to the functional limitations occasioned by disease.

### *Adherence to Treatment*

The area of patients' adherence to therapeutic regimens is the prototype for behavioral issues involved in clinically managing heart, lung, and blood diseases. Adherence is the linchpin of treatment; without patients' adherence, beneficial therapies cannot yield positive outcomes. Yet, almost irrespective of the nature of the therapy or the treated condition, large proportions of patients fail to adhere adequately to prescribed treatments and therefore fail to receive the full benefit for which such treatments were intended.

Estimated rates of nonadherence range from 30 percent to 70 percent and may be higher than 80 percent for very difficult treatment programs. Nonadherence can result in failed treatment, unnecessary or imprudent intensification of treatment, costly diagnostic procedures, disease complications, additional hospitalizations, and possibly death. Nonadherence includes failure to take prescribed medicines and any other behavior that contravenes the purpose of therapy, such as continuing to smoke after suffering an MI,

neglecting to wear a ventilator mask in the workplace, or failing to adhere to iron-chelation therapy for thalassemia.

Failure to adhere is not clearly related to patients' gender, race, education, income, or personality, but appears to be most common when a treatment is preventive, complex, inconvenient, or lengthy, or when the disorder that is being treated is asymptomatic or the benefits of treatment are not evident.

Assessing adherence is difficult because instruments that rely on patients' self-reports often lack adequate reliability and may be invalid because of patients' deliberate or inadvertent overestimation, bias, or limited memory. Recent advances in measurement techniques, such as electronic monitoring devices, biochemical assays, reviews of pharmacy databases, and improved self-report strategies, offer new opportunities for improving researchers' and clinicians' abilities to track patients' adherence.

Behavioral strategies to improve adherence have been useful for adult and pediatric populations and have been applied to medication regimens, smoking-cessation programs, and weight-control efforts. These strategies include using environmental cues to prompt patients to take their medications, integrating the use of medications with daily habits, and actively monitoring adherence by patients and/or parents or partners. Other promising strategies for enhancing adherence include interventions to recruit the support of patients' families, spouses, or members of structured treatment groups; application of cognitive–behavioral principles to increase patients' motivation; and educational efforts to facilitate communication between health care providers and patients.

For some conditions, such as tuberculosis, adherence problems are especially critical. This disease is of great public health concern and has increased markedly among low-income, indigent populations that have a high rate of drug abuse. Here, recourse to "directly observed therapy," involving provider–patient contact for the delivery of each medication dose, has improved rates of compliance significantly.

Although generic approaches to adherence have been successful, adherence problems are often idiosyncratic or tied to the unusual nature of a particular therapeutic regimen or patient population. Novel interventions tailored to specific adherence problems must be designed and tested for their efficacy in these instances.

## *Cardiovascular Diseases*

Many Americans are living with heart disease, including more than 13 million persons who have angina pectoris or who have suffered an MI. Management of their disease and prevention of recurrent or subsequent disease have thus increasingly attracted the attention of behavioral scientists and clinicians. Most of this effort has been focused on controlling or modifying lifestyle risk factors such as smoking, physical inactivity, and adverse diet.

Therapeutic interventions also have been developed to ameliorate the enhanced risk conferred by certain psychosocial variables, such as personality, psychological stress, and social support, which also contribute to heart disease. There is now evidence that psychosocial interventions can reduce morbidity and mortality beyond that achieved by standard cardiac rehabilitation regimens in CHD patients. Supplementing "usual care" following acute MI with behavioral counseling may lower recurrence rates by as much as 50 percent over 5 years. Preliminary reports also suggest that a rigorous, multimodal program of stress management, diet modification, and exercise can cause regression of atherosclerosis in the coronary arteries. Similarly, stress management in heart disease patients was recently shown to reduce the occurrence of myocardial ischemia, as well as other cardiac events, when compared with usual care.

Behavioral or pharmacological treatment of depression also may improve the prognosis of CHD patients. As previously noted, clinical depression is highly prevalent among patients who have had an MI, and depression is an important predictor of recurrent events and survival after an MI. A randomized, multicenter clinical trial is now being conducted to evaluate the effects of behavioral and pharmacological treatments for depression in patients with CHD.

## *Lung Diseases*

Chronic lung diseases affect 29 million Americans. Management of these diseases presents a diverse set of challenges. In asthma, for example, the relevant behavioral issues include avoidance or control of allergens and other asthma triggers, self-monitoring of symptoms, adherence to preventive medications, and appropriate management of acute attacks.

A variety of social, cultural, and economic factors affect asthma management, often impeding efforts to control the clinical course of this disease. For example, the likelihood of slow-onset, fatal asthma may be predicted, in part, by inadequate self-management associated with poor social support, social isolation, or pressing psychological and social problems. Educational interventions to enhance patients' self-management of asthma, on the other hand, have been shown to reduce patients' exposure to environmental precipitants, improve control of symptoms, promote correct use of metered-dose inhalers, and reduce hospitalizations for asthma and the costs of health care.

One strategy that has been developed for self-monitoring of presymptomatic airway obstruction is peak-flow monitoring. Data on the efficacy of this strategy show mixed results, but some studies suggest that it can reduce overall symptoms, the frequency of urgent-care visits, and days lost from work. Peak-flow monitoring may be especially helpful for patients who have difficulty perceiving increased levels of airway obstruction before symptoms become overt.

COPD, another common pulmonary disease, is characterized by irreversible airway obstruction and mainly affects middle-aged and older adults. Cigarette smoking causes COPD in the vast majority of cases, which makes the disease almost entirely preventable. The severe disability and limitation of activities that occur with advanced COPD are common targets of behavioral intervention. Approaches that combine education in self-management techniques and exercise training have improved patients' exercise capacity, work performance, dyspnea, and overall quality of life. Progressive COPD is also associated with cognitive impairment in some individuals, which may result from chronic hypoxia; however, there is some evidence that long-term oxygen therapy can reduce this cognitive decline.

Advances in the treatment of genetically determined diseases of childhood have given patients longer lives, and in consequence, have created problems in disease management that did not exist in previous generations. For CF, these problems include adherence to complex drug regimens, postural drainage, exercise, and nutritional interventions. While children with CF report that their primary difficulties relate to the demands of self-care, parents report a wider spectrum of difficulties, such as anxiety, disruption of family life, and problems carrying out the home management of their child's disease. The efficacy of behavioral interventions to improve the management of CF has not yet been studied extensively and represents a priority area for future research.

## *Sleep Disorders*

Significant advances have been made in treating OSAS nonsurgically. The most prominent of these advances is the development of means to deliver air through the nose continuously. This

strategy is known as continuous positive airway pressure (CPAP). It is highly effective, but patients' rates of nonadherence are also high. Although adherence appears to improve with length of treatment, interventions to enhance patients' adherence to CPAP need to be evaluated in controlled studies.

Weight loss is also an important target of intervention when treating OSAS. Existing studies report somewhat mixed outcomes, but there is evidence that significant weight loss can reduce sleep-related respiratory disturbances and enable some patients with OSAS to discontinue their reliance on CPAP.

## *Blood Diseases*

Like CF, many blood diseases are congenital, produce debilitating symptoms, and entail complex and often inconvenient treatment regimens. Because they also affect children, behavioral issues pertaining to a child's normal development and psychosocial adjustment and to the functioning of the child's family often must be addressed along with other, more common problems of disease management, such as ensuring patients' adherence to treatment and handling acute symptoms.

Sickle cell disease presents many of these behavioral issues. Sickle cell disease predominantly affects blacks and varies widely in clinical severity. The disease involves unpredictable, periodic episodes of severe pain; significant risk for cerebrovascular, respiratory, and infectious complications; and, for older children, the possibility of delayed growth and development and associated problems with peer relationships and social adjustment. Mental health problems arising from the stress of coping with this disease are common, with up to 50 percent of patients suffering depression, anxiety, and other psychological disorders.

Another set of genetic diseases is the thalassemia disorders. Although different from sickle cell disease, these conditions are equally severe and are difficult to manage. To sustain life, patients must undergo frequent blood transfusions and intravenous administration of chelating agents to remove excess iron from blood that is transfused. As with CF, patients with thalassemia now live much longer than before, but must adhere to an inconvenient, expensive, and uncomfortable treatment regimen for their entire lifespan.

Ensuring patients' adherence to iron-chelation therapy is a major challenge. Indeed, one-half of adolescents with thalassemia disorders do not adhere to this therapy. As a result, they risk development of congestive heart failure and other iron-induced damage to organs.

A third genetic disorder, hemophilia, also poses unique difficulties for patients' adjustment. Bleeding episodes, which occur spontaneously or because of trauma, are accompanied by damage to the joints and pain and may lead to other complications. The life expectancy of patients with hemophilia has been lengthened because of advances in transfusion medicine, including the development of home treatments for arresting bleeding episodes by using factor concentrates. Because of the time-demanding and complicated nature of this treatment, however, adherence has become a central problem in managing this disease.

For each of these blood diseases, much research is needed to elucidate the social, emotional, and behavioral dimensions of treatment, including factors that determine patients' adjustment to disability and long-term care. The effects of these diseases on the normal development of children and adolescents also must be evaluated. Accumulation of this knowledge will enable behavioral scientists and clinicians to design effective interventions for enhancing the management of this diverse set of blood diseases.

## Quality of Life

Increasingly, health status is viewed as encompassing more than the biological processes of disease alone, but in addition, the individual's own sense of well-being and an ability to perform well in the multiple roles that define a normal life. In this context, an individual's performance and function range from simple matters of mobility and self-care to the fulfillment of family, social, and occupational responsibilities. These patient-centered characteristics, which may also be considered medical outcomes, are referred to as health-related quality of life.

Behavioral research on health-related quality of life involves the evaluation of such outcomes—the sequelae of disease and of treatments for disease—from the broader perspective of patients' functional capacities and life satisfaction. Specific outcomes, or measures of quality of life, may be assigned numerical values and used to quantify the balance between expected benefits of treatment and compensating sources of disability and discomfort associated with particular disorders or therapies. Recently, these assessments have also been used to express the costs and benefits of alternative treatments, as when prioritizing health care services.

Measures of health-related quality of life have been found to predict a number of health end points, including mortality, and are useful in characterizing the effects of diseases and interventions on patients' physical, cognitive, emotional, and social functioning. For example, research shows that untreated hypertension is associated with many subtle changes in cognitive performance, including deficits in attention, learning, memory, mental flexibility, and abstract reasoning. In contrast, the several classes of medication used to treat hypertension generally do not impair patients' quality of life, except with respect to sexual function, which appears to be affected most by diuretic therapy.

Other studies of health-related quality of life show that coronary artery bypass surgery and coronary angioplasty predict similar rates of recurrent MI and mortality in patients with CHD, but that patients' performance of daily activities is improved more with bypass surgery. On the other hand, cardiac surgery has been shown to cause some deterioration in cognitive functioning (particularly attention, memory, and mental acuity); these effects are both acute and, occasionally, persistent.

Health-related quality of life is a relatively new area of behavioral research. Nevertheless, it is likely to assume growing importance as the medical community and public increasingly recognize that patients' abilities to participate in life's major activities are an essential component of medical evaluation and decision-making. Ensuring patients' quality of life will also be a key concern when developing and applying new treatments.

# Recommendations for Future Research

The Task Force identified more than 100 areas of significant opportunity for behavioral research. These topics range from risk factor associations and risk reduction to pathophysiology, expression of symptoms, and the clinical management of disease. The many specific recommendations for new research are listed in the report for each of the research areas addressed by the Task Force.

Many of the recommendations in the report reflect similar research concerns, as applied to different diseases and clinical care issues, and therefore may be expressed as thematic objectives for behavioral investigation. These objectives, which are viewed by the Task Force as representing areas of highest priority for behavioral research, are summarized below.

### 1. Foster Interdisciplinary Research and Research Teams

The scientific accomplishments summarized in this report illustrate that research on the behavioral dimensions of disease and its clinical management progresses most vigorously when conducted by interdisciplinary research teams. For example, the best evidence that psychosocial factors contribute to risk for CVD comes from population studies joining the expertise of both behavioral scientists and epidemiologists. Similarly, the experimental and clinical evidence that behavior influences the pathophysiology of CHD, including atherosclerosis, myocardial ischemia, and cardiac arrhythmia, results from extensive research collaborations among many experts, including psychologists, neurobiologists, cardiologists, and comparative pathologists.

Because the application of behavioral science to the problems of heart, lung, and blood diseases and to sleep disorders implies interdisciplinary investigation, the collaborative arrangements necessary for conducting such research must continue to be fostered.

*The Task Force therefore recommends that the NHLBI strengthen existing strategies of collaboration and develop new methods for fostering communication among the disciplines addressing heart, lung, blood, and sleep disorders.*

Appropriate efforts might include solicitation of cross-discipline pre- and postdoctoral training programs in behavioral medicine; development of new initiatives for interdisciplinary research on behavioral aspects of heart, lung, blood, and sleep disorders; and promotion and maintenance of research review panels with interdisciplinary expertise.

### 2. Encourage Research on Behavioral Factors in Lung and Blood Diseases

Research on the behavioral aspects of lung and blood diseases must be expanded. Behavioral scientists have given relatively little attention to these two areas even though lung and blood diseases are prevalent, disproportionately affect children, and present numerous challenges for patients' psychosocial adjustment and long-term clinical management.

Contemporary treatments significantly extend the life expectancy of patients with diseases such as CF, sickle cell disease, thalassemia, and hemophilia, but they also create new difficulties for these patients and their families. These difficulties include adhering to treatment regimens that are often painful and complex and handling the effects of debilitating symptoms on patients' social and emotional development, as well as overall family functioning.

*The Task Force therefore recommends that the NHLBI encourage research on behavioral issues relevant to lung and blood diseases.*

For most of these diseases, even the scope of relevant behavioral issues remains to be elucidated—such as the cognitive and emotional sequelae of disease, the determinants of symptom exacerbation, patients' perceived quality of life, level of treatment adherence, and problems in disease self-management. Progress in these areas, however, could lead to significant improvements in clinical care and treatment, as the barriers to optimal adjustment and disease management are identified and subjected to targeted behavioral intervention.

### 3. Promote Investigation of Previously Understudied Populations

Like other biomedical research, most of the evidence on behavioral predictors of disease is based on studies of middle-aged white men. The prevalence of lifestyle and psychosocial risk factors, however, often varies across different demographic groups. For example, tobacco use and physical activity vary according to race, gender, and socioeconomic status. Understanding

these differences may assist in reaching underserved populations and in designing interventions that will have the greatest benefit.

The nature and strength of associations between risk factors and disease outcomes also may differ among population groups. For example, some evidence suggests that behavioral factors predict CVD more strongly in men than in women. However, such findings are difficult to evaluate because of a dearth of investigations in this area and the methodological deficiencies of existing studies. Thus, reported gender differences in behavior–disease associations may be erroneous, resulting from reliance on psychosocial measures that are validated only for men or, possibly, from inadequate statistical power due to the lower incidence of cardiac events in middle-aged women. Another possibility is that behavioral factors are equally important among women and men, but the specific variables that predispose to disease in women may differ from those that are predictive in men.

Similar issues may also pertain to studies of minority populations. Behavioral risk factors may vary in these populations because of different cultural and learning experiences, exposure to different environments, and different genetic backgrounds. Current understanding of the behavioral aspects of disease across all segments of the population must be increased.

*The Task Force therefore recommends that the NHLBI promote research focused on previously understudied population groups and that special attention be given to the development and use of appropriate methodologies and study designs.*

### 4. Incorporate Behavioral Science Into Existing Epidemiological and Clinical Studies

The effect of behavioral factors on risk for disease must be better understood. However, establishing associations between putative risk factors and subsequent development of new or recurrent disease usually requires large-scale investigations, often involving population sampling or extensive recruitment of patients and repeated observations over several years. Incorporation of behavioral measurements into existing studies offers a cost-effective means of evaluating the disease relevance of newly hypothesized risk factors and the usefulness of new techniques or instruments to measure specific variables of interest.

*The Task Force therefore recommends that measurements of relevant behavioral variables be included in ongoing and new major observational and prospective epidemiological studies and in large clinical trials, as appropriate.*

For example, research indicates that enhanced cardiovascular responsiveness to stress may increase an individual's risk for CHD and essential hypertension. To clarify this possible association, the NHLBI recently supported development of a psychophysiological test battery that has high reliability and may be applied in population-based epidemiological investigations. Incorporating such instruments into ongoing, prospective studies of risk factors for CVD is now appropriate. Similarly, inclusion of ambulatory blood pressure monitoring in longitudinal studies can enhance understanding of behaviorally evoked variations of blood pressure and the influence of this variability on the development of hypertension and its end-organ effects.

In addition, behavioral research should be integrated into studies of the occurrence of CHD events. Such work can help illuminate the onset, triggers, and course of MI, myocardial ischemia, and malignant arrhythmias. Psychological measures also could be included usefully in studies identifying precipitants of clinical asthma. In addition, other instruments for assessing psychosocial risk factors, such as socioeconomic status, should now be incorporated routinely in epidemiological investigations, as should measures of

treatment adherence and health-related quality of life in studies of patient populations and major clinical trials.

### 5. Identify Further the Biological Mechanisms That Underlie Behavior–Disease Associations

Recent research has linked individuals' behavior not only to the incidence of disease, but also to important pathophysiological processes, especially those related to CHD. This research must now be followed by more intensive investigations of the biological mechanisms that mediate behavioral influences on clinical disease.

*The Task Force therefore recommends that the NHLBI encourage further research on the biological mechanisms that underlie associations between behavior and disease.*

Recent research efforts point to potentially promising areas of study. For example, experiments on nonhuman primates have identified some of the neuroendocrine factors that promote atherosclerosis. This work should lead to more detailed studies of pathophysiology and mechanism, focusing on such disease-relevant events as early changes in the function of arterial endothelium, the proliferation of cells in the intima of the artery, and processes involved in plaque formation, complication, and rupture.

Both clinical and experimental research also are needed to establish the hemodynamic, neuroendocrine, hemostatic, and neural mechanisms for behavioral influences on acute cardiac events, including infarction, coronary thrombosis, myocardial ischemia, ventricular fibrillation, and sudden death in susceptible individuals, as well as the development of behaviorally induced hypertension. Studies of patients with sleep disorders should similarly seek to determine how sleep apnea affects myocardial perfusion and cardiac electrical stability, in addition to clarifying the circadian mechanisms that may underlie diurnal variations in morbidity and mortality from cardiovascular and pulmonary disease.

In addition, preliminary evidence that psychological stress can exacerbate the symptoms of asthma should prompt research aimed at identifying immunological and autonomic–neuroendocrine mechanisms by which behavioral and emotional states might influence inflammatory and bronchomotor processes in clinical asthma.

### 6. Identify Psychological Factors Responsible for the Aggregation of Behavioral Risk Factors

Many behavioral risk factors for disease often aggregate within individuals. That is, people who have one lifestyle risk factor, such as smoking, obesity, physical inactivity, or high alcohol consumption, are also likely to have other health-impairing habits. Psychosocial risk factors for CVD also often occur together. Hostile individuals, for example, are more likely than nonhostile persons to have symptoms of depression and few sources of social support.

This clustering of disease-predictive attributes suggests that a more limited set of psychological variables may underlie the diversity of behavioral risk factors documented in epidemiological research. Attempts to identify these variables may yield a more parsimonious understanding of the behavioral origins of disease risk and suggest new directions for designing preventive and therapeutic programs for risk reduction.

*The Task Force therefore recommends that behavioral scientists seek to identify the psychological factors that may be responsible for aggregation of behavioral risk factors within individuals.*

### 7. Develop Interventions to Promote Sustained Improvements in Lifestyle Risk Factors

Behavioral researchers have made substantial progress in developing and evaluating interventions to modify lifestyle risk factors. These interventions include programs for smoking cessation, weight loss, physical exercise, and diet modification. However, individuals' initial successes in altering their high-risk behaviors are commonly followed by relapse or failure to maintain the lifestyle changes achieved during the intervention.

*The Task Force therefore recommends that researchers be encouraged to design specific therapeutic strategies for improving individuals' long-term maintenance of behavioral changes.*

A related problem is the lack of empirical guidelines for selecting appropriate treatment goals. For example, the amount, duration, and intensity of exercise needed to best protect against CVD are not clear. In the case of obesity, even a modest reduction in weight will improve other risk factors, but whether this benefit also reduces an individual's risk for morbidity and mortality is not known. These examples illustrate the importance of establishing the relationship between *degrees* of risk factor change and relevant health outcomes, in addition to encouraging long-lasting changes, in efforts to improve the health of individuals and populations.

### 8. Develop Interventions to Improve Patients' Adherence to Treatment

In addition to maintaining long-term changes in lifestyle risk factors, patients who are being treated for cardiovascular, lung, and blood diseases often have difficulty adhering to the treatments prescribed. Failures in adherence are ubiquitous, affecting nearly all categories of treatment and thereby undermining much of the therapeutic enterprise. Although many interventions have been developed to promote improved adherence (some of generic design and others tailored to specific treatment modalities), the efficacy of these approaches needs to be established. In addition, ways to enhance patients' adherence within managed care settings and to improve the adherence-counseling skills of primary care physicians, nurses, and paraprofessionals need to be developed and evaluated.

*The Task Force therefore recommends that the NHLBI support the development and evaluation of interventions to improve patients' adherence to treatment.*

### 9. Develop Efficient Preventive Interventions for Reducing Risk for Disease

Trial programs to prevent smoking and to help individuals develop healthful dietary and activity patterns have been somewhat successful. However, recent trends such as increased smoking among some adolescent groups and population-wide increases in obesity underscore the deleterious effects that larger cultural influences can have on individuals' adoption of healthful behaviors.

The effect of the broader environment (e.g., mass-media messages, popular role models) on children and adolescents' adoption of dietary patterns, physical activity, and use of alcohol and tobacco needs to be better understood. This knowledge should be used to develop more effective policies and interventions for primary prevention, making use of existing social institutions and medical resources.

*The Task force therefore recommends that more efficient interventions of primary prevention be developed to reduce children and adolescents' risk for heart, lung, and blood diseases.*

### 10. Foster Development of New Research Methodologies and Measurement Techniques

Like all areas of science, behavioral research is constrained by the methodologies and

measurement tools available. As new research methods and techniques become available, behavioral science will advance more rapidly. Some of the methodologies of the future may come from other sciences but will nonetheless benefit behavioral research.

Examples of recent technological developments include ultrasound techniques for noninvasively evaluating extracranial carotid artery disease and various imaging techniques for assessing changes in cardiac function and myocardial perfusion. The first of these techniques is now being used to evaluate behavioral influences on the development and progression of atherosclerosis, while imaging techniques have already figured prominently in the study of myocardial ischemia.

In other areas, there is a need to improve or expand the measurement of disease-relevant psychosocial and behavioral variables. For example, validated instruments are needed to assess individuals' functional health status and perceived well-being, two important aspects of health-related quality of life. Similarly, the availability of improved, cost-effective methods for measuring visceral obesity and consumption of fat and other dietary components would enhance studies of obesity and diet modification.

Researchers who are studying the psychosocial and socio-environmental predictors of disease would benefit from the availability of scales having established validity in demographically heterogeneous populations. This research also would be enhanced by the availability of multidimensional instruments capable of capturing the diverse features of such broadly defined concepts as socioeconomic status, social integration, and psychological stress.

In addition, ambulatory techniques for "real-time" assessment of behavioral and psychological states in natural environments need to be further refined. Such techniques promise to assist in understanding of the behavioral triggers for episodic symptoms and events related to pulmonary and cardiovascular diseases. Finally, documenting treatment compliance would be improved substantially by the development of adherence measures that are objective, valid, practical for use in customary clinical settings, and applicable to a variety of patient and research populations.

*The Task Force therefore recommends that the NHLBI foster the development and application of new methodologies and measurement techniques for use in behavioral research on heart, lung, and blood diseases.*

### 11. Integrate Behavioral and Pharmacological Approaches to the Reduction of Risk Factors

Medications to redress lifestyle risk factors, such as smoking, obesity, and unhealthy dietary preferences, are emerging as important components of risk management. For example, nicotine replacement therapies are a new and effective means for promoting and maintaining smoking cessation, and new drugs to suppress appetite and reduce food intake are now widely used to help individuals lose weight and control obesity. These medications, however, do not offer sufficient benefit to justify their use as the only means of treatment. This is not surprising given the important role that environmental, social, and learning factors play in the initiation and maintenance of health-impairing behaviors. Indeed, preliminary evidence suggests that medication may be most effective when it is prescribed in conjunction with a broader program of behavioral modification and counseling.

*The Task Force therefore recommends that the NHLBI encourage further research to establish optimal interventions that combine behavioral approaches with existing and emerging pharmacological therapies to reduce the risk factors for heart, lung, and blood diseases.*

**12. Incorporate Genetic Research Strategies Into Behavioral Research on Heart, Lung, and Blood Diseases**

In addition to abundant evidence that genetic differences among individuals account for a substantial portion of population variability in many disease risk factors, it is now well established that most complex behavioral traits result from a combination of genetic and environmental influences. Therefore, both the independent and the interactive effects of genes and environments must be identified to fully understand the development of behavioral risk factors for disease.

It is already known that many of the behavioral variables implicated in CVD have significant heritability. These variables include patterns of physical activity, smoking, obesity, diet-induced weight gain, certain dietary preferences, physiological responsiveness to stress, hostile personality characteristics, and depression. Quantitative genetic studies also enable researchers to estimate environmental influences on individual differences in behavior and to distinguish between those environmental effects that cause related persons to be either similar (e.g., shared family environments) or different. Future behavioral genetics research should be directed toward clarifying the nature of genetic and environmental influences on the development of behavioral risk factors and, possibly, elucidating the common origins of risk factors that often tend to cluster within individuals.

Recent advances in the molecular genetics of disease and disease risk can also be incorporated fruitfully into behavioral research. The identification of major genes regulating lipid metabolism and body weight, for instance, provides specific markers of genetic vulnerability, in the context of which behavioral interventions (such as diet modification or weight loss programs) should be evaluated. Studies of this type may identify persons who would be expected to derive either more or less benefit from a particular form of treatment.

Genetic technologies also are producing new animal models that may be useful in behavioral research on the pathogenesis of disease. For example, the creation of transgenic and "knockout" mouse strains that are susceptible to human-like atherosclerosis offers the opportunity for studying social effects on atherogenesis using an animal model that is much less expensive, and therefore more feasible, than nonhuman primates. Such models may also lead to a better understanding of the physiological mechanisms that underlie effects of behavioral risk factors on disease.

*The Task Force therefore recommends that strategies for genetics research be incorporated into behavioral research on heart, lung, and blood diseases*.

The aforementioned high-priority recommendations are intended to stimulate behavioral research on cardiovascular, lung, and blood health and disease. The rationale for these recommendations is presented in detail in the Task Force's full report, which follows. This report includes specific recommendations for each topic addressed by the Task Force. All of these recommendations deserve careful review and consideration. Behavioral science has already contributed significantly to the prediction, prevention, and amelioration of disease. Given recent exciting developments, considerable additional progress may be expected in the future.

National Heart,
Lung, and
Blood Institute
Report
of the
Task Force on
Behavioral Research in
Cardiovascular, Lung,
and Blood Health and Disease

# I. Behavioral Antecedents of Disease

# I. Behavioral Antecedents of Disease

Diseases of the heart, vasculature, lung, and blood are major sources of morbidity and mortality in the United States. To understand fully the development and progression of these diseases, many behavioral and psychosocial factors must be considered. For example, many of the causes of heart disease relate to habits of living—lifestyles and behaviors that individuals can control. Indeed, the decrease in mortality from cardiovascular diseases (CVD) that has occurred during the past 30 years is due only partly to dramatic medical developments, such as new drugs and improved technology. It also is substantially attributable to population-wide changes in the lifestyle variables that are risk factors for heart disease.

Major research advances have clarified the influence of behavioral and psychosocial factors on the prevention, development, and treatment of cardiovascular and pulmonary disorders. These advances have been made possible by the increasing integration of behavioral science with biomedical knowledge and techniques. Recent work in this area exemplifies *biopsychosocial* or *biobehavioral* research as described by the Office of Behavioral and Social Science Research at the National Institutes of Health (NIH). This research model emphasizes the interaction of biological (e.g., physiological, genetic), behavioral, and psychosocial factors in determining health and illness.

A large body of evidence demonstrates that behavior contributes to the risk for cardiovascular and pulmonary disorders. This evidence derives from several research strategies:

- Epidemiological and population-based studies of associations between behavioral and psychosocial variables and cardiovascular or pulmonary disorders
- Clinical studies of patients and individuals predisposed to disease
- Experimental behavioral research using appropriate animal models of human pathology.

This research has helped establish the importance of behavior in the etiology, treatment, and prevention of heart and lung diseases.

In contrast to heart and lung diseases, which are strongly influenced by environment, most of the major blood diseases, such as sickle cell disease, thalassemia, and hemophilia, are genetic in origin. For example, children inherit sickle cell genes from their parents and have sickle cell disease throughout their lives. The severity of the symptoms may vary widely during their lifespan, and their symptoms may differ from those of others with the disease. Behavioral factors are not involved in the onset or development of the disease, but may be relevant to treatment. Because behavioral factors are not specifically relevant to the *acquisition* of blood diseases in general, this group of disorders is not addressed in Part I of the report. Behavioral research on blood diseases primarily addresses issues related to strategies for managing these diseases and issues pertinent to genetic screening and counseling. This interventional research is discussed in Part II of the report.

In Part I, the Task Force summarizes recent advances in understanding the behavioral antecedents of heart and lung diseases. Evidence from epidemiological, clinical, and animal research is presented to demonstrate the link between behavioral characteristics and the onset, development, and expression of these diseases and to illustrate the mechanisms for behavior's influence on the pathophysiology of disease. The Task Force's review is divided into two major sections:

- *Behavior–disease associations* (i.e. behavioral variables that increase individuals' risk for cardiovascular and pulmonary diseases)

- *Behavior–disease processes* (i.e., biological mechanisms for behavior's influence on the pathophysiology of these diseases).

Each section includes a review of the state of the science, a discussion of research opportunities, and a list of recommendations for future research.

# Behavior–Disease Associations

The associations between behavior and heart and lung diseases have been widely studied and are understood far better today than in the past. Much, but not all, of this behavioral research has been focused on two disorders: arterial hypertension and ischemic heart disease. These conditions account for most of the morbidity and mortality resulting from CVD. Behavioral research on lung diseases has centered on the effects of smoking.

The behavioral risk factors implicated in cardiovascular and pulmonary disease include:

- *Lifestyle factors*, such as cigarette smoking, lack of exercise, adverse diet, alcohol dependence, and obesity

- *Individual characteristics*, including personality and psychological traits (e.g., depression, hostility, and anger) and physiological responsiveness to stress

- *Psychosocial and other environmental variables*, including socioeconomic status, race and ethnicity, lack of social support, and occupational and social stress.

These three sets of factors are discussed separately in the sections that follow.

## Lifestyle Factors

Research has extensively examined cigarette smoking, physical inactivity, diet, and obesity as behavioral risk factors for cardiovascular and pulmonary diseases. Alcohol dependence and abuse also have important consequences for cardiovascular health. These behavioral or lifestyle factors often are rooted deeply in social and cultural practices, and many are more prevalent among lower socioeconomic classes than among higher classes. These health-impairing behaviors often are initiated because of social influences; for example, adolescents may begin to smoke because of peer pressures and a need for the approval of their peers. The behaviors may also be maintained by the interaction of biological and behavioral mechanisms. Thus, the combination of addiction to nicotine and fear of weight gain may help to maintain smoking and impede smoking cessation.

The National Heart, Lung, and Blood Institute (NHLBI) Report of the Task Force on Research in Epidemiology and Prevention of Cardiovascular Diseases (1994) provides an extensive review of the progress made in understanding the associations between these lifestyle factors and coronary heart disease (CHD), essential hypertension, and pulmonary disorders. These associations are therefore not described in detail here.

Rather, the present report summarizes current knowledge of the development, maintenance, and modification of behaviors that increase the risk for cardiovascular and pulmonary diseases. Five specific behavioral variables are reviewed in this section on lifestyle factors: cigarette smoking,

physical inactivity, diet, obesity, and alcohol dependence and abuse. These variables are also important risk factors for many other diseases that are being addressed by NIH components other than the NHLBI.

## *Cigarette Smoking*

Cigarette smoking is the greatest single preventable cause of premature death in the United States. Researchers have documented the health consequences of tobacco use in thousands of research studies. Currently, they estimate that cigarettes are responsible for approximately 434,000 deaths each year in the United States.

Cigarettes are a major contributor to CVD and the primary cause of chronic obstructive pulmonary disease (COPD) and lung cancers. Smoking reduces the effectiveness of antianginal medications and may compromise the long-term benefits of thrombolytic agents used to treat and prevent heart attacks. Cigarette use has declined in the United States in recent years, but the consumption of tobacco products continues to increase worldwide.

The average age at which smoking is initiated has declined during the past 40 years, probably because of aggressive advertising campaigns promoting cigarette use. Today, nearly all smokers begin their smoking habit before age 19. Scientific evidence increasingly indicates that nicotine is addictive and that the development of tobacco addiction may take a number of years.

Trends of cigarette smoking among adolescents are particularly important. The National Academy of Sciences' Institute of Medicine reports that, between 1980 and 1993, the prevalence of smoking among teenagers remained relatively constant, at approximately 30 percent, even though smoking among adults decreased significantly. Studies also indicate that initiation rates for smoking have been increasing among women and Asian Americans. In addition, recent evidence suggest that the prevalence of smoking is increasing among black men even though it had previously been on the decline.

Ethnic variations in the prevalence of smoking among teenagers clearly suggest that tobacco smoking is not distributed randomly, but is associated with psychosocial and biological factors. For example, smoking is noted more frequently among individuals of low socioeconomic status and among less educated adults, both of whom are less likely to want to quit smoking or to be successful if they attempt to quit, than among individuals of higher status or among more educated adults. Among teens who experiment with smoking, those with a predisposition to certain mental health disorders, such as major affective disorder or antisocial personality disorder, are more likely to become dependent on smoking by the time they reach adulthood.

Researchers have recently identified genetic influences on the onset and persistence of tobacco dependence and have noted that the heritability of tobacco dependence is comparable to that of alcohol dependence. Investigators are increasingly interested in the mechanisms of desensitization among the brain's receptors after acute and chronic exposure to nicotine. Desensitization may be genetically influenced and is likely to be critical to the onset of dependence. Various environmental and biological factors operate at different stages in the initiation and maintenance of the smoking habit. Figure 2 depicts the potential influences of these factors.

Smoking behavior in men and in women may be reinforced by slightly different factors. For example, nicotine addiction may be more influential among men, whereas nonpharmacological and social aspects may be more important among women. Research shows that concerns about weight predict initiation of smoking among teenage women and that, among women in general, lasting concerns about weight are associated

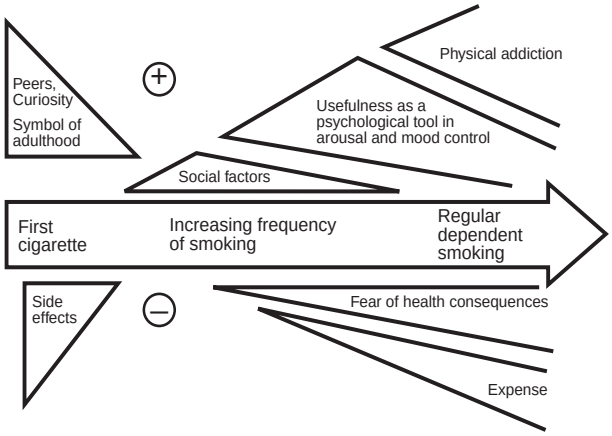


**Figure 2.** Psychological, behavioral, social, economic, and biological factors affecting different stages in the development of smoking. Adapted and reprinted with permission from Stephney R: Smoking behavior. A psychology of the cigarette habit. Brit J Dis Chest 1980;74(4):325-344.

with smoking and with difficulties of smoking cessation.

Use of alcohol, caffeine, and/or illicit drugs is positively associated with smoking and can have independent pathophysiological effects on the cardiovascular system (e.g., acute cardiac damage from cocaine use, exacerbation of hypertension from alcohol use). The reasons for the relationship between smoking and use of other drugs are not clear, but may involve cross-drug tolerance, conditioned associations between drug-taking behaviors, and a common underlying biological predisposition to the use of drugs.

In addition, the dietary habits of smokers may differ from those of nonsmokers. Diets of smokers may be less healthful and may be higher in fats and lower in fiber. These dietary habits can have implications for smokers' cardiovascular health. The association of smoking with these factors and with other biological and behavioral variables needs to be examined carefully to better understand smoking and to devise strategies for preventing and controlling tobacco use.

## *Research Opportunities*

Although researchers now better understand the general actions of nicotine in the body, they know relatively little of the specific effects of nicotine in the brain that reinforce tobacco use. Many of these effects are aversive initially, but tolerance to these effects can develop quickly and positive effects may increase with tobacco use. Better understanding of nicotine's effects and the sites of action would speed development of effective treatments. Genetic factors involved in the control of these effects are being explored in animals, but have not been examined in humans.

Another critical gap in knowledge is the lack of understanding about specific mechanisms involved in the ways that biological and behavioral factors work together to promote the onset of tobacco dependence. Development of dependence is typically a slow process; for an individual to move from experimenter to addicted smoker may take a number of years. Dependence does not automatically result from individuals' biological exposure to nicotine. Furthermore, conditioned associations between nicotine intake and environmental stimuli set the stage for maintenance of smoking, and these associations may lead to relapse in the presence of conditioned stimuli after a quit attempt.

The factors that increase the risk of tobacco dependence among certain economic and ethnic groups need to be investigated. Contributing factors include psychosocial and cultural variables (e.g., targeted advertising conducted by the tobacco industry) and, possibly, genetic factors. An understanding of ethnic differences in smoking may be gained, for example, by exploring the reasons for the recent increase in the prevalence of smoking among black teenagers.

Smoking rarely occurs independently of other harmful health behaviors. The relationships

between smoking and these harmful behaviors, such as excess fat intake, inappropriate dieting for weight loss, and use of other addictive substances, need to be understood better. The detrimental effects of smoking on health may be increased when smoking occurs in association with other harmful behaviors.

### *Recommendations*

Recommendations for behavioral research on smoking as a risk factor for heart and lung diseases are:

1. Investigate the specific effects of nicotine and the corresponding actions in the brain that reinforce tobacco use. Identify the genetic factors controlling these effects.
2. Determine more specifically how biological mechanisms interact with behavioral factors (including a person's history of mental health problems) to foster dependence on smoking.
3. Investigate the factors, including cultural influences and susceptibility to targeted advertising, that may account for the greater vulnerability of certain population groups to tobacco dependence.
4. Examine the influence of smoking on other harmful health behaviors such as high intake of fats, use of other addictive substances, and the influence of these behaviors on smoking.

## *Physical Inactivity*

Physical inactivity is a significant and independent risk factor for CHD. Regular physical activity in the form of endurance exercises, such as jogging, walking, swimming, and biking, can increase an individual's functional capacity and can be important for primary and secondary prevention of CVD and other chronic diseases.

The risk of CHD among sedentary persons is estimated to be two times higher than the risk of CHD among physically active persons. Physical activity and risk of CHD seem to have an inverse dose-response relationship. That is, studies show that as physical activity increases, risk of CHD decreases.

Most data indicate that the reduced risk of mortality associated with physical activity largely derives from a shift from an inactive lifestyle to a nonsedentary lifestyle. Research also indicates that reduced mortality risk is more strongly associated with increase in the frequency and duration of activity (measured as kilocalories per week) rather than increases in the intensity of activity. These findings suggest that individuals should give greater emphasis to activities such as climbing stairs, gardening, and walking, which can be done frequently, as well as other, more vigorous forms of exercise such as sports.

Cross-sectional studies show that active individuals have better CVD risk factor profiles than their sedentary counterparts. Active individuals have lower blood pressure levels, lower rates of obesity, higher levels of high density lipoprotein (HDL) cholesterol, lower levels of low density lipoprotein (LDL) cholesterol and very low density lipoprotein (VLDL) cholesterol, and low triglyceride levels. Active persons also may have lower hematocrit readings, decreased plasma fibrinogen, increased fibrinolysis, and improved glucose tolerance and insulin sensitivity. Moreover, fit persons, compared with unfit persons, may also show reduced hemodynamic and neuroendocrine responses to behavioral stressors.

The amount of physical activity needed to achieve health benefits remains controversial. Some clinicians have suggested that, ideally, individuals should exercise three to five times each week. Others have recommended more recently that, optimally, individuals should accumulate at least 30 minutes of any activity on most days of

the week. Because the greatest potential for reductions in cardiovascular morbidity and mortality can be achieved by sedentary individuals who become moderately active, strategies to help these persons initiate and maintain a nonsedentary lifestyle are critically important.

No more than 25 percent of Americans engage in physical activity regularly, even though relatively little skill, minimal expense, and only about 2 percent of a person's time is needed for many forms of exercise. Individuals at greatest risk for inactivity include women (especially black women), less educated persons, overweight individuals, blue-collar workers, and elderly persons. Individuals can increase their physical activity by engaging in regular aerobic exercise at home or in supervised sessions or by increasing their occupation-related and leisure-time physical activity.

The mode, complexity, convenience, and costs of exercise programs can affect individuals' participation in exercise. Research shows that individuals who participate in supervised home-based exercise programs have higher adherence rates than, and at least comparable cardiovascular benefits to, individuals who participate in programs outside the home. The availability and proximity of community facilities and safe environments that are conducive to exercise may be important factors in individuals' participation in exercise. The support of families and other social networks also predicts whether individuals adopt and maintain an exercise program. In addition, a variety of psychological factors affect a person's decision to exercise. These factors include self-motivation, readiness for change, self-efficacy, and perception of benefits and enjoyment of exercise.

For individuals who already have CVD, exercise training can be highly beneficial. Indeed, this type of training is a core element of most cardiac rehabilitation programs. Exercise improves the functional capacity of most cardiac patients, including patients with very low cardiac ejection fractions and limited exercise tolerance, and this functional improvement occurs without significant cardiovascular complications or other adverse outcomes.

More than 4,500 cardiac patients have participated in more than 35 randomized controlled trials of exercise training for cardiac rehabilitation. No increase in morbidity or mortality was observed among the patients who participated in this training, as compared with those who did not participate. Exercise is a relatively safe activity, even for patients with stable CHD. Results of cardiac rehabilitation programs are further described in Part II of this report.

### *Research Opportunities*

The type, frequency, duration, and intensity of physical exercise necessary for achieving maximal health benefits need to be determined for a range of disease outcomes. As noted, most clinicians currently recommend that individuals accumulate at least 30 minutes of activity on most days of the week. Better methods of assessing lifestyle activity are needed to determine whether this level of activity should be recommended for achieving different health outcomes.

Most Americans do not engage in regular physical exercise, and of those who start an exercise program, more than 50 percent will discontinue it. The influence of cultural, demographic, and environmental factors such as social support, convenience, and cost on physical activity and exercise is being increasingly recognized and appreciated. These effects and the behavioral factors that influence the choice to be active (or inactive) and contribute to long-term maintenance of physical activity deserve further attention.

In addition, researchers have recently demonstrated the importance of studying sedentary behavior as well as physical activity. The variables associated with increased time spent in sedentary activities need to be identified. Because

habits that are developed in childhood are likely to be continued into adulthood, the variables specifically associated with children's sedentary activity deserve special attention. The interrelationship of exercise with other risk factors such as cigarette smoking, adverse diet, excessive alcohol use, and depression also needs to be better understood.

Recent evidence suggests that exercise may be associated with mental health benefits, as well as physical benefits, for both healthy and unhealthy populations. Regular exercise also may forestall some of the decline in functional status (the ability to engage in activities of daily living) that accompanies aging. The effect of increased physical activity on psychological well-being and quality of life requires further investigation, especially with respect to the effects for patients with heart, lung, and blood diseases and for elderly persons and for patients with mental health disorders.

### *Recommendations*

Recommendations for behavioral research on physical inactivity as a risk factor for heart and lung diseases are:

1. Determine the optimal and minimal dose of physical activity needed to reduce morbidity and mortality associated with different end points of heart and lung diseases. Development of assessment approaches for better quantifying lifestyle activities is an important first step.
2. Identify the variables that influence the initiation and maintenance of regular physical activity, especially among groups with the lowest levels of physical activity.
3. Determine the reasons for sedentary activity in children and adults.
4. Examine further the relationship of physical inactivity to other harmful health behaviors such as cigarette smoking, adverse diet, and alcohol use. Determine how interventions for one behavior influence other behaviors.
5. Examine the psychological impact of physical activity on patients with heart, lung, and blood diseases, giving particular emphasis to elderly persons and to patients with depression, anxiety, and other mental health disorders.

## *Diet*

Various components of an individual's diet are related to CVD risk factors and to CVD. Most notable is the relationship between high intake of saturated fat and cholesterol and high serum cholesterol. Intake of saturated fat also affects blood pressure levels. Data also indicate that more than one-half of the individuals with hypertension are sensitive to salt and that a reduction in their salt intake will decrease their blood pressure. Blacks and elderly persons are particularly prone to salt-sensitive hypertension.

Whereas fat is the major dietary culprit affecting CHD and its risk factors, other dietary habits such as consumption of fruit and vegetables may be protective. Data from a recent trial show that a diet rich in fruits and vegetables can reduce blood pressure levels in a matter of weeks, particularly when combined with low-fat dairy foods and reduced intake of saturated and total fats (see figure 3, combination diet). Other research indicates that a low consumption of fruits and vegetables independently predicts risk of stroke.

Fruits and vegetables may be protective because of their potassium and antioxidant content. Antioxidants such as beta-carotene, a precursor of vitamin A, ascorbic acid (vitamin C), vitamin E, and selenium appear to protect against atherosclerosis. Intake of soluble fiber and soy protein also reduces CHD risk factors.

Genetic influences likely modify the effects of diet on CHD risk factors. Some individuals, for

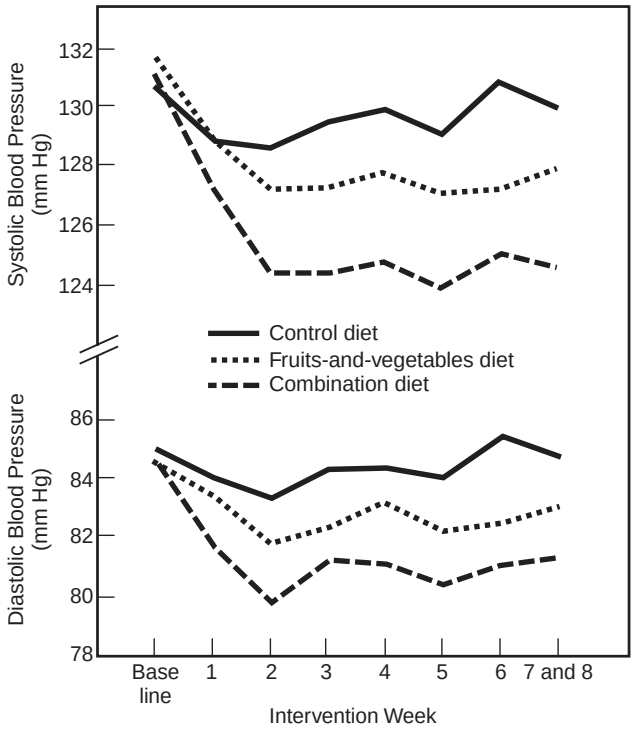


**Figure 3.** Mean systolic and diastolic blood pressures at baseline and during each intervention week according to dietary intervention. Reprinted with permission from Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin P-H, and Karanja N: A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336(16):1117-1124.

example, may be genetically more responsive than others to changes in their saturated-fat intake.

*Changes in the American diet*. The American diet has changed in important ways during the past 10 years. In 1976-80, Americans consumed approximately 36 percent of their calories as fat; today, this percentage has decreased to about 34 percent. Americans have decreased their consumption of certain foods, such as red meats, eggs, and whole milk, and have increased their consumption of poultry and fish. They also have increased their intake of fruits and vegetables to an average of 4.3 servings each day. These changes are associated with recent population-wide decreases in cholesterol levels and rates of CHD mortality.

Despite these improvements, however, most Americans still consume more than the recommended level of fat, which is 30 percent of calories. Less than 20 percent of children and adolescents and only 21 percent of adult men and 25 percent of adult women restrict their fat intake to this degree. In addition, only 32 percent of Americans achieve the recommended level of five servings of fruits and vegetables each day.

*Assessing dietary intake*. Accurate assessment of dietary intake is essential for studying the relationship between diet and CVD. Typically, epidemiological and behavioral researchers have relied on individuals' self-reports of dietary intake. However, these studies, conducted among free-living adults, consistently show a weaker relationship between diet and CHD risk factors than do studies conducted in metabolic (hospital) wards, where intake can be assessed and controlled directly. Use of recently developed methods for assessing dietary intake objectively (e.g., the doubly-labeled water technique) reveals that many individuals underreport food intake, particularly those who are obese or concerned about their weight.

*Food preferences*. Improved knowledge of the relationship between diet and health may result in reduced intake of dietary fat and increased intake of fruits and vegetables. But increased knowledge does not appear to be a sufficient incentive for changing dietary behavior. Food preferences, the strongest predictor of dietary intake, also are important. Behavioral researchers have therefore sought to understand the development of food preferences and to devise strategies for modifying them.

Understanding the body's regulation of calorie and fat intake over time is one aspect of this research. Previously, research on eating was focused on internal cues that produce hunger and satiety and on a model of eating based primarily on homeostatic principles. More recently, researchers have emphasized the study of food

preferences and the importance of learning and past experiences in developing these preferences. Findings show, for example, that satiety is sensory-specific. That is, when a specific food is consumed, the perceived palatability of that food decreases and sensations of fullness increase. If a new food is introduced, however, consumption of the new food will be higher than that of the previous food.

Researchers also have shown that preference for salty and sweet tastes and avoidance of sour and bitter sensations are universal and innate, but other food preferences are learned. For example, the diet a mother eats during pregnancy influences a child's initial food preferences.

Behavioral techniques can be used to modify an individual's food preferences. Increasing a person's exposure to a given food, pairing a "neutral" food with a liked food, presenting food in a positive social context, and pairing food with positive postingestive consequences are effective techniques for increasing an individual's preference for a given food.

Understanding food preferences is further complicated by the recent and increasing availability of fat-modified foods. Recent studies suggest, for example, that individuals differ in their response to these foods. Some individuals, particularly those of normal weight, compensate for reduced fat by increasing their total intake of calories or fats, but other individuals do not compensate and therefore lose weight. The availability of other foods affects this compensation. If all the available foods are low in fat, an individual will compensate less and will maintain the overall volume of food consumed, although the total calories from fat will be reduced.

### *Research Opportunities*

Investigators who have been studying food preferences have emphasized short-term laboratory studies of children. The possibility of modifying food preferences in adults has not been explored adequately. Also unclear is whether food preferences must be modified in order to produce permanent changes in eating behavior, or whether changes in eating behavior eventually will lead to changes in food preferences.

The availability of a large array of fat-modified foods offers a unique opportunity for studying the effect of these foods on individuals' preferences for fat and consumption of fat, as well as the overall healthfulness of their diets. Issues to be addressed include whether individuals will consume fat-modified foods in addition to their usual diet, or instead of their usual foods, and whether they will compensate for these foods over time to maintain a constant fat and/or calorie intake.

Studies of the relationship between dietary intake and CVD are severely limited by researchers' inability to measure dietary intake directly and accurately. Techniques are critically needed for assessing the amount of fat and calories individuals consume. More objective approaches are especially desirable.

Although research shows that some individuals respond better than others to dietary changes, the variables underlying individual differences are still undetermined. Genetic variations are implicated, but the specific genes controlling the responses have not been identified. In recent studies, for example, researchers examined the association between individuals' genetic phenotypes (e.g., the APO-E phenotype) and the effect of a dietary change on their serum cholesterol levels. These studies, however, were inconclusive, and more research is needed to identify the genetic phenotypes that influence individuals' responses to dietary modification.

### *Recommendations*

Recommendations for behavioral research on diet as a risk factor for CVD are:

1. Determine the effect of food preferences on food intake in comparison with the effect of increased knowledge about foods, reduced cost and increased availability of foods, and other factors. Assess the possibility of modifying food preferences and determine the effectiveness of approaches that encourage individuals to choose a healthful diet.

2. Examine the effect of individuals' consumption of fat-modified products on their food preferences, intake of calories and fats, diet's overall nutrition quality, and biological variables such as body weight and serum cholesterol levels.

3. Develop ways to assess the intake of calories and fats accurately during everyday life in noninstitutionalized individuals.

4. Identify genetic factors that influence individuals' responses to dietary modification.

## *Obesity*

When the *Healthy People 2000* guidelines were formulated in 1990, excess weight was a problem for about 25 percent of Americans. One of the goals stipulated in *Healthy People 2000* was to reduce the percentage of Americans who were overweight to less than 20 percent. Unfortunately, the American population has gained weight instead. Currently, 35 percent of women and 31 percent of men aged 20 and older, as well as 25 percent of all children and adolescents, are considered overweight.

The prevalence of obesity is particularly high among minorities, especially minority women. Approximately 50 percent of black, Mexican American, and Native American middle-aged women are considered obese. Obesity also occurs disproportionately among individuals of low socioeconomic status.

Increases in the percentage of individuals who are overweight cannot be explained by changes in smoking habits, and they contrast with apparent decreases in dietary fat intake. The increased prevalence is a particular concern because excess weight is associated with hypertension, hypercholesterolemia, diabetes, and CHD. Being overweight increases an individual's risk of dying, particularly of CHD, and is associated with altered respiratory function, particularly sleep apnea.

Being overweight also has psychological costs. Overweight individuals are less likely to be hired for a job and less likely to get married than individuals who are not overweight. Children choose not to play with overweight peers, and even physicians report that they hold negative attitudes toward their overweight patients.

*Distribution of body fat*. Research indicates that distribution of body fat, independent of overall obesity, is related to CVD and all-cause mortality. A more central distribution of body fat, or "masculine" fat distribution (defined as a higher ratio of waist-to-hip circumferences), is associated with hypertension, hyperinsulinemia, glucose intolerance, hypertriglyceridemia, myocardial infarction (MI)—heart attack—angina, stroke, and death.

Recent studies of these effects suggest that visceral (or intra-abdominal) obesity is responsible for the increased health risk associated with the central accumulation of fat. Research also indicates that genetic factors are associated with distribution of body fat and that several behavioral factors, including stress, low physical activity, and smoking, are associated with visceral fat. Although smokers tend to weigh less than nonsmokers, a higher proportion of their fat is visceral.

*Weight loss/weight cycling*. Numerous studies show that modest weight loss can lower blood pressure levels, decrease LDL cholesterol levels, increase HDL cholesterol levels, reduce insulin

resistance, improve glycemic control, and reduce sleep apnea. These positive benefits have been observed in individuals who have lost only 10 percent of their body weight, and larger weight losses produce even greater improvements.

In several epidemiological studies, researchers have shown that weight cycling (i.e., repeated episodes of weight loss and subsequent weight gain) is associated with increased mortality, especially from CVD. These negative effects appear primarily to result from involuntary weight cycles which are probably associated with underlying diseases. Most prospective studies have not shown any negative effects of weight cycling on metabolic parameters, psychological variables, or CVD risk factors.

*Determinants of body weight*. A number of genetic, behavioral, and other factors determine body weight. Family, twin, and adoption studies indicate that obesity has a strong genetic component that explains approximately 50 percent of individual differences in body weight. In addition, researchers have shown that obese infants with obese parents are twice as likely to develop obesity in adulthood as infants with nonobese parents. A low metabolic rate, a tendency to utilize carbohydrate fuel rather than fat, and higher insulin sensitivity are associated with subsequent weight gain but not with maintenance of obesity. Studies of the recently discovered obesity gene and its protein (leptin) will enhance understanding of these complex factors.

Physical inactivity, pregnancy, smoking cessation, and stress are some of the behavioral factors associated with weight gain. Studies indicate that large weight gains are most likely to occur between the ages of 25 and 34 in both men and women, possibly because of decreased physical activity. Pregnancy, implicated in some studies, is not associated with marked weight gain for women in general, but women who gain much weight during pregnancy are likely to retain excessive weight 1 year after their pregnancy. Black women are disproportionately represented in this group.

Women also continue to gain weight as they age, averaging almost 1 pound a year during menopause. Smoking cessation is known to lead to weight gain in both men and women, and this effect is particularly pronounced in women. Anecdotal evidence suggests that weight gain also is associated with stress.

In addition, extensive data document the importance of environmental and dietary factors for body weight. In the studies available, researchers compared individuals of the same genetic background who lived in rural versus urban areas and in industrialized versus nonindustrialized countries. For example, migration studies show that Japanese individuals residing in Japan are thinner than Japanese persons residing in Hawaii, who are thinner than their counterparts residing in the continental United States.

*Causes of obesity*. Obesity results from an imbalance between caloric intake and energy expenditure. Low levels of physical activity and high intake of dietary fat are important risk factors for obesity. High-fat diets, in particular, promote obesity, perhaps because they are more palatable than other diets and contain excess calories that are consumed easily and stored more readily in the body than excess calories from carbohydrates.

Epidemiological studies suggest that obese individuals often consume diets that are high in fat but equal in calories to diets of leaner individuals. Other research indicates that individuals consuming a low-fat/high-carbohydrate diet often lose weight partly because this diet results in greater satiety and therefore reduced caloric intake. Also noted is a relationship between consumption of high-fat diets and genetic predisposition to obesity.

Substantial evidence indicates that obese individuals are less active than lean individuals. The major difference observed is the amount of time spent on physical activity. Obese individuals spend more time in sedentary activities, such as watching television. Other factors that contribute to energy expenditure include resting energy expenditure and the thermic effect of food.

Clearly the development of obesity is multifactorial. This fact is best demonstrated by an impressive 100-day "overfeeding" study of 12 monozygotic twins and a separate study of the same twins that included increased exercise. In both studies, the weight change that occurred with manipulation of the twins' environment varied markedly between the twin pairs, but the variability within pairs was very small. These results suggest that individuals vary in their genetic susceptibility to different environmental changes.

### *Research Opportunities*

The recent marked increase in the prevalence of excess weight is a national concern. The reasons for this increase need to be understood better, especially in relation to the apparent decreased consumption of dietary fats during the same period.

Other important areas of study include identification of the most successful way of modifying environmental factors and psychosocial variables that may affect weight and determination of the effect of these modifications on dietary behavior.

The physiological factors that control dietary intake, energy expenditure, and energy regulation also must be understood better. In particular, studies of the recently discovered obesity gene and its product (leptin) could enhance understanding of energy regulation. The relationship between physical activity and dietary intake and their relative contributions to obesity also need to be investigated.

Differences in the prevalence of obesity among ethnic and socioeconomic groups need to be clarified. The effect of differences in genetic susceptibility, access to healthful foods and to exercise facilities, and attitudes about appropriate body weight need to be examined further in these groups. Individuals at high risk of becoming obese could be identified based on this information.

Additional research could explain the development of visceral obesity and its effect on cardiovascular morbidity and mortality. Development of a simple, cost-effective technique for assessing visceral obesity will advance this research.

### *Recommendations*

Recommendations for behavioral research on obesity as a risk factor for heart and lung diseases are:

1. Identify the changing environmental factors responsible for the increased prevalence of obesity in the United States.
2. Investigate environmental variables that affect energy intake and physical activity. Examine the effects of the availability and cost of food and exercise facilities, as well as the influence of knowledge and attitudes on dietary intake and energy expenditure.
3. Investigate genetic and physiological variables controlling energy balance, including the effect of changes in intake or exercise on this balance and on body weight. Determine the relative contributions of intake and expenditure of energy to the risk for obesity.
4. Identify environmental and genetic factors that explain differences in the prevalence of obesity among ethnic and socioeconomic groups.

5. Increase understanding of the variables that influence visceral obesity and the effects of visceral obesity on CVD. Develop a cost-effective approach for measuring visceral obesity.

## *Alcohol Dependence and Abuse*

Alcohol dependence and abuse are responsible for at least 100,000 deaths annually in the United States, as well as $200 billion annually in medical care, lost productivity, and other social costs. Fifty percent of the increased risk of mortality among alcoholics is due to CVD. Up to one-fourth of all cases of hypertension are associated with alcohol, and heavy drinking, defined as three or more drinks each day, is related significantly to hypertension in men and women regardless of age or weight—an association that has been observed in more than 60 population studies worldwide.

High levels of alcohol consumption also increase the risk of fatal and nonfatal strokes, arrhythmias, sudden cardiac death, ischemic heart disease, and cardiomyopathies. Cardiomyopathy is evident in about one-third of alcoholic men and women. And although the lifetime intake of alcohol among alcoholic women is less than one-half that of alcoholic men, cardiomyopathy is equally common to both. Clinical studies also show that, for women, alcohol has more toxic effects on the myocardium.

*Benefits vs. risks of alcohol consumption*. Recent epidemiological studies suggest that low-to-moderate intake of alcohol decreases the risk of CHD. Reports also indicate that light drinkers have lower mortality rates than nondrinkers. However, persons consuming three drinks daily have an increased risk of mortality from CHD. These findings—the apparent benefits of low-to-moderate consumption of alcohol, but the known harmful effects of high levels of alcohol intake—need to be studied further. Additional studies of cardiovascular function and risk across a broad range of intake levels must be conducted to clarify the implication of the findings for the nation's public health. The NHLBI, which traditionally has not supported much research on alcohol dependence, should give careful consideration to the research needed in this area.

For example, the mechanisms of alcohol's influence on cardiovascular health are not well understood. Acute intake of alcohol can have deleterious effects on the cardiovascular system, such as short-term increases in blood pressure and heart rate, and at high doses, impairment of diastolic LV function. In patients with CHD, alcohol increases angina and decreases exercise capacity. In animal models, acute alcohol intake activates the sympathetic nervous system and stimulates the release of corticotropin-releasing hormone and cortisol. These findings suggest that alcohol's influence on acute cardiac events may be mediated by the central nervous system.

Long-term *moderate* alcohol intake, defined as no more than one to two drinks daily, is associated with increased serum levels of HDL and improved lipid profiles. These factors reduce the risk of coronary artery disease (CAD) among moderate drinkers, compared with nondrinkers.

However, long-term *excessive* use of alcohol is associated with depressed cardiac output, ventricular hypocontractility, and atrial fibrillation. Samples of LDL from alcoholic patients show oxidatively modified epitopes and acetyl aldehyde adducts, as well as decreased vitamin E content. These changes may make LDL more atherogenic and thereby negate the antiatherosclerotic effects of low levels of alcohol consumption.

The strength of association between risk of CHD and low alcohol consumption also is directly related to serum concentrations of LDL; individuals with the highest levels of LDL show the greatest protective effects of moderate alcohol consumption. These findings indicate that low levels of drinking may benefit only some

individuals, whose characteristics have not yet been completely defined.

In sum, a review of the literature on alcohol and CVD raises concern that the deleterious health effects of alcohol consumption may outweigh alcohol's beneficial effects on the risk for CHD. Although the mechanisms of the cardiovascular benefits associated with low-to-moderate consumption of alcohol are not understood, data suggest that this benefit may be partly related to lipid changes resulting from drinking.

*Causes and effects of alcohol use*. Alcohol abuse and dependence are heterogeneous disorders that have multiple causes and are characterized by wide variations in patterns of substance use. Some of the predisposing factors for alcohol abuse and dependence are similar to those for smoking; for example, use of other drugs, diet, and socioeconomic status are all known to influence the risk of CVD.

Both biological and behavioral factors are associated with an increased risk of alcohol abuse and dependence. Alcohol disorders are far more likely to occur in men than in women, but whether this discrepancy results from biologically or behaviorally based sex differences is not clear. Personality factors associated with alcohol abuse in young adults include high activity level, attention deficits, inability to control emotions, and antisocial characteristics. Other drug use, including smoking, is also much more common in those who abuse alcohol, and consumption of alcohol can increase the desire to smoke or use cocaine, behaviors which also increase the risk for cardiovascular morbidity. Development of cross-drug tolerances, conditioned associations between drugs, and a basic underlying predisposition to the abuse of drugs may increase individuals' potential for using multiple drugs.

Alcohol appears to provide relief from unpleasant subjective states such as anxiety and frustration. Many of these effects vary, depending on the amount of alcohol consumed and the time that has passed since it was consumed. For example, alcohol can enhance an individual's mood within about 30 minutes, when alcohol levels in the blood are rising, but it may have more sedative effects later, when alcohol levels in the blood are falling.

Although research indicates that alcohol consumption can reduce anxiety under certain conditions, the mechanisms for this effect are still being debated. Researchers have attributed alcohol's effects on anxiety to biological influences (e.g., direct effects on the central and peripheral nervous systems) and to psychological processes (e.g., changes in self-awareness, self-evaluation, or allocation of attention resources). Tolerances to alcohol's effects may develop and, in response, individuals may need to increase their alcohol consumption to maintain the reward effects.

Most drinkers drink in moderation, a pattern which may have few harmful health effects. A primary aim of research is to identify the drinkers who are likely to consume alcohol in excess.

Individuals' expectation of positive effects from drinking alcohol is associated with their initial and later consumption of alcohol. An individual's continued use of alcohol may become associated with environmental situations such as stress or socializing with friends, which subsequently will elicit the urges to drink.

A family history of alcohol dependence also is an important risk factor for the development of alcohol-related problems. Research shows that persons with a positive family history for alcohol dependence experience greater reinforcing effects from alcohol intake when blood alcohol is rising, and fewer unpleasant effects when blood alcohol is declining. In addition, the anxiety-reducing effects of alcohol may be enhanced in individuals who have a family history of alcohol dependence. A familial predisposition to alcohol dependence undoubtedly results, in part, from genetic influences, but the social and psychological dysfunction from living with at least one alcoholic parent

probably also contributes to increased risk of alcohol abuse.

The quality of parent-child interaction patterns appears to be an important risk factor for both conduct disorders and alcohol use among teenagers. Use of alcohol and drugs usually begins during early adolescence and is reinforced by substance use among peers. Additional research on the differences in behavioral, family, and peer characteristics that distinguish children at risk of excessive alcohol use from those not at risk may provide critical information for understanding how to prevent alcohol abuse and dependence.

### *Research Opportunities*

Most researchers have examined the effects of temperamental characteristics or environmental demands on alcohol use. The ways that different environmental influences affect different types of individuals to promote alcohol use are not understood. The genetic and environmental interactions that may influence the development of alcohol abuse and dependence need to be better understood.

Most research on alcohol abuse in human populations has been conducted with men. Little is known about the determinants of alcohol abuse among women. Gender differences in alcohol abuse need to be better understood. The problem of alcohol abuse among women should be given more attention, especially because, at comparable levels of consumption, alcohol has a greater physiological effect on women than on men.

The ways that alcohol promotes acute cardiac events and chronic CVD are not well understood. Additional research is needed to understand the influence of behavioral characteristics, socioeconomic status, family history of alcohol abuse, and life stress on patterns of alcohol consumption and on the short- and long-term cardiovascular effects of alcohol.

### *Recommendations*

Recommendations for behavioral research on alcohol dependence and abuse as a risk factor for CVD are:

1. Identify environmental determinants of alcohol abuse among persons at different risk for this disorder because of family history or temperament. Elucidate gene-environment interactions that contribute to the development of alcohol abuse or dependence and their relation to risk for CVD.
2. Identify factors that contribute to gender differences in alcohol use and examine the determinants of alcohol use and dependence in women.
3. Determine the mechanisms for the influence of heavy social drinking and alcohol abuse on the development of acute and chronic CVD, including hypertension, CAD, and cardiomyopathy.

## Individual Characteristics

In addition to the health habits and lifestyle behaviors described above, individual characteristics related to personality and emotions and to patterns of physiological responses to acute stress have been associated with CVD. Behavioral research on these individual characteristics is summarized in this section under two topics: psychological traits and personality, and reactions to acute psychological stress.

### *Psychological Traits and Personality*

*Hostility, anger, and related traits.* Psychological traits such as hostility and Type A behavior pattern, and negative emotions such as anxiety and depression have been studied widely for their possible association with increased risk for CVD. In epidemiological studies, these qualities

typically are assessed by the use of self-administered questionnaires. Occasionally, researchers use clinical interviews to assess objectively certain stylistic manifestations of personality (e.g., gestures, body posture, hostile voice tone, voice volume) in the individuals being interviewed.

Reports from several epidemiological studies show that individuals with a Type A behavior pattern, which is characterized by extremes of competitiveness, sense of time urgency, ambition, and easily aroused hostility, have about twice the risk of CHD as individuals with non-Type A behavior patterns. This finding holds true even when statistical adjustments are made for other standard risk factors, such as high blood pressure level, high cholesterol level, smoking, and family history of CHD. In a number of recent studies, however, researchers report no effect of Type A behavior on risk of CHD.

Because Type A behavior is a constellation of behavioral characteristics, some Type A behaviors may be more important than others for the development of CHD. To explore this possibility, researchers recently coded the separate dimensions of the Type A behavior pattern from self-reports and clinical interviews and attempted to relate these dimensions to risk for CHD.

This research demonstrated the importance of one dimension—hostility—to risk for CHD. Cognitive, affective, and behavioral components of hostility have all been shown to be important. The cognitive component consists of negative beliefs about other people and negative attitudes toward others, including cynicism and mistrust. The affective component refers to frequent and intense experience of anger. The behavioral component refers to overt aggression or the attempt to harm others by insults, sarcasm, or opposition.

In addition to this research, recent meta-analytic evaluations of the epidemiological literature indicate definite associations between hostility and risk for CHD. After controlling for other risk

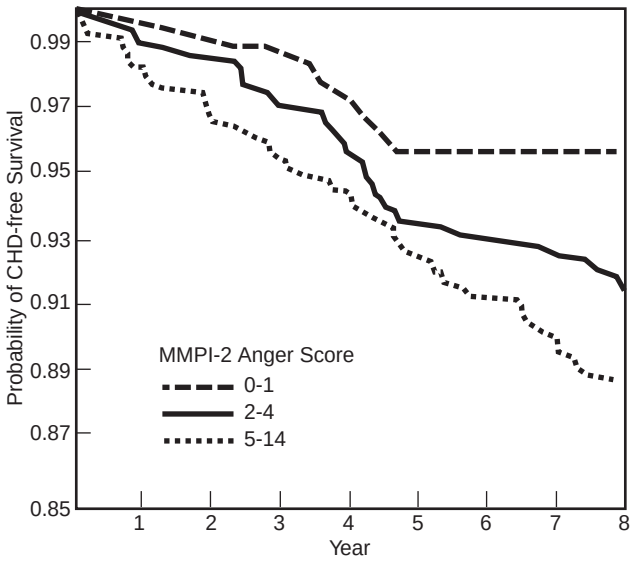


**Figure 4.** Probability of coronary heart disease-free survival among patients grouped according to anger content scores on the revised Minnesota Multiphasic Personality Inventory (MMPI-2). Reprinted with permission from Kawachi I, Sparrow D, Spiro A, Vokonas P and Weiss ST: A prospective study of anger and coronary heart disease: The Normative Aging Study. Circulation 1996;94(9)2090-2095.

factors, the researchers have found that cognitive measures of hostility were most predictive of all-cause mortality and, to a lesser degree, morbidity from CHD (see figure 4).

Studies also have documented an association between the cognitive and affective dimensions of hostility and the extent of carotid artery disease. However, as in previous research on CHD, most of the participants in these investigations were men. Whether a similar association between hostility and risk for CHD exists among women is not known.

The influence of hostility on health appears early in life. Prospective studies, which were initiated with adolescents and college students who were then followed for 3 to 20 years, show that hostility and Type A behavior predict smoking and alcohol use in later years, as well as high lipid levels and increased body mass index. In addition, adolescents and young adults who are rated as hostile, anxious, and pessimistic tend to have more conflicting and less supportive relationships with

their families and with their peers. The presence of conflicting family relationships predicts increased hostility in adolescence, which is likely to continue to encourage others' conflicting and nonsupportive behavior. The findings from this research suggest that prevention programs may be effective for reducing hostility and other behavioral risk factors among young adults.

*Depression, anxiety, and fatigue and exhaustion*. In addition to hostility, negative emotions such as depression and anxiety are important factors for individuals' prognoses after a CHD event. These characteristics are assessed clinically by the use of self-report questionnaires and diagnostic interviews, as well as self-report measures of subclinical ratings of negative mood.

Several studies indicate that almost two-thirds of patients with MI have some mental disorder, primarily depression, or anxiety. Major (clinical) depression is apparent in approximately 20 percent of patients who have experienced an MI. Another 27 percent of MI patients report minor symptoms of depression. In contrast, the prevalence of major depression at any point in time in community samples of individuals of comparable age and gender is only 3 percent.

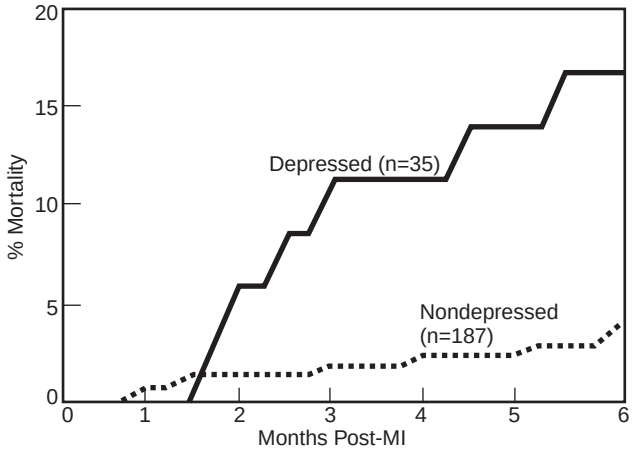


**Figure 5.** Six-month cumulative mortality in depressed and nondepressed post-myocardial infarction patients. Reprinted with permission from Frasure-Smith N, Lesperance MD, and Talajic M: Depression following myocardial infarction: Impact on 6-month survival. JAMA 1993;270(15):1819-1825.

For MI patients, depression increases the risk of future CHD events such as reinfarction, cardiac arrest, and death, regardless of the severity of disease (see figure 5). In addition, high levels of depressive symptoms are associated with the incidence of stroke, and depression is the most common diagnosis among women who have a history of mental health disorders, with the latter placing them at increased risk for sudden death.

Clinical depression following an MI not only leads to a poor long-term medical prognosis, but also reduces the likelihood that an individual will return to normal levels of occupational and social activities. Subclinical characteristics of depression have also been associated with worsened long-term prognosis of CHD patients. Pessimistic attitudes about the future are related to poor prognosis following coronary artery bypass surgery and to poor quality of life regardless of the initial severity of disease.

A combination of traits, known as "vital exhaustion," has been described in CHD patients and individuals at risk for CHD. Vital exhaustion is a mental state characterized by unusual fatigue, a feeling of being dejected or defeated, and increased irritability. It has predicted both restenosis after successful coronary angioplasty and incidence of angina and nonfatal MI during a 4-year period.

Symptoms of anxiety also are linked with enhanced CVD risk. In-hospital anxiety after an MI predicts subsequent ischemic and arrhythmic events, including recurrent MI and sudden cardiac death. In prospective studies, a high level of tension predicted increased blood pressure levels and development of hypertension.

The association of cardiac events with depression, anxiety, and hostility may result from patients' poor adherence to medication because of negative emotions or from other factors such as smoking, dietary practices, and autonomic function. With respect to the latter, arousal of the

sympathetic nervous system can have specific adverse effects on the heart, including increased basal tone of the coronary arteries, platelet aggregation, and intraluminal shear stress; enhanced myocardial consumption of oxygen; and decreased fibrillation threshold. These effects are described in the section on Acute Cardiac Events.

### *Research Opportunities*

New evidence suggests that many of the psychosocial characteristics associated with increased CVD risk tend to cluster or group together. For example, hostile persons may have less social support and more symptoms of depression than nonhostile persons. Because of this type of clustering, more parsimonious ways are needed to define and measure relevant psychosocial risk factors in epidemiological and clinical studies. These refinements may improve understanding of the translation of psychosocial factors into disease processes.

Almost all of the existing psychosocial measures were developed initially for studies of middle-aged white men. The validity of these measures needs to be established for other ages and ethnic groups and for women. In addition, valid measures should be developed for measuring clusters of psychosocial factors among diverse groups in future epidemiological studies.

Researchers have shown that a number of putative psychosocial risk factors for CVD emerge by adolescence and young adulthood. The environmental and genetic factors that promote these traits need to be understood, and strategies for preventing their development need to be devised.

Studies among children and adults in primary care settings and communities reveal surprisingly high rates of mental health disorders. As noted above, researchers have shown that mental health disorders such as depression and anxiety are associated with CVD. Patients who are diagnosed with CHD and with clinical depression or increased anxiety have shorter survival times and a poorer quality of life, and data indicate that mental health disorders may be highly prevalent among patients admitted to a hospital with suspected MI. Investigations conducted in primary care settings and communities could help clarify the association between mental health disorders and heart, lung, and blood diseases.

Investigators will want to explore the pathways for increased risk of CVD from psychosocial risk factors, including those associated with mental health disorders, to the extent that these associations become strongly established. Possible mechanisms include alterations in the autonomic nervous system control of the heart. Researchers have shown that heart rate variability and circulating catecholamine responses are altered in depressed patients. The fact that inhibitors of serotonin re-uptake are among the most effective and common treatments for depression suggests that changes in serotonergic function also may occur. The presence of depression also may make treatment less effective, and the possible cardiotoxic effects of some psychotropic medications may increase the risk of complications from CVD in some patients.

### *Recommendations*

Recommendations for behavioral research on the association of psychological traits and personality with heart, lung, and blood diseases are:

1. Develop new, valid measures of clusters of psychosocial risk factors for CVD to use in epidemiological and clinical studies of diverse populations.
2. Study the environmental and biological determinants of adverse psychological traits for CVD in diverse populations to better inform interventions for preventing the development of these traits.

3. Establish whether mental health disorders predict the occurrence of heart, lung, and blood diseases in community settings.

4. Clarify the biological and behavioral pathways that account for the association between cardiovascular conditions and mental health disorders and negative emotions in general.

## *Reactions to Acute Psychological Stress*

Individuals vary markedly in the magnitude of their cardiovascular reactions to acute psychological stress. For example, some individuals' blood pressure levels may increase 30 to 40 mmHg when performing daily tasks that they view as aversive or challenging, whereas, under the same circumstances, other individuals' blood pressure levels may change little or not at all. Such individual differences in cardiovascular "reactivity" are present early in life and endure over time.

Risk for CVD may be elevated among those persons who respond to stress with particularly large increases in blood pressure levels and heart rate. For example, individuals who are behaviorally predisposed to CHD because they have Type A attributes or traits of anger and hostility experience larger cardiovascular reactions to stress than more placid individuals.

Other evidence associates increased cardiovascular reactivity with the occurrence of myocardial ischemia (inadequate supply of blood to heart tissue) during mental stress in individuals who have CHD. One preliminary study showed that increased cardiovascular reactivity also may be associated with subsequent cardiovascular events among individuals who have survived an acute MI.

Persons who are highly reactive to stress also may be at higher risk of hypertension. Two longitudinal studies indicate, for example, that exaggerated responses of blood pressure levels to a cold pressor test involving immersion of an individual's hand in cold water predict the individual's hypertensive status 3 or 4 decades later.

Other studies suggest that reactivity to stress may predict changes in blood pressure levels over shorter durations in individuals with normal blood pressure. Additionally, some recent evidence indicates that individual differences in blood pressure reactivity may correlate with echocardiographic indices of LV mass among hypertensive individuals and among some groups of young adults and children (see section on Hypertension and Left Ventricular Hypertrophy).

The influence of this heightened reactivity to psychological stress on the promotion of CVD is not clear. Researchers currently are examining various possible pathophysiological mechanisms. Heightened reactivity may influence the development and progression of atherosclerosis through hemodynamic effects (see the section on Behavior-Disease Processes), alter the dynamics of the circulation to increase the workload of the heart, and influence a variety of metabolic processes, such as unfavorable lipid profiles and decreased insulin sensitivity, by activating the sympathetic nervous system.

### *Research Opportunities*

Prospective evidence for an association between reactivity and development of CVD among initially healthy individuals is sparse, except for the few longitudinal studies of reactivity to cold pressor tests, which were initiated many years ago. Recently, the NHLBI supported the development of a protocol to assess individual differences in behaviorally elicited cardiovascular reactivity in population-based epidemiological investigations. This work resulted in the development of a computerized battery of psychophysiological tests that are well standardized, have good reproducibility, and may be applied readily to different testing sites.

In addition, other researchers have improved the reliability of assessing individuals' reactivity to a variety of stressors. These instruments should be applied in prospective studies of arterial hypertension and CHD and in investigations involving serial noninvasive measurements of relevant pathophysiological processes such as atherosclerosis and vascular and end-organ complications of hypertension.

Assessment of the interactive effects of environmental factors and individual characteristics is important. For example, individuals who are highly reactive to acute stress might be at increased risk for hypertension and cardiovascular morbidity only when exposed to high levels of occupational or personal life stress. Study designs and methods should include evaluation of environmental factors so that the effects of reactivity can be examined in these cases.

In addition, recent psychophysiological research shows that individuals differ not only in the magnitude of their cardiovascular responses to stress, but also in the underlying hemodynamic adjustments that support the increases in blood pressure levels. For example, an increase in blood pressure in response to a behavioral provocation may be due to an elevated cardiac output (*cardiac* reactivity) or to an elevated peripheral resistance (*vascular* reactivity). Different patterns of hemodynamic response to stress may influence different aspects of CVD (e.g., atherosclerosis, hypertension) through effects on the dynamics of blood flow or metabolic correlates. Continued research is needed to clarify these interactions and relationships.

Patterns of cardiovascular reactivity also differ significantly between men and women and between different ethnic groups. For example, men tend to have a greater vascular response to stress than do women. And, during stress, blacks tend to show greater vascular reactivity than whites, whereas whites show greater cardiac reactivity than blacks. Further research is needed to elucidate the significance of various patterns of hemodynamic reactivity to psychological stressors, and the distribution of these patterns across population groups that have different risks of CVD.

Cardiovascular reactions to acute psychological stress typically are evaluated in laboratory or clinical settings, and the measurements in these settings are generally assumed to reflect, and be a proxy for, individuals' reactivity to the challenges and events of daily life. Recent advances in ambulatory measurement of cardiovascular function and psychological states make it possible to evaluate the expression of reactivity in individuals' customary environments.

In addition, the development of new statistical techniques for analyzing physiological data obtained in ambulatory conditions enables scientists to quantify individuals' cardiovascular responses to naturally occurring stressors. These responses also can be compared with cardiovascular adjustments induced by other behaviors such as changes in posture, physical activity, and sleep. Using these techniques, scientists can test hypotheses about the reactivity–disease association based on measurements of cardiovascular response obtained in "real" life and "real" time. This capability may be especially valuable for studies of clinical events such as myocardial ischemia, which occurs episodically and may not be detected unless it is assessed in an ambulatory context.

### *Recommendations*

Recommendations for behavioral research on the association between reactions to stress and CVD are:

1. Evaluate prospectively stress-elicited cardiovascular reactivity as a predictor of CVD and progression of CVD.

2. Elucidate patterns of hemodynamic adjustment underlying blood pressure responses to psychological stress, including the distribution of these patterns across population groups that differ in CVD risk, pathophysiological correlates, and relevant disease end points.

3. Exploit ambulatory measurement techniques to evaluate cardiovascular reactivity in daily life and the relationship between reactivity and various manifestations of CVD.

## Psychosocial and Other Environmental Variables

Environmental factors also may predispose individuals to risk for CVD independently or in combination with lifestyle factors and individual characteristics. For considering these factors, the Task Force adopted a broad view of the term "environmental." Included within the Task Force's definition are psychological, social, cultural, ethnic, and occupational variables, as well as the physical environment. Four areas of behavioral research on environmental variables implicated in CVD are addressed in this section: socioeconomic status, race and ethnicity, psychological stress and job strain, and social resources.

### *Socioeconomic Status*

Health correlates systematically with an individual's position in society. Compared with individuals who are more advantaged, persons of lower socioeconomic status die earlier from all causes and have higher rates of heart disease, diabetes, high blood pressure, chronic bronchitis, emphysema, and tuberculosis. The relationship between socioeconomic status and health is not simply due to the relationship between poor health and poverty. For each increment in socioeconomic status, health improves, even among relatively affluent classes. This gradient of socioeconomic status and health is found in most Western cultures.

In the United States, socioeconomic status also influences the degree to which the population has benefited from the decline in mortality from CVD during the past 30 years. This decline has been more pronounced among those of higher socioeconomic status, thereby increasing the slope of the gradient between social position and health. Deaths from CHD and arteriosclerosis account for a large proportion of the differences in mortality rates between different socioeconomic strata.

Researchers do not agree on the reasons for the widely observed link between health and socioeconomic status. Poor nutrition, inadequate hygiene, and lack of access to medical care may be factors. However, although they may help explain the negative effects of poverty among persons of lower socioeconomic status, they do not explain the differences in health between middle and higher socioeconomic strata. Similar differences are also found in countries that have universal health care or prepaid health care plans, which provide health care coverage to all socioeconomic strata. Thus, the association between socioeconomic status and health cannot be explained solely by a difference in access to medical care. Other factors must be involved.

Health behaviors, including smoking, physical activity, weight control, and alcohol consumption, are closely tied to both socioeconomic status and health outcomes. Even in studies that included statistical controls for health behaviors, health outcomes were still associated with socioeconomic status.

Recently, investigators proposed that personal and social characteristics of individuals may help explain the gradient of socioeconomic status and health. Certain characteristics, such as exposure to stressful life events, work environment, social

support, coping mechanisms, hostility, depression, and sense of personal control, vary with both socioeconomic status and health status (see the previous section on Psychological Traits and Personality). Whether these characteristics account for some of the linkage between socioeconomic status and health is not known.

## *Race and Ethnicity*

In the United States, race and ethnicity are strongly associated with differences in the burden of illness. Blacks, for example, are at greater risk than whites for stroke, hypertension, diabetes, electrocardiographic abnormalities, and obesity (among women). Compared with whites, blacks also have three times the age-adjusted mortality rate for asthma. Asthma is more prevalent among black children and causes greater limitation of activity and more frequent hospitalizations than among whites of European origin.

The biological and environmental determinants of ethnic differences in the rates of disease and mortality are not well understood. In the United States, membership in minority racial or ethnic groups is disproportionately associated with lower occupational prestige, income, and educational attainment. This association suggests the possibility that the relationship between ethnicity and health may reflect socioeconomic status differences, at least in part. It has been difficult to disentangle the differential effects of socioeconomic status and ethnicity on health.

The nature of the gradient in health and socioeconomic status may be somewhat different between minority and majority groups. For example, education and income are common measures of socioeconomic status. Among both blacks and whites, these indicators are associated with the prevalence of CHD and measures of carotid artery disease. However, the gradient of socioeconomic status and carotid disease is steeper among whites than among blacks. The flatter gradient for blacks may be due to the smaller number of affluent individuals (i.e., restricted range of socioeconomic status) in this minority group or to differences in the relation of education and income to social status among blacks and whites.

## *Psychological Stress and Job Strain*

Psychological stress can be defined as a negative internal state resulting from an individual's perception that environmental demands exceed the resources available to cope effectively. Stress is most commonly measured by assessing exposure to traumatic events such as natural disasters or to unusual, aversive, or challenging life experiences. Researchers have shown that, in vulnerable individuals, stressful life experiences may trigger clinical events such as MI and sudden cardiac death (see the section on Acute Cardiac Events).

Stress also can affect an entire population. For example, increased rates of cardiac mortality can be observed in populations exposed to earthquakes, war, or blizzards. On the day of the Northridge earthquake in California, the Los Angeles County coroner's records show a fivefold increase in the number of sudden deaths from cardiac causes, compared with the preceding week. Most of these deaths occurred within the first hour of the earthquake. And, during the 1991 Iraqi missile crisis, compared with the same period a year earlier, the number of acute MIs increased in the areas of Tel Aviv, Israel, that were attacked.

*Job strain*. Occupational activities are an important and common source of stress for many individuals in the workforce. "Job strain" results from holding demanding jobs that offer little opportunity for employee control or independent decisions. In studies involving white men, job strain is associated with an increased prevalence and incidence of CHD, stroke, and hypertension. Men employed in effortful jobs that offer few rewards for good work (e.g., handling freight,

working on an assembly line) are at increased risk for MI.

The influence of occupational stress on CVD among women has been investigated in relatively few studies, even though most middle-aged women are employed outside the home and often in low-status jobs. In studies of young women, job strain has not been associated with increased blood pressure levels. This finding may reflect researchers' failure to measure women's total work strain resulting from their multiple roles at home and work and the need to balance home, family, and work responsibilities.

*Additional stressors*. Individuals who are chronically struggling against a demanding and nonsupportive environment have an increased risk of hypertension. For example, blacks who score highly on a measure of "John Henryism," a style of excessively effortful coping in a stressful economic environment, and who are of a lower socioeconomic status are likely to become hypertensive. A mismatch between financial or educational resources and expenditures also may be associated with hypertension.

## *Social Resources*

Limited access to social resources also increases individuals' vulnerability to disease. Psychosocial researchers have conceptualized and measured two aspects of social resources: social isolation and social support.

Social isolation is defined as having few intimate relationships or social contacts. It is often measured by indices such as being unmarried, living alone, or belonging to few organizations such as clubs or churches.

Low social support is defined as having few friends or family members who can provide emotional or tangible support in times of trouble. It is measured by individuals' responses such as, "There is no one I can turn to when I have personal problems" or "There is no one I can count on to provide help to get to the doctor."

Data from large-scale epidemiological studies show that individuals who are socially isolated are more likely to die prematurely from all causes when compared with their counterparts who are more socially integrated (see figure 6). This association is apparent when deaths from CVD are

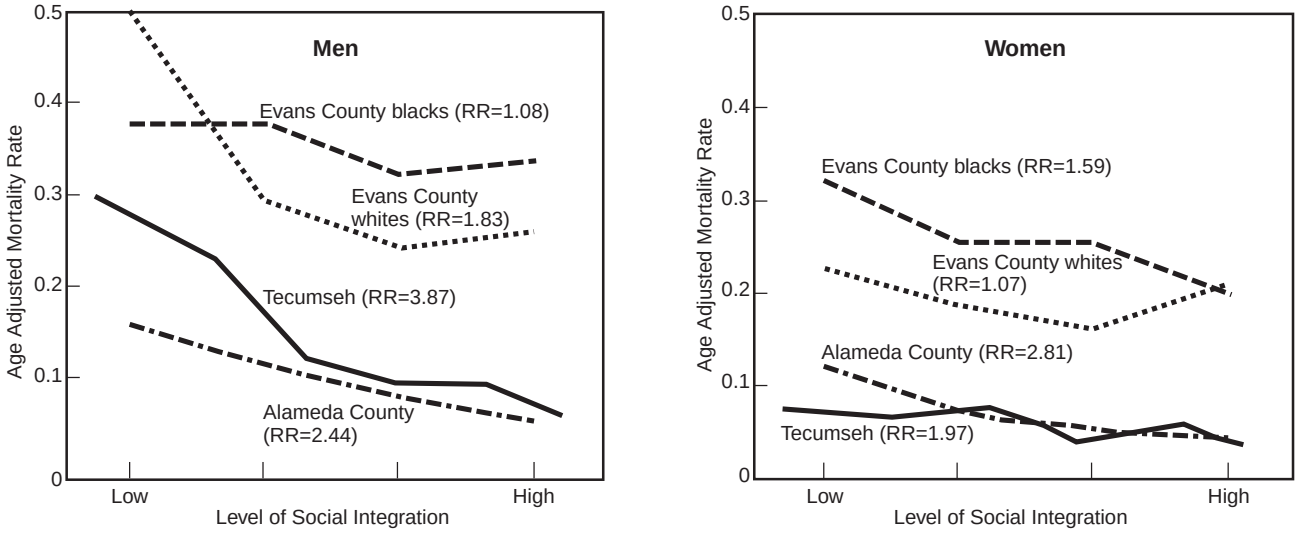


**Figure 6.** Age-adjusted mortality by level of social integration for men (left) and women (right) in three prospective studies. RR = relative risk ratio of mortality at the lowest versus highest level of social integration. Adapted and reprinted with permission from House JS, Landis KR, and Umberson D: Social relationships and health. Science 1988;241:540-545.

examined separately, and the association is especially strong among men.

Recent data also suggest that social isolation and low social support may be particularly important determinants of the length of survival following initial diagnosis of MI, angina, or other manifestations of CAD. In one study, post-MI patients who lived alone had increased risk of mortality, as did patients who were unmarried or reported no close confidants. In one clinical trial, men who had an MI, were socially isolated, and had high life stress had a fourfold risk of mortality. In elderly men who had an MI, the most powerful predictor of reduced survival after the MI was lack of sufficient emotional support before their heart attack. Social isolation and low social support are also important determinants of recurrent events and poor quality of life following an initial diagnosis of CAD.

Social resources are thought to affect physical recovery in patients with MI through several mechanisms. Patients who have social support may be more adherent to medical therapy and may make positive changes in their health behaviors. In addition, supportive interactions may reduce the potentially damaging effects of negative emotional states on neuroendocrine and physiological regulatory mechanisms. For example, research shows that social support can moderate an individual's blood pressure responses to acute mental stress.

### *Research Opportunities*

Socioeconomic status is defined broadly as a set of characteristics that includes differences in learning experiences and opportunities, as well as exposure to different environmental demands. The mechanisms responsible for the relationship between socioeconomic status and CVD and other diseases are not understood. Even as mortality rates have declined in the United States for all causes and for CVD, recent studies show that the disparities in death rates by socioeconomic status are increasing. In addition, high variability of income in specific geographic areas (e.g., states, census tracts, countries) is associated with higher mortality rates in these areas.

The widening disparity in income and health in the United States presents a unique opportunity for investigating the mechanisms that account for the effects of socioeconomic status on health. The socioeconomic status differential cannot be eliminated, but a better understanding of the behavioral and psychosocial mechanisms that account for the differences can provide a foundation for developing interventions to improve health and prevent disease among all socioeconomic strata.

Ethnicity is also a marker for a diverse set of cultural and learning experiences, exposure to different environments, and genetic characteristics. Ethnicity correlates with socioeconomic status, but we do not understand to what extent the effects of ethnicity on health are due to differences in socioeconomic status. Because minority groups, compared with whites, are disproportionately gaining in population in the United States, additional epidemiological data are needed to understand the health-promoting and health-damaging behaviors of different ethnic groups, the cultural meaning of these behaviors, and the extent to which socioeconomic status differences accounts for the effects of ethnicity.

Researchers have examined the independent effects of psychosocial variables, an approach that has been driven by epidemiological standards for establishing causation which include determining consistency of effect in all populations. In general, researchers have not examined the *interactive* effects of environmental and vulnerability (diathesis) factors in the development of disease. For example, they have not analyzed widely the synergistic effects of stressful life events and lack of social resources on CVD risk, even though such relationships are predicted. Research on the

development of mental health disorders suggests that vulnerability factors may enhance the effects of stress on the risk of disease in some cases.

Many of the relationships between psychosocial factors and the natural history of CVD have been stronger in men than in women. The reasons for this difference are not clear. They may include the following: (a) researchers' use of measures of psychosocial factors that are more valid for men than for women (i.e., existing assessment instruments are insensitive when applied to women); (b) delayed development of clinical disease in women, resulting in more age-related, comorbid conditions among women which may "mask" psychosocial effects; (c) infrequent CVD events among women during mid-life, resulting in studies that are statistically inadequate; and (d) the existence of different factors that are important for women. Future studies should include sufficient numbers of women so that researchers can adequately analyze the psychosocial factors that are important to the initiation and progression of CVD in women.

The concept of psychological stress may be measured most appropriately as a multidimensional construct. Researchers make theoretical distinctions between acute and chronic stress; sources of stress (e.g., family, work); accumulation of different types of stress; and self-reports of stress based on single vs. multiple time points. The usefulness of these distinctions has been examined for understanding mental, but not physical, health. Psychological stress must be defined and measured in sufficient detail, and the relation of different aspects of stress to disease processes must be investigated.

Most epidemiological investigators use measures of social isolation as proxies for measures of social resources. Research on mental health suggests that measures of perceived social support, which include the type and quality of social relationships, may be important correlates of psychological well-being. Identifying the specific aspects of social resources that protect against cardiovascular and pulmonary conditions, such as the quality of social relationships, also may be important. The possible protective mechanisms offered by social resources include direct provision of aid, services, or tangible assistance; ready access to medical care; promotion of positive health behaviors; enhanced coping with stress; and, possibly, beneficial autonomic or neuroendocrine influences (e.g., reduced physiological responses to stressful stimuli).

In epidemiological studies to identify the risk factors for cardiovascular, lung, and blood conditions, clinical disease has been the outcome variable of interest, while earlier, preclinical manifestations of disease in asymptomatic individuals have been ignored. Studying clinical disease has required the use of long follow-up periods because atherosclerosis, hypertension, and other chronic diseases have a prolonged developmental course. If preclinical manifestations of disease could be studied, shorter follow-up periods would be required.

Fortunately, sensitive, noninvasive measurements of atherosclerosis can now be accomplished using ultrasound techniques. These techniques enable researchers to study the prevalence and progression of disease in clinically asymptomatic individuals. Ultrasound scanning is used to detect markers of atherosclerosis in carotid arteries. The measurements have been shown to be reliable and to be correlated with CAD and an individual's risk for clinical events. Other indicators of preclinical disease are also available.

Preliminary studies suggest that environmental and behavioral factors, such as low socioeconomic status, hostility, and hopelessness, are associated with the progression of atherosclerotic disease in carotid arteries. These studies indicate that ultrasound measurements of atherosclerosis can be applied broadly to elucidate the associations between psychosocial risk factors, modifications of these risk factors, and CVD.

### *Recommendations*

Recommendations for behavioral research on the association of psychosocial and other environmental variables with heart, lung, and blood diseases are:

1. Incorporate into existing and planned observational studies the means to measure and evaluate psychosocial mechanisms for the influence of socioeconomic status and ethnicity on initiation and progression of diseases in men and women.

2. Analyze relevant, existing epidemiological data sets for expected interactive relationships between biological risk factors and psychosocial characteristics, and between environmental and vulnerability factors in terms of their effect on disease outcomes.

3. Refine the methods for measuring environmental characteristics of diverse cultural groups and of women in natural history and clinical studies, and test gender differences in the social environment's effect on disease risk.

4. Apply recent theoretical distinctions in the assessment of stress and social resources in clinical studies of heart, lung, and blood diseases to determine the aspects of stress and social resources that may be candidates for secondary prevention.

5. Enhance existing and planned observational studies that use noninvasive indicators of early disease by adding the means to measure and evaluate psychosocial characteristics of the environment, including stress and social resources, in relation to the natural history of preclinical disease.

## Behavior-Disease Processes

During the past decade, behavioral scientists have not only documented associations between behavioral factors and heart, lung, and blood diseases, but also explored physiological mechanisms that link behavioral processes to disease. Research on physiological mechanisms has typically distinguished between long-term pathogenic processes, such as those that underlie individuals' vulnerability to CHD, essential hypertension, and some chronic lung diseases (conditions that develop over decades), and short-term, acute events that comprise the symptomatic expressions of underlying health conditions (e.g., episodic airway obstruction in asthmatic patients, sudden death and MI in persons with CVD).

In this section, the Task Force addresses the influence of lifestyle behaviors, psychosocial stress, and sleep disorders on both short- and long-term pathological processes associated with cardiovascular and pulmonary diseases. These relationships are explored under six topic areas: atherosclerosis, acute cardiac events (i.e., myocardial ischemia, thrombosis, MI, cardiac arrhythmias, and sudden death), hypertension, insulin and glucose metabolism, lung diseases, and sleep disorders. Also considered are behavioral factors that modulate the clinical manifestations of disease, such as the perception of symptoms, pain sensitivity, and circadian variations in symptom expression.

### Atherosclerosis

Atherosclerosis is a pathological process of the large muscular and elastic arteries of the body, in which the intima, or inner layer of the artery wall, is thickened by an accumulation of cholesterol and other lipids, the influx and proliferaction of cells, and the growth of fibrous connective tissue. When occurring in the coronary arteries, which supply blood to the heart itself, atherosclerosis is a primary cause of symptomatic CHD. As noted previously, psychosocial factors may increase risk for coronary disease by influencing the development of atherosclerosis.

Clinical studies demonstrate that persons with behavioral attributes that are thought to predispose to symptomatic coronary disease, such as easily evoked anger or hostility, also exhibit greater coronary artery atherosclerosis when referred for diagnostic angiography than do individuals without these characteristics. Because atherosclerosis develops over a long period of time and because experimental studies are needed to document causal associations, most behavioral research on atherogenesis has been conducted using animal models, such as birds, rodents, and nonhuman primates. Mice raised in socially deprived environments, for example, develop thickening of the coronary arteries and aorta when interacting with animals reared under normal social conditions.

Nonhuman primates provide a closer model of coronary artery atherosclerosis in humans than do other animals, particularly with respect to the characteristics of lesions. Not only do many species of monkeys develop atherosclerosis readily when fed cholesterol-containing diets, but monkeys also exhibit complex social behaviors. Many of these behaviors are analogous to attributes that figure prominently among psychosocial antecedents of coronary disease in humans, such as competitiveness, aggression, and social status.

Recent experiments among male and female cynomolgus monkeys have greatly advanced understanding of the effect of certain behaviors on atherosclerosis. When these monkeys are housed in small social groups, periodically redistributing animals to new groups requires that they reestablish dominance hierarchies ("pecking orders") and affiliative relationships. Under these conditions, high-status males (dominant monkeys) develop more extensive coronary atherosclerosis than do males of lower social rank, termed "subordinates." Because a similar result is not obtained among dominant animals that are housed in groups of fixed or stable membership, these results suggest that the behavioral demands of retaining predominance in an unstable, or stressful, social environment promote atherosclerosis.

In addition, the heightened susceptibility to atherosclerosis seen among socially dominant, stressed animals results from activation of one of the body's principal neuroendocrine axes, the sympathetic–adrenal medullary system. Administering a sympathetic antagonist (beta-blocker) to stressed animals, for example, prevents the worsening of atherosclerosis otherwise seen among socially dominant monkeys.

Among female monkeys, social behavior is as strongly related to atherosclerosis as in males, although differently. Among the females, subordinate, rather than dominant, social status accelerates atherogenesis. This effect appears to result from the disruption of menstrual cycles that is typically induced by social subordination. In turn, loss of ovarian function, whether it is partial, as induced by behavior, or complete, by removal of the ovaries, deprives females of their relative protection against atherosclerosis. Conversely, administration of oral contraceptives retards the development of atherosclerosis, and does so preferentially among socially subordinate animals (see figure 7).

These findings suggest that ovarian deficiency in premenopausal women, which can also stem in part from emotional distress, increases risk for atherosclerosis, and that use of oral contraceptives may inhibit atherogenesis. Of additional interest, psychosocial stress also can accelerate the age at menopause among women entering the perimenopausal transition. Overweight premenopausal women also tend to have anovulatory cycles and infertility problems, which can be relieved by losing weight. However, after menopause, overweight women tend to have higher circulating estrogen levels because of the secondary conversion of androstenedione in fat tissues. Another factor—cigarette smoking—also affects women's risk of CVD by suppressing estrogen production and enhancing estrogen metabolism.

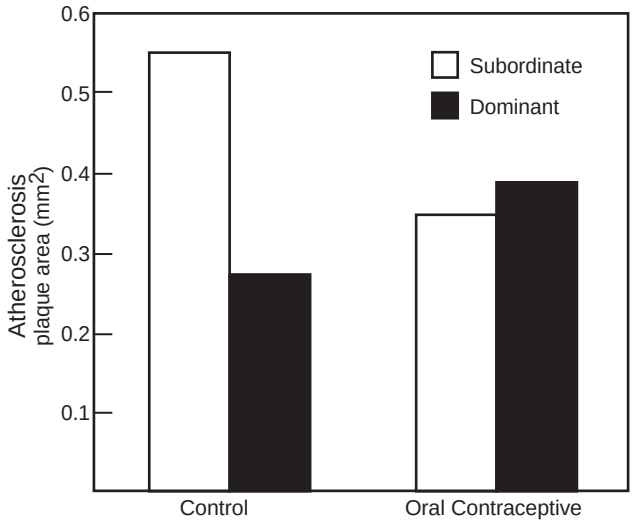


**Figure 7.** Iliac artery atherosclerosis among socially dominant and subordinate female cynomolgus monkeys either untreated (control) or treated with an oral contraceptive. Adapted with permission from Kaplan JR, Adams MR, Anthony MS, Morgan TM, Manuck SB, and Clarkson TB: Dominant social status and contraceptive hormone treatment inhibit atherogenesis in premenopausal monkeys. Arterioscler Thromb Vasc Biol 1995;15(12):2094-2100.

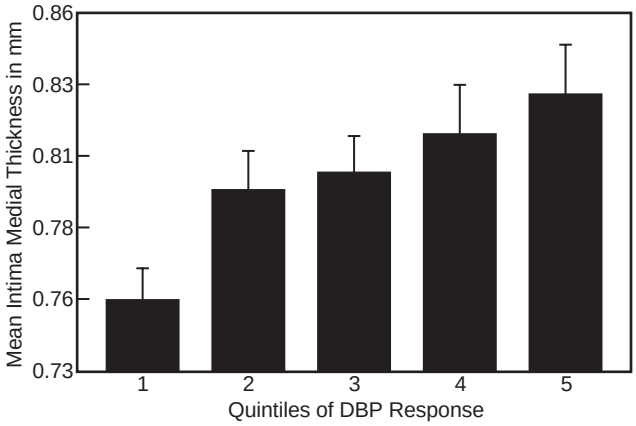


**Figure 8.** Association between diastolic blood pressure reactivity to mental stress and intimal medial thickness (measure of carotid artery atherosclerosis) among 46-52 year-old men from Eastern Finland. Adapted and reprinted with permission from Kamarck TW, Everson SA, Kaplan GA, Manuck SB, Jennings JR, Salonen R, and Salonen JT: Exaggerated blood pressure responses during mental stress are associated with enhanced carotid atherosclerosis in middle-aged Finnish men: Findings from the Kuopio Ischemic Heart Disease Study. Circulation 1997;96(11): 3842-3848.

Like humans, cynomolgus monkeys differ in the magnitude of their cardiac reactions to behavioral stimuli. For example, when fed a high-cholesterol diet, animals that exhibit the largest heart rate responses to stress also develop the most extensive atherosclerosis. This association between heart rate reactivity and atherosclerosis is observed in both male and female monkeys and in both pre- and postmenopausal (ovariectomized) females. The results of recent studies suggest that a similar relationship occurs in humans. For example, individuals with an exaggerated cardiovascular reactivity to laboratory stressors have been found to show accelerated thickening in the carotid arteries, a measure of atherosclerosis (see previous sections on Reactions to Acute Psychological Stress and Social Resources). In a recent epidemiological study of Finnish men, the Kuopio Ischemic Heart Disease Study, this association was strongest among persons under 55 years of age (see figure 8).

## *Research Opportunities*

Studies of nonhuman primates have established a valid animal model for investigating the behavioral antecedents of CAD and have elucidated some of the neuroendocrine mechanisms for behavior's potentiation of atherosclerosis. The same model can now be used to address more detailed aspects of the pathophysiology and mechanisms of atherosclerosis, such as the determinants of early alterations in the function of endothelial cells that line artery walls and the proliferation of cells within the intima of the artery.

As described above, ovarian dysfunction resulting from social subordination promotes the development of atherosclerosis in female monkeys. Although studies have identified behavioral correlates of estrogen deficiency in women, individual differences in ovarian function have rarely been examined in relation to risk of CHD in humans and have not been studied in conjunction with psychosocial parameters. These relationships

should be evaluated among women in epidemiological and clinical studies.

The clinical implications of the results of behavioral studies of atherosclerosis in primates need to be explored. As noted, primate studies show that certain pharmacological interventions inhibit atherogenesis selectively among animals behaviorally predisposed to atherosclerosis. The clinical implications for humans can be addressed by incorporating relevant psychosocial measures into clinical trials designed to evaluate the effects of such interventions.

Alternative animal models of behavioral influences on atherogenesis need to be developed. Primate studies have been very valuable, but may be impractical for studying complex questions concerning gene–environment interactions or molecular and cellular events during the development of early lesions. Primates also are often unsuitable for experimental designs that require large numbers of animals.

The development of convenient rodent models was hampered previously by the resistance of most rodent species to the development of atherosclerosis similar in the characteristics and anatomical distribution of lesions to that in humans. Application of recently developed genetic techniques, such as transgenic and "knockout" mouse strains, makes new models of atherosclerosis possible, principally by genetically altering the factors that affect the metabolism of lipids. Like humans, these mouse strains respond to dietary lipids, develop lesions at analogous artery sites, and show progression from fatty streaks to fibrous plaques. These models should be exploited to evaluate the mechanisms by which behavioral factors promote atherogenesis, particularly as expressed against a defined genetic background.

### *Recommendations*

Recommendations for research on behavioral factors and atherosclerosis are:

1. Determine the effects of behavior on basic processes of atherogenesis, such as endothelial injury, cell proliferation, and plaque formation and rupture.
2. Establish whether ovarian dysfunctions such as chronic menstrual irregularity, functional amenorrhea, and their psychological correlates predict atherosclerotic disease in women.
3. Determine whether beta-receptor antagonists and oral contraceptives (in women) retard the progression of atherosclerosis in persons who are putatively at risk for CHD because of their behavioral attributes or social environment.
4. Study the modulation of genetic susceptibility to atherosclerosis by behavioral processes (i.e., gene–environment interactions), utilizing atherosclerosis-susceptible mouse strains created by the application of new genetic technologies.

## Acute Cardiac Events: Myocardial Ischemia, Infarction, and Sudden Death

Coronary artery disease develops without symptoms over many years, and the clinical manifestations of CAD occur relatively late during the course of disease. Despite CAD's lengthy course, however, about one-half of the cases involving death will occur in individuals who have no preexisting symptoms. Other important acute events are myocardial ischemia and malignant arrhythmias.

In CAD, long-term pathogenic processes include the development of coronary atherosclerosis and, possibly, chronic challenges to the integrity of arterial cells. Acute processes include myocardial ischemia, rupture of atherosclerotic plaque, formation of thrombi, and development of arrhythmias.

Different psychosocial parameters may influence early and later (or chronic and acute) processes in

the natural history of CAD. Acutely stressful events may precipitate cardiac ischemia or arrhythmia, whereas enduring features of the psychosocial environment or personality, such as low socioeconomic status, persistent stress, and hostile temperament, may be more likely to affect long-term progression of disease. In addition, common factors mediated by the same or different physiological mechanisms could be relevant to both the development of lesions and the acute clinical manifestations of disease.

Although widely debated for many years, there is now increasing evidence for acute and chronic stress as risk factors for myocardial ischemia, MI, malignant arrhythmias, and sudden death. This evidence has been provided by animal research, epidemiological research, and clinical studies.

The significance of behavioral triggers of acute cardiovascular events is supported by recent studies demonstrating the importance of vulnerable plaque for the onset of acute MI. Evidence suggests that acute events involving plaque rupture frequently are triggered in susceptible patients by physical and mental stress. In other studies, investigators have used a variety of current techniques for assessing cardiac function in the laboratory and field to demonstrate convincingly the pathophysiological mechanisms and effects of emotional and behavioral stress as triggers of myocardial ischemia.

The physiological pathways linking stress and myocardial ischemia, MI, and sudden death are mediated by the central nervous system (i.e., brain and spinal cord) and the autonomic nervous system (i.e., sympathetic and parasympathetic nervous systems). Figure 9 depicts the "cascade" of physiological responses to stress that may trigger acute events in susceptible individuals. These responses include increased heart rate, increased catecholamine and blood pressure levels, and changes in factors relating to hemostasis and thrombosis.

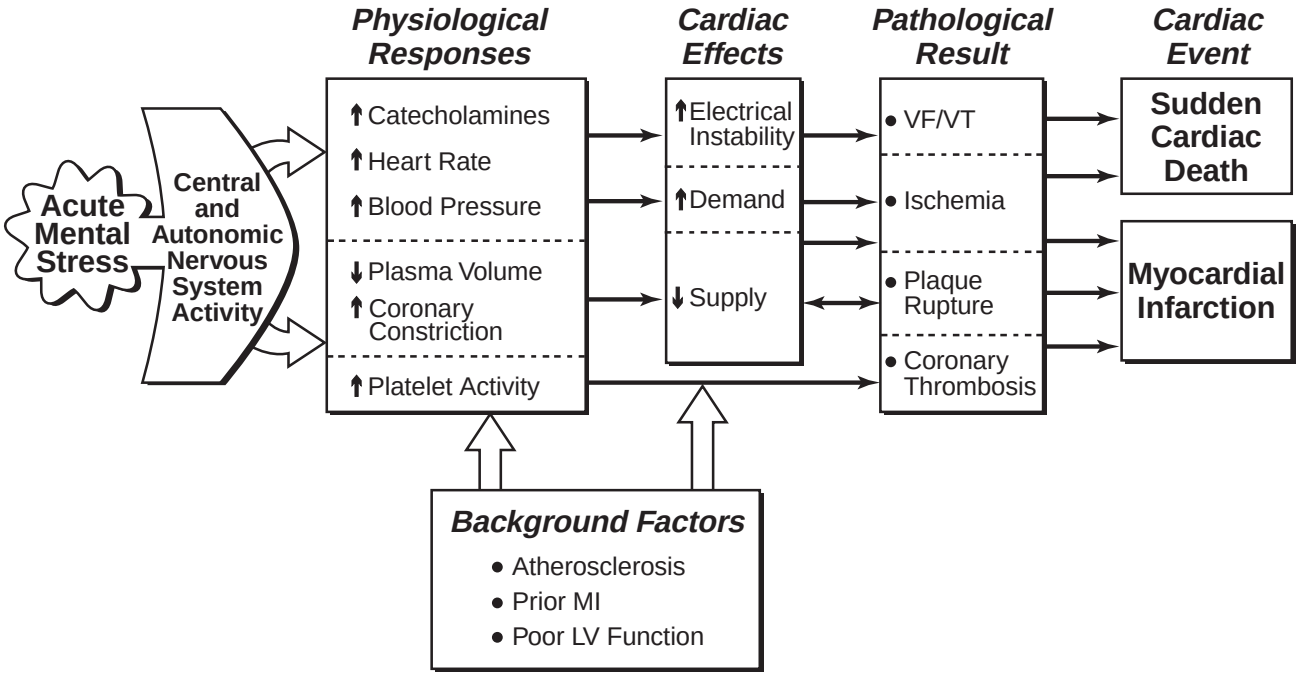


**Figure 9.** Pathophysiologic model of the actions of acute stress as a trigger of myocardial infarction and sudden death in vulnerable individuals. LV = left ventricular; VF/VT = ventricular fibrillation/tachycardia; MI = myocardial infarction. Adapted and reprinted with permission from Krantz DS, Kop WJ, Santiago HT, and Gottdiener JS: Mental stress as a trigger of myocardial ischemia and infarction. Cardiol Clin 1996;14(2):217-287.

The effects of psychosocial factors, and particularly stress, are described below for five acute cardiac events: sudden cardiac death and arrhythmias, MI, thrombosis, myocardial ischemia, and angina. The link between these events and circadian rhythms is also considered.

## *Sudden Cardiac Death and Arrhythmias*

Approximately 1.5 million heart attacks occur each year in the United Status, and about one-sixth of these (approximately 250,000) culminate in sudden death (i.e., death occurring within 1 hour of symptoms) and can be attributed to a malignant arrhythmia—most frequently, ventricular fibrillation. Most victims of sudden death have significant atherosclerosis, and a previous MI is identified in up to three-fourths of those who die suddenly.

Emotional stress is thought to precipitate sudden cardiac death by stimulating central nervous system pathways that affect cardiovascular functioning, possibly those that involve the neurotransmitter serotonin. When the heart becomes vulnerable because of atherosclerotic disease, some of the responses to stress may result in constriction, or vasospasm, of the coronary arteries or plaque rupture in the coronary vessels.

In recent years, researchers have made considerable progress in defining the mechanisms of behavioral influences on the central nervous system that result in instability of the heart and life-threatening arrhythmias. Investigators have developed experimental procedures to examine acute cardiovascular effects of intense emotional states, and they have applied sophisticated neuroanatomical techniques to map brain sites that mediate emotional influences on the heart. This research indicates that anger is the emotional state most commonly associated with ischemia and life-threatening arrhythmias. Ischemia following stress, which is known as “post-stress ischemia,” can develop within 2 to 3 minutes of intense arousal and has been shown clinically to follow exercise as well as anger elicitation.

Evidence for the role of the sympathetic nervous system in life-threatening arrhythmias is extensive. Activation of this system by stimulation of central and peripheral adrenergic structures, infusion of catecholamines, or imposition of behavioral stress can increase the vulnerability of the normal as well as the ischemic heart to arrhythmias. Administration of beta-adrenergic blockers substantially reduces this vulnerability.

Substantial evidence also indicates that enhanced parasympathetic activity exerts an antifibrillatory effect on the heart. Activation of the vagus nerve appears to protect by several mechanisms: inhibiting release of norepinephrine from adrenergic nerve endings, interfering with cellular signaling processes, and reducing the heart rate and attendant metabolic demands on the heart.

During the past decade, heart rate variability has emerged as a highly promising index for assessing the functioning of the autonomic nervous system. High-frequency heart rate variability is thought to represent the parasympathetic component of the autonomic nervous system, whereas low-frequency variability is thought to reflect interaction between the sympathetic and parasympathetic nervous systems. This index has been useful for stratifying patients’ risk after an MI. Among patients who have had an MI, those who have a diminished heart rate variability are at increased risk of death.

Heart rate variability is also sensitive to physiological and pharmacological interventions. For example, health-promoting behavioral influences such as exercise conditioning result in an autonomic pattern that enhances parasympathetic activity, reduces sympathetic activity, increases heart rate variability, and reduces individuals' susceptibility to arrhythmias.

The hypothalamus, which receives commands from the amygdala and the prefrontal cortex, is the

primary site for the central nervous system's control of the autonomic nervous system. Researchers have long known that stimulation of the hypothalamus induces a variety of emotional states, including defense reactions, and increases the incidence of ventricular arrhythmias resulting from a discharge in the sympathetic nervous system. Hypothalamic activity is thought to mediate the effects of behavioral stress on arrhythmias induced by the autonomic nervous system. Interference with the function of other brain areas such as the amygdala, the output of the thalamus from the frontal cortex to the brainstem, has been shown to delay or prevent ventricular fibrillation in stressed animals.

The triggering of arrhythmias by central nervous system activity may depend on several intermediary mechanisms. These include direct effects of neurotransmitters on the myocardium and its specialized conduction system, and changes in myocardial perfusion resulting from alterations in coronary vasomotor tone and/or enhanced platelet aggregability (see figure 9). The net influence of these effects on the heart depends on a complex interplay between the specific neural pattern elicited and the presence of cardiac pathology.

## *Myocardial Infarction*

As noted previously, epidemiological data suggest that psychosocial stress can trigger acute MI in individuals with preexisting CAD (see the section on Psychosocial and Other Environmental Variables). In addition, physiological outcomes after an MI are worsened significantly in the presence of psychological risk factors, such as clinical depression or distress, as well as social risk factors (e.g., social isolation). Patients who have had an MI and who have a combination of these physiological and behavioral variables have a poor prognosis.

## *Thrombosis*

Recent laboratory research on the physiology of stress in humans suggests that acute stress can affect processes related to the formation and dissolution of blood clots (thrombosis and hemostasis). These processes are key physiological antecedents of MI and other acute coronary events. Activation and inhibition of blood platelets are central features of arterial thrombosis. Epinephrine, and possibly shear stress, stimulate platelet activity. Acute psychological stress increases epinephrine levels, blood pressure levels, and heart rate and, temporarily, can decrease plasma volume and increase blood viscosity.

Platelet reactivity during psychological stress may be an important mechanism in coronary events. Indeed, available data show that patients experiencing an MI or stable and unstable angina have elevated levels of substances associated with increased clotting (beta-thromboglobulin and platelet factor-4). Preliminary data also indicate that psychological stress increases platelet activity in patients with stable CHD, though not more than in healthy volunteers.

## *Myocardial Ischemia*

Research on myocardial ischemia, the inadequate blood flow to cardiac tissue, has furthered understanding of the ways that mental stress triggers clinical events. This topic has emerged as an important area of investigation with clinical implications. Electrocardiographic monitoring of patients with CAD has revealed that mental stress during daily life triggers transient myocardial ischemia with a potency comparable to that of strenuous physical exercise. Using sensitive measures of cardiac contractile function, investigators have also shown that acute psychological stress provokes myocardial ischemia in about

one-half of patients with CAD. This ischemia, which primarily appears among patients who have exercise-inducible ischemia, is most frequently silent, or asymptomatic. It also typically occurs at lower heart rates than exercise-inducible ischemia in the same patient, but at comparable blood pressure levels.

These characteristics suggest that factors associated with decreased blood supply to the heart during stress may be involved in the pathophysiology of this ischemia. This suggestion is supported by recent observations that acute mental stress can cause constriction of diseased epicardial coronary arteries (see figure 10) and failure of the resistance vessels of the heart to dilate normally. Impairment of the integrity of the endothelium, or inner lining, of arteries may be responsible for these effects. Endothelial integrity is important for normal vasomotor functioning, and is often impaired in atherosclerotic arteries.

Complementary research on cynomolgus monkeys demonstrates that chronic social stress also impairs vasomotion of coronary arteries when moderate or extensive atherosclerosis is present.

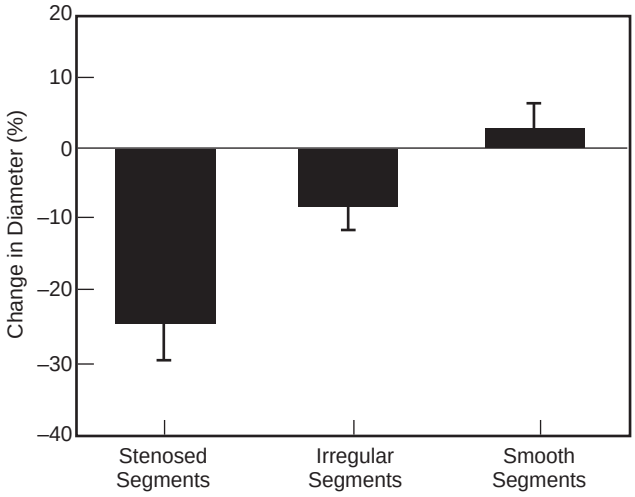


**Figure 10.** Effect of acute mental stress on diameter of stenosed, irregular, and smooth epicardial coronary artery segments in patients with coronary artery disease. Reprinted with permission from Yeung AC, Vekshtein VI, Krantz DS, Vita JA, Ryan TJ, Ganz P, and Swelwyn AP: The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. N Engl J Med 1991;325(22):1551-1556.

This impairment is shown by a paradoxical constriction of arteries in stressed monkeys infused with the vasoactive substance acetylcholine. The effects of chronic stress on vascular function in these animals is mediated by a mechanism involving nitric oxide.

Researchers have shown that patients who exhibit myocardial ischemia during acute mental stress also are likely to have more frequent episodes of ischemia during the stresses of daily life. CAD patients who display mental stress ischemia may also be at risk of poorer physiological outcomes. For example, in one recent study of patients with CAD and a history of ischemia on previous exercise stress tests, the presence of ischemia evoked by mental stress testing predicted cardiac prognosis over 3 years.

## *Anginal pain*

Anginal pain, the classic symptom of CAD described by Heberden in 1772, is the reason many CHD patients first seek medical attention. Although anginal pain is a marker for myocardial ischemia, evidence increasingly indicates that episodes of ischemia do not always result in pain, but may more often be painless or "silent." One-third of MIs also occur silently, without symptoms.

Both biological and behavioral factors contribute to the presence of anginal pain with myocardial ischemia. Indeed, the research literature documents extensively the importance of behavioral and psychological factors in the perception of pain. Perception of anginal pain has been related to the pattern or intensity of discharge of pain-related afferent fibers in the heart and to greater beta-endorphin responses to exercise and to mental stress. Patients with psychological traits such as anxiety and depression appear to perceive and report more anginal pain. In addition, depression appears to be related to an earlier onset of anginal pain and to a decreased response of beta-endorphins to treadmill exercise.

Some patients have both painful and silent episodes of ischemia during daily life. The reason why these different types of episodes occur in the same patient is not clear. However, researchers know that exercise is more likely to trigger symptomatic (painful) episodes of ischemia, whereas mental stress is more likely to trigger silent episodes.

## *Circadian Rhythms and Behavior*

Myocardial ischemia, MI, and sudden cardiac death occur more often in the morning and are linked to daytime neural, endocrine, and behavioral patterns. These facts are well established. Research also indicates that physical and mental activities play a role in this circadian rhythm.

For CHD patients, daily activities associated with awakening, such as changes in posture and activity level, are thought to be causally related to the increased rate of myocardial ischemia, MI, and sudden cardiac death during the morning and to the mechanisms responsible for this increase (e.g., increases in circulating catecholamines, increased platelet aggregation). During daily life, the occurrence of ischemia has been shown to increase markedly in the morning at the same time that morning activities begin. Increases in blood pressure levels, heart rate, and arterial tone in relation to psychological and physical activity may also initiate disruption of atherosclerotic plaques and result in thrombosis.

Studies of the circadian rhythm of cardiac events have resulted in new prevention and treatment measures, such as beta-adrenergic blockade, which have significantly reduced the incidence of MI in CHD patients during the morning hours. Beta-adrenergic blockers may block the consequences of increased activity in the sympathetic nervous system that occurs during morning activities.

## *Research Opportunities*

Patients who are predisposed to clinical events because of preexisting atherosclerosis, endothelial dysfunction in the coronary arteries, prior MI, and/or poor LV function are susceptible to a number of intermediate pathophysiological processes that may increase their vulnerability to myocardial ischemia, malignant ventricular arrhythmias, coronary thrombosis, or plaque rupture. However, the influence of psychosocial factors and their neuroendocrine and hemodynamic effects on fundamental processes in artery walls has yet to be elucidated.

Additional research is needed in animals and humans to identify (a) the central nervous system structures and neurochemical pathways involved in triggering MI and sudden cardiac death in response to behavioral stress and (b) the influence of vasospasm of the coronary arteries and disruption of plaque in these arteries when cardiovascular events occur in response to behavioral stress. Nonhuman primates and other animal models can be used to study the acute effects of behavior on the biology of artery walls (e.g., impairment of vasomotor function due to endothelial injury, creation or rupture of vulnerable plaque, and formation of thrombi).

By applying available new techniques and methods to behavioral studies of CVD, many of the physiological processes that link behavior to cardiac events and endothelial function can be studied. These new techniques and methods include, but are not limited to, the following:

- Brain imaging, which can be combined with behavioral tests to explore brain mechanisms responsible for cardiac arrhythmias.

- Noninvasive methods for assessing autonomic functioning (e.g., heart rate variability) and for

measuring electrophysiological parameters (e.g., T-wave alternans) of cardiac electrical instability. These methods can be used to identify the most informative electrophysiological variables for tracking the prognostic effects of behavioral stress on ischemia-induced cardiac arrhythmias.

- Behavioral assessment paradigms for monitoring patients in the clinic and in ambulatory conditions. These paradigms can be used to study the influence of mental stress on cardiac ischemia and on markers of vulnerability to malignant arrhythmias and to examine the influence of biological and behavioral factors on individuals' perception of anginal pain.

- Biochemical measures, which can be used to study the effects of acute and chronic stress on hemostasis and thrombosis in animal models and humans.

By applying these techniques in studies of patients who are vulnerable to clinical cardiac events, important information can be gained regarding the frequency and potency of potential behavioral triggers of these events. Studies of patients who are at high risk of sudden cardiac death and who have implantable cardiac defibrillators would be especially informative. It is also important to study potential behavioral triggers in patients with vulnerable plaque and/or other risk factors for MI and ischemia.

Another research opportunity derives from applying the new techniques and methods described above to studying the relationship between psychosocial factors and CVD. Researchers should investigate the mechanisms that link psychosocial traits and circumstances with morbidity and mortality from CAD. The critical features of successful psychosocial interventions also could be studied using these methods.

New evidence linking neurochemical changes in the central nervous system to emotion and new advances in brain imaging also may provide a basis for exploring the relationships among emotions, central nervous system processes, and cardiac vulnerability. These investigations would be useful for clarifying the influence of emotional states such as anger and anxiety on ischemia, arrhythmia, and sudden cardiac death.

### *Recommendations*

Recommendations for research on the association of behavioral factors with acute cardiac events are:

1. Determine the hemodynamic, neuroendocrine, hemostatic, and neural mechanisms for the triggering effect of stress and other behavioral and psychosocial factors on acute cardiac events, including MI, coronary thrombosis, myocardial ischemia, ventricular fibrillation, and sudden cardiac death, in susceptible individuals.

2. Encourage the application of new and currently used technologies in cardiology, molecular biology, and the behavioral sciences in research on behavioral influences that trigger acute cardiac events. Using these technologies, identify the psychological and pathophysiological characteristics of individuals who are predisposed to and at greatest risk of acute, behaviorally triggered events (e.g., patients who have vulnerable plaque, documented myocardial ischemia, and/or malignant cardiac arrhythmias).

3. Investigate the physiological and behavioral mechanisms that link psychological traits and psychosocial environmental circumstances with morbidity and mortality from CAD.

4. Use advances in brain imaging and other methods for studying the functioning of the central and autonomic nervous systems to

examine the relationships between central nervous system processes, emotions, and cardiac vulnerability and the onset and course of MI, ischemia, and malignant arrhythmias.

## Hypertension and Left Ventricular Hypertrophy

Hypertension—a major risk factor for CHD and stroke—affects 50 million Americans. It is a multifactorial disease having both genetic and environmental antecedents. Studies of twins suggest that genetic factors account for up to 50 percent of the variation in blood pressure among individuals; thus, at least 50 percent of such variation must also be environmental in origin, or reflect the influence of gene–environment interactions.

The major environmental variables contributing to hypertension are presumed to be dietary factors, physical inactivity, and psychosocial stress. Epidemiological studies indicate that body weight is one of the most important determinants of hypertension. These studies also indicate that alcohol intake is related more consistently to blood pressure levels than is salt intake. The variable relationship between salt intake and blood pressure levels may be attributable to individual differences in salt sensitivity.

Dietary and psychosocial factors often occur together. For example, individuals who live in a poor, urban, high-crime neighborhood are also likely to eat a high-salt, low-potassium, and high-fat diet. This combination of factors may be one reason for the observation that hypertension is common among individuals of lower socioeconomic status and blacks, and that migration from a traditional, rural society to an industrialized, urban society is associated with increases in blood pressure.

Behavioral factors may contribute to the development and persistence of two phenomena related to elevated blood pressure: sustained hypertension and "white-coat" hypertension. Individuals with sustained hypertension have elevated blood pressure levels throughout the day or in the workplace. Individuals with white-coat hypertension have elevated blood pressure levels when they are tested in a doctor's office or clinic, but normal blood pressure levels at other times. Whether persons with white-coat hypertension should be considered "true" hypertensives is not clear. Current understanding of the behavioral aspects of these different types of hypertension is described below.

### *Sustained Hypertension*

Studies of animals consistently show that the areas of the brain that are involved in emotional, aggressive, and sexual behaviors also influence blood pressure levels. Chronic electrical stimulation of these brain regions (which are linked to hyperactivity of the sympathetic nervous system) can provoke sustained hypertension. Hypertension also results when animals, especially strains that are genetically susceptible to hypertension, are continually exposed to aversive stimuli.

The behavioral effects demonstrated in these studies can be moderated by changes in the environment. For example, the offspring of spontaneously hypertensive rats, a genetically susceptible strain, develop less hypertension when raised by normotensive mothers (WKY strain) than when raised by their natural mothers. By understanding the mechanisms of behaviorally induced hypertension in these animals, researchers may be able to gain clues to similar pathogenic processes in humans.

In humans, increased prevalence of hypertension is associated with individuals' long-term exposure to daily stressors such as residing in low-income and high-density neighborhoods or having high-demand and low-control jobs. The prevalence of hypertension in the United States is greater among blacks than among whites, and environmental

factors appear to be as important as genetic factors in explaining this difference. Blacks are often exposed to racism and, compared to whites, a greater proportion live in poorer, higher-crime neighborhoods, are of lower socioeconomic status, and have less education. All of these variables may possibly affect blood pressure levels.

Some mechanisms have already been revealed by behavioral research in both animals and humans. These include activity of the sympathetic nervous system, altered sodium retention in response to stress, activity of the HPA axis, vascular remodeling, and behavioral conditioning of the baroreflexes.

The sympathetic nervous system is a key component of sustained hypertension. Its involvement is confirmed by the fact that hypertension is delayed or prevented by removal of the sympathetic nerves, surgical isolation of the kidneys from their sympathetic nerves, or long-term treatment with sympathetic (adrenergic) antagonists. In addition, overactivity of the sympathetic nervous system during early stages of hypertension has been documented extensively in humans.

In addition to the direct effects of the sympathetic nervous system, high dietary salt intake may enhance the blood pressure-raising effects of exposure to stress in some animal models. In these studies, slower renal elimination of excess sodium and water during stress may be an important factor.

Studies in humans indicate that slow elimination of sodium in response to stress is also a factor for vulnerable individuals, particularly blacks and men who have a family history of hypertension or marginally elevated blood pressure levels. Compared with whites, blacks also have a greater propensity to respond to stress with peripheral vasoconstriction, a characteristic that may be relevant to hypertension (see the section on Individual Characteristics).

Other potential mechanisms of behaviorally induced hypertension include changes in the activity of the HPA axis that may occur after prolonged exposure to aversive stimuli, and thickening of the vessel wall (vascular remodeling), which may occur in response to frequent elevations in blood pressure levels. Researchers have shown that the HPA axis may have a role in hypertensive patients' blunted sensitivity to painful stimuli. One hypothesis is that reduced pain sensitivity is reinforcing and contributes to the development of hypertension, perhaps due to increased HPA and opioid activity.

Vascular remodeling has been shown to occur in animal models when cardiac output and blood pressure levels are increased because of enhanced activity of the sympathetic nervous system. Classical or Pavlovian conditioning of baroreflex function may also contribute to the development of hypertension.

Individuals' blood pressure responses to real life events can now be assessed by ambulatory, noninvasive, 24-hour monitoring. With this capability, researchers can more accurately determine an individual's "true," representative mean blood pressure, as well as short-term variations and diurnal patterns in the blood pressure levels. Patients can be classified according to whether they do or do not experience the normal nocturnal decline in blood pressure, and how this is related to hypertension.

Using 24-hour ambulatory monitoring, researchers have been able to demonstrate associations between long-term exposure to stress and high blood pressure—associations that are not apparent when measuring an individual's blood pressure only in a doctor's office or clinic. Ambulatory measurements thus help distinguish between patients with sustained hypertension and patients with white-coat hypertension.

## *White-Coat Hypertension*

White-coat hypertension occurs in about 20 percent of patients with mild hypertension. In most studies, patients with white-coat hypertension exhibit normal geometry and function of the heart, whereas patients with sustained hypertension exhibit increased LV mass. A recent study indicated that white-coat hypertension was not related to increased risk of morbidity or mortality from CVD, whereas sustained hypertension was associated with greater CVD morbidity. This study also demonstrated that hypertensive patients whose blood pressure did not drop at night (nondippers) had greater morbidity from CVD than those whose blood pressure did drop (dippers) (see figure 11); this association was particularly evident among women.

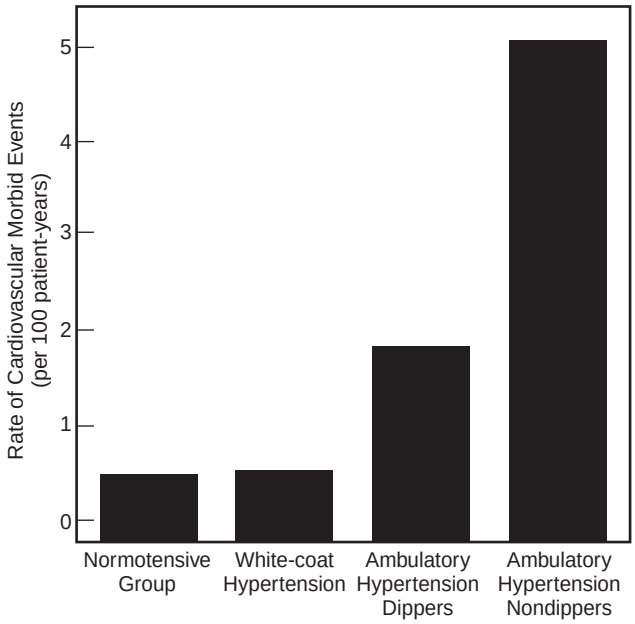


**Figure 11.** Incidence of major cardiovascular morbid events grouped according to four blood pressure categories. The difference between categories was significant ($p<.0001$). Reprinted with permission from Verdecchia P, Porcellati C, Schillaci G, Borgioni C, Cucci A, Battistelli M, Guerieri M, Gatteschi C, Zampi I, Santucci A, Santucci C, and Reboldi G: Ambulatory blood pressure: An independent predictor of prognosis in essential hypertension. Hypertension 1994;24(6):793-801.

The psychological or other factors that distinguish patients with white-coat hypertension from patients with sustained hypertension are not known. The reasons for the establishment of a pattern of responsiveness to blood pressure checkups in the clinic (white-coat hypertension) also are not known, but the tendency is not associated with a general enhancement of stress-related cardiovascular reactivity.

## *Left Ventricular Hypertrophy*

Increased LV mass and wall thickness are important intermediate predictors of CVD. The Framingham Heart Study and other investigations have indicated that, second only to age, these variables are the strongest predictors of risk for death from CVD.

Blood pressure level is one of the major determinants of LV mass. Other determinants may be equally significant. As with hypertension, intake of salt is related to LV mass, and the sympathetic nervous system and renin-angiotensin systems may contribute to increased LV mass. Measurements of LV geometry, including measurements of LV mass and wall thickness, have provided important information on the significance of behavioral factors for hypertension.

Recent studies demonstrate that job strain is associated with increased LV mass. In addition, the propensity to experience exaggerated blood pressure responses to stress may also be related to greater LV mass in black and white adolescents and adults. For the same level of clinically obtained blood pressure, blacks have a greater LV mass than whites.

### *Research Opportunities*

Ambulatory monitoring of blood pressure has already begun to prove its value as a superior method of assessing the daily load on an individual's cardiovascular system and as a stronger predictor of morbidity from CVD than traditional measurements of blood pressure obtained clinically. The ability to obtain accurate information about blood pressure levels at work, at home, and during sleep is valuable because this information can be used to document the relationship of behavioral events to blood pressure and the development of hypertension. Expanded behavioral assessments obtained concurrently with repeated measurements of blood pressure during ambulatory monitoring can provide additional important information on changes in work, home, and social factors that may affect individuals' blood pressure levels in their natural environments.

At the time of preparation of this report, none of the large-scale U.S. epidemiological studies has included ambulatory monitoring of all patients. By incorporating this capability into these studies, researchers would be able to obtain important information from large prospective databases that includes women and minorities. Studies such as Atherosclerosis Risk in Communities (ARIC) and Coronary Artery Risk Development in Young Adults (CARDIA) are examples of these types of studies.

Considerable evidence indicates that stress can cause acute elevations of blood pressure levels. Some research also indicates that exaggerated responses of blood pressure during stress may be associated with the development of hypertension. However, the ways that frequent transient increases in blood pressure, in response to repeated bouts of stress, lead to sustained increased blood pressure are poorly understood.

Prospective research in animal models and humans could illuminate the relationship of blood pressure and hemodynamic responses to repeated exposure to stress. Alterations in glycemic and neurohumoral function, potential mediators of these responses, deserve careful consideration. The effects of cardiovascular reactivity on both shorter-term (e.g., LV mass and geometry, intimal thickening of carotid arteries) and longer-term cardiovascular outcomes (e.g., hypertension and CHD) could be examined in these investigations.

In addition, echocardiographic assessments of LV structure and function should be incorporated into behavioral research on hypertension. Echocardiography can provide a good cross-sectional end point and an assessment of lowered or increased risk during relatively brief intervals. By using echocardiography, researchers can assess the influence of behavioral factors on the heart that may be independent of their effects on blood pressure levels.

Despite recent studies suggesting that the relative risk of white-coat hypertension is lower than that of sustained hypertension, additional clinical research is needed on white-coat hypertension. Measurement of blood pressure in the clinic will continue to be the principal basis for establishing treatment of hypertensive patients in cost-conscious medical practices. The possibility of developing a clinic-based test that combines measurement of blood pressure with information on a patient's medical history and psychological status should be explored as a way of screening for patients with probable white-coat hypertension. The combined clinic-based test could be used to identify patients who are most likely to have white-coat hypertension; they could then be verified, at reduced expense, by additional ambulatory monitoring.

Genetic linkage studies in animal models or humans may be useful in the near future for relating behavioral factors to risk for hypertension and CVD. As noted previously, human and animal research indicates that genetic factors are involved in processes (e.g., sodium sensitivity, reactivity of

the sympathetic nervous system) that likely play a role in the development of hypertension. Because of the many linkages suggested between behaviorally related hypertension and excessive activity of the sympathetic nervous system, combined genetic and environmental approaches that focus on autonomic and neuroendocrine markers appear especially promising.

### *Recommendations*

Recommendations for research on the association of behavioral factors with hypertension and LV hypertrophy are:

1. Evaluate the determinants of stability and change in blood pressure over time by incorporating repeated, ambulatory blood pressure monitoring, combined with behavioral assessments of stress and stress buffers, into existing and planned longitudinal or observational studies.
2. Clarify the physiological processes of the hypothetical transition from frequent, transient increases in blood pressure, arising from repeated exposure to stress, to sustained hypertension. As potentially contributory mechanisms, consider in particular mediation by the sympathetic nervous system, vascular remodeling, and slow elimination of sodium.
3. Use cross-sectional and prospective research designs to investigate further the relationship of behavioral factors (e.g., job strain or other long-term exposure to stress; psychological variables such as expressed hostility, anxiety, or depression; high blood pressure reactivity to stress) to increases in LV mass, as determined by echocardiography.
4. Study the behavioral origins of white-coat hypertension, and develop and validate a clinic-based screening test for identifying individuals with white-coat hypertension.
5. Encourage genetic studies in animal models or humans to identify the determinants of increased susceptibility to behaviorally induced hypertension.

## Insulin and Glucose Metabolism

Epidemiological studies have identified a constellation of risk factors for CHD that appear to be interrelated and constitute an insulin metabolic syndrome. These variables include central obesity, hypertension, glucose intolerance, dyslipidemia (lipid disorders such as hypertriglyceridemia, hyperapobetalipoproteinemia, and low HDL cholesterol), and atherosclerosis. While the occurrence of all these abnormalities in one individual is quite rare, persons who exhibit any one of these conditions are more likely to also exhibit other features of the syndrome.

Insulin sensitivity (responsiveness of metabolic pathways to insulin) and insulin resistance (impaired responsiveness and decreased effectiveness of insulin) are related both to behavioral variables and to CHD. Behaviors that increase insulin resistance (e.g., smoking, eating excessive calories, physical inactivity, psychosocial stress) also increase the risk factors for CHD that constitute the insulin metabolic syndrome. Conversely, behaviors that decrease CHD risk factors (e.g., weight loss, physical activity) generally increase insulin sensitivity.

*Biological pathways*. Although the biological pathways linking behavior with the various components of the insulin metabolic syndrome have not been fully elucidated, it is apparent that interactions involving insulin resistance, hyperinsulinemia (a persistently high insulin concentration in the blood), and activation of the sympathetic nervous system may be involved. With respect to interactions among the latter variables, for example, individuals who are insulin resistant but maintain normal glucose tolerance can compensate for their insulin resistance by

hypersecreting insulin. Similarly, investigators have shown that insulin causes a dose-related increase in norepinephrine level, which is in turn related to systolic blood pressure. The sympathetic nervous system may also influence the extraction of glucose in skeletal muscles, which is the site of insulin resistance in both noninsulin-dependent diabetes mellitus and hypertension, by inducing tonic vasoconstriction of the skeletal muscles.

*Behavioral effects.* The interrelationships among the components of the insulin metabolic syndrome may reflect, in part, a correlation among lifestyle variables. For example, less physically active individuals tend to be more obese than more physically active individuals. In addition, the interactive relationships among insulin resistance, hyperinsulinemia, and activation of the sympathetic nervous system may contribute to a clustering of risk factors that predispose individuals to CHD.

Evidence indicates that the tendency to develop insulin resistance is inherited. However, aspects of behavior, including lifestyle, do appear to play a major role in the expression of insulin resistance. Researchers have related insulin resistance and sensitivity to psychosocial stress, psychological traits, diet and obesity, physical activity, and smoking.

For example, preliminary data suggest that psychosocial stress and/or psychological traits may be related to augmented insulin and C-peptide response during an oral glucose tolerance test, and also to elevated triglycerides, diminished HDL cholesterol, and increased abdominal obesity. Statistical adjustments for body mass index, age, smoking, alcohol use, and physical activity do not alter these associations.

In addition, studies using the Sprague-Dawley rat model show that excess consumption of dietary sugar contributes to increased plasma insulin, insulin resistance, and activity of the sympathetic nervous system, thereby increasing blood pressure levels. The effects of overeating on activity of the sympathetic nervous system seem to be mediated by insulin.

Physical activity also increases insulin sensitivity, decreases triglycerides, and elevates HDL cholesterol. These changes occur independently of changes in body weight, diet, or smoking. It has been shown that reduction in blood pressure following aerobic exercise training is mediated by increased insulin sensitivity rather than by weight loss.

Smokers display both insulin resistance and hyperinsulinemia and are relatively glucose intolerant. The differences in insulin resistance between smokers and nonsmokers are related to smokers' higher total cholesterol levels and lower concentrations of HDL cholesterol.

Although some of the behavioral factors that increase insulin resistance (e.g., the excessive caloric intake that results in obesity) tend to contribute to each component of the insulin metabolic syndrome, other behavioral factors do not. For example, cigarette smoking causes an increase in insulin resistance and induces hyperinsulinemia as well as hypertriglyceridemia, glucose intolerance, and lower HDL cholesterol levels, but does not increase chronic blood pressure levels. The independent and combined effects of each component are not fully understood.

## *Research Opportunities*

Researchers have demonstrated important relationships among behavior, activity of the sympathetic nervous system, and insulin metabolism in relation to separate and combined components of the insulin metabolic syndrome. They have shown that psychological stress or an increase in caloric intake independently increases activity of the sympathetic nervous system, insulin resistance, and hyperinsulinemia.

However, the manner in which these interactions promote atherosclerosis and increase risk for CHD in relation to changes in insulin and glucose metabolism has not yet been assessed. The availability of a nonhuman primate model useful for demonstrating that psychosocial stress and diet interactively promote atherosclerosis presents an opportunity for studying the interrelationships among behavior, diet, activation of the sympathetic nervous system, insulin metabolism, and atherosclerosis. The independent and combined contributions of psychosocial stress and physical inactivity to the insulin metabolic syndrome also could be examined with this animal model.

The effects of particular behaviors on specific physiological and metabolic processes that interact with insulin resistance should also be explored. However, all behaviors do not contribute to the insulin metabolic syndrome in the same manner. For example, as already noted, cigarette smoking does not increase resting blood pressure, although it does affect other components of the syndrome. The influence of smoking on abdominal obesity also needs to be clarified, particularly since cigarette smokers tend to have a lower body mass index than nonsmokers.

Opportunities are available for determining whether the different behavioral factors that influence insulin metabolism affect risk factors for the insulin metabolic syndrome in an additive or synergistic manner. For example, researchers have shown that psychosocial stress increases the number of cigarettes smoked and the amount of alcohol consumed by individuals, but whether these behaviors influence insulin resistance in a linear (additive) manner or have a synergistic effect on the insulin metabolic syndrome is not known. Multivariate statistical techniques could be used to examine the interrelationships among various behaviors, aspects of insulin and glucose metabolism, and clustering of risk factors.

The extent to which insulin resistance and its relationships to CHD risk factors may be moderated or mediated by behavioral and lifestyle variables needs to be studied further as a function of ethnicity, age, and gender. For example, why is insulin sensitivity inversely associated with atherosclerosis in Hispanic and non-Hispanic white Americans but not in black Americans? Why are older individuals more likely to develop insulin resistance than younger persons? Why is insulin resistance more closely related to CHD in women after, rather than before, menopause?

Other studies are needed to define the importance of gene–behavior interactions to the metabolism of insulin and glucose and to risk factors for CHD. Epidemiologists have identified differences in the relationships among lifestyle variables, insulin and glucose metabolism, and risk factors for CHD within and between populations, but formal genetic studies of these relationships have not yet been conducted.

### *Recommendations*

Recommendations for research on the association of behavioral factors with the insulin and glucose metabolic syndrome are:

1. Identify the causal relationships among aggregations of behavior, aspects of insulin metabolism, and the clustering of risk factors.
2. Study the interaction of psychosocial stress and diet in the development of atherosclerosis in nonhuman primates to clarify the influence of insulin metabolism on the development of CHD.
3. Investigate the separate and combined effects of behavioral risk factors and changes in insulin sensitivity on the development of CHD in humans and nonhuman primates.
4. Assess differences in the association among behavioral variables, insulin metabolism, and risk of CHD according to ethnicity, age, and gender.

5. Identify the genetic determinants of insulin sensitivity and covariation among CHD risk factors.

## Lung Diseases

Considerable research has examined the influence of behavior on the two most common types of chronic lung conditions in the United States: COPD and asthma. Both of these diseases are characterized by diminished expiratory airflow due to narrowing of the airways. In COPD, the abnormalities of expiratory flow are persistent and resistance to change, whereas airway obstruction in asthma is ordinarily reversible, either spontaneously or with treatment.

### *Chronic Obstructive Pulmonary Disease*

In nearly 90 percent of cases, COPD is caused by smoking. Therefore, this disease is almost entirely preventable. Although it has traditionally affected mostly men, COPD now increasingly affects women. In fact, the incidence of COPD is rising more rapidly among women than among men because of increased cigarette smoking by women.

Besides smoking, other risk factors for COPD include age, airway hyperreactivity, hereditary defects (e.g., alpha-1-antitrypsin deficiency), infection, and some forms of occupational exposure (e.g., to mineral dusts, abrasives, certain metals, plant and grain dusts). Lower socioeconomic status also is believed to increase risk for COPD, possibly because of individuals' enhanced exposure to damaging agents in the physical environment such as oxidant gases, active and passive cigarette smoke, and air pollution. Although the precise preclinical course of most patients with COPD is not known, cigarette smoking—alone or in conjunction with other variables—is clearly the predominant risk factor for this disease.

### *Asthma*

Asthma affects approximately 15 million Americans, and about one-half of these are children. In childhood, asthma is more common in boys; in adulthood, prevalence is higher among women aged 15 to 45 years, then higher in men in later years. Familial predisposition to asthma is significant and probably reflects many genetic (polygenic) influences. The various risk factors for wheezing early in life include exposure to tobacco smoke, respiratory infections, and diminished lung function at birth. Some research suggests that breast-feeding may protect against the development of asthma.

Airway hyperreactivity, an exaggerated airway response to an array of stimuli, is a universal feature of asthma. Triggers for airway constriction include viral respiratory influences, environmental allergens, air pollution, smoke and other irritants, certain chemical and food additives, exercise, and exposure to cold. In addition, psychological stress may exacerbate asthma. Whether this association is mediated through asthma-provoking behaviors, such as decreased medication adherence and exposure to asthma triggers, or through direct physiological links is unclear.

Research suggests that asthma symptoms display a diurnal pattern; increased symptoms that interfere with sleep frequently occur during the early morning. Behavioral factors (e.g., patterns of medication adherence) may exacerbate this pattern.

For some asthmatics, episodes of symptoms are linked to periods of heightened emotion. Although the direction of causation is not known, preliminary evidence suggests that airway resistance can be altered by exposure to acute laboratory stressors. Bronchial constriction or dilation can also be induced in about 20 percent of asthmatics in response to simple administration of saline by telling patients that the "drug" they have been given is either a "constricting" or a "dilating"

agent. These effects occur independently of a patient's age, gender, or severity of asthma and of the method of pulmonary assessment. These observations suggest that central nervous system processes involving emotions, reactions to stress, or conditioning can affect pulmonary function in susceptible individuals and, therefore, may play a role in symptom expression and the exacerbation of clinical asthma.

Emotional states also may be related to inflammatory processes that are important in asthma. The recent demonstration that emotions can alter T-lymphocyte function, including the production of cytokines, provides a potential link between emotional experiences and the regulation of inflammation. However, direct evidence associating emotional responses with inflammatory processes in the lung is not yet available.

*Fatal asthma*. The majority of asthma deaths, approximately 4,000 per year, are preventable. Two patterns of fatal asthma have been suggested: rapid-onset and slow-onset. Investigators have not identified any commonalities among the patients experiencing rapid-onset fatal asthma. However, they have noted that slow-onset fatal asthma appears to occur most often among patients who have severe disease, poor medical management, and complicating psychosocial variables, such as poor adherence, family stress, substance abuse, or mental health problems.

*Socioeconomic factors*. Epidemiological studies suggest that morbidity and mortality from asthma are highly prevalent in certain areas, primarily inner-city, minority communities. Economic factors, including access to quality medical care, have been associated with the prevalence of asthma. Some studies have suggested that exposure to cockroach antigen, which is more common in low-income, urban neighborhoods, may be an important contributing factor to both asthma prevalence and severity. Other researchers have focused on understanding the contributing role of behavioral factors, such as overreliance on emergency departments and inadequate asthma knowledge and self-management skills, to the high morbidity in low-income, minority communities.

*Perception of symptoms*. Another area of interest to behavioral researchers is the differences in the ability of asthmatics to perceive varying levels of airflow obstruction. The perception of dyspnea (shortness of breath) can vary dramatically among individuals who have comparable levels of bronchial constriction, and diminished perception of symptoms can result in dangerous delays in seeking medical treatment. For this reason, poor perception of symptoms has been implicated as a possible important contributing factor to the exacerbation of high-risk asthma and to death from asthma.

## Other Lung Diseases

Infectious diseases such as tuberculosis and influenza have been studied by behavioral researchers because of the effects of exposure-related behaviors on the onset and development of these diseases. Appropriate preventive behaviors, such as taking medications (e.g., isoniazid), obtaining flu vaccines, and washing one's hands can, of course, help prevent these diseases.

Occupational lung diseases such as asbestosis and black lung are associated with exposure in the workplace to airborne particles that cause chronic lung damage. Behavioral research in this area has centered on the physical environment and personal factors that promote adherence to protective measures, such as use of personal ventilators that limit exposure to particles in the workplace.

## Research Opportunities

*Asthma*. Behavioral scientists can further knowledge regarding several aspects of the onset, development, and management of asthma. For example, the mechanisms by which central

nervous system activity may influence airway resistance need to be elucidated. Inflammatory processes and their initiation and modulation by the immune system are seen as essential in understanding asthmatics' vulnerability to reversible airway obstruction. Acute psychological stress has been shown to induce rapid changes in cellular immune function, including T-cell mitogenesis and the numbers of circulating natural killer and T-suppressor/cytotoxic (CD8+) lymphocytes. Such associations also suggest the possibility that stress may influence asthma through alterations in cytokines or granular leukocytes.

Additionally, autonomic function affects airway resistance. Parasympathetic activation causes constriction of bronchial smooth muscle (particularly in the upper airways) and stimulation of adrenergic receptors promotes bronchial dilation. Because emotional stimuli can evoke pronounced changes in autonomic activity, such autonomic reactions may conceivably contribute to the precipitation and amelioration of bronchial constriction in susceptible asthmatics.

Although some evidence suggests that psychological factors can affect airway resistance in asthmatics, the direction and strength of these effects need to be further documented. Individuals whose airways are most susceptible to these influences also need to be identified. A common difficulty in studying the precipitants of symptoms that occur episodically (as in asthma) concerns the elusive nature of daily activity. New methodologies for the "real time" assessment of psychological states in ambulatory individuals, in conjunction with portable devices permitting simultaneous measurement of pulmonary function, may be applied usefully in addressing these questions.

Differences in patients' awareness of airflow obstruction and bronchial spasm may be important for managing asthma. Some research suggests that "poor symptom perceivers" may be at higher risk of dangerous exacerbations of asthma and/or delays in seeking medical care than better symptom perceivers. Additional research can improve understanding of the variables associated with asthmatics' accurate perception of symptoms.

Exposure to cigarette smoke prenatally or during early childhood also may affect the development of asthma, and this relationship needs to be studied. For example, the amount and timing of exposure that constitute a risk for asthma are not clear, and whether a combination of other predisposing factors and exposure to cigarette smoke increases the likelihood of asthma has not been established.

*COPD.* Cigarette smoking is the primary behavioral issue involved in the development of COPD. The research opportunities in this area are thus the same as those already identified in the section on Cigarette Smoking in Part I, Behavior–Disease Associations.

### *Recommendations*

Recommendations for research on the association of behavioral factors with lung diseases are:

1. Elucidate the immunological and autonomic–neuroendocrine mechanisms of influence of the central nervous system on inflammatory and bronchomotor processes in individuals with clinically diagnosed asthma.
2. Determine the influence of psychological and sociocultural factors on the regulation of airway resistance and the precipitation of symptomatic asthma.
3. Evaluate individual characteristics and outcomes associated with individuals' perception of symptoms of lung disease.
4. Evaluate the contributory effects of prenatal and early childhood exposure to cigarette smoke on the development of lung diseases.

## Sleep Disorders

Sleep disorders have a number of neurophysiological consequences that can affect cardiovascular and pulmonary conditions. The behavioral changes that accompany sleep are profound, and the physiological changes are various, numerous, and complex.

Sleep-related changes affect hormonal secretion, sexual arousal, circulatory activity, and autonomic (both sympathetic and parasympathetic) function. Insufficient, ill-timed, or disturbed sleep can disrupt an individual's functioning during awake periods and cause significant physiological and behavioral problems. In turn, behaviors during awake periods, from exercise to use of substances (e.g., alcohol, nicotine, caffeine) or ingestion of prescription medications, can alter sleep in many ways.

Daily organization of the sleep/wake cycle, like many other body processes, is controlled by brain mechanisms that include circuitry linked to an intrinsic timekeeper, or oscillator, which functions as a daily (circadian) clock. One example of the many functions linked to this clock is the secretion of cortisol, which increases in the early morning. Another example is the daily fluctuation in platelet aggregation, which is higher in the morning and may account for an increased likelihood of MI during the early morning.

As noted in the section on Acute Cardiac Events, sleep and circadian rhythms have a major influence in determining the risk, treatment, outcomes, quality of life, and other factors related to cardiovascular and lung diseases. Behaviors that alter the relationship between intrinsic circadian rhythms and an individual's daily activities—for example, waking up or exercising at inappropriate phases of the circadian cycle—may affect CVD risk.

*Rapid-eye-movement (REM) sleep.* During the past 5 years, investigators have amassed considerable evidence indicating that the profound surges in activity of the sympathetic nervous system during sleep may constitute an important trigger of myocardial ischemia and life-threatening arrhythmias. REM sleep is associated with major surges in activity of this system, which can result in decreased blood flow to coronary areas that are partially obstructed. Studies of heart rate variability in post-MI patients suggest that sleep is associated with impaired function of the autonomic nervous system and reduced activity of the vagus (parasympathetic) nerve. Because activity of the vagus nerve protects against ventricular fibrillation, these findings are important for understanding the enhanced risk for sudden death for post-MI patients.

REM sleep may have an important role in precipitating MI and sudden death in patients who already have CHD, a prior MI, heart failure, or cardiac irregularities. Each year in the United States, about 42,500 persons die from sudden cardiac death during the night. This number nearly equals the number of fatalities from automobile accidents in this country and is 60 percent higher than the number of deaths due to human immunodeficiency virus (HIV) infection.

REM sleep also may have an important role in precipitating MI and sudden death in infants at risk for sudden infant death syndrome (SIDS) and in Southeast Asians who die from sudden unexpected nocturnal death syndrome (SUNDS). The relationship of sleep to SIDS has received much attention because most cases of SIDS occur when a child is presumed to have been sleeping. Recent efforts to prevent infants from sleeping on their stomachs (e.g., the widespread Back to Sleep program) have helped reduce the incidence of SIDS.

*Sleep deprivation.* The specific relationships of chronic and acute sleep deprivation to behavioral and biological risk factors for CVD are largely unknown. Insufficient sleep is pervasive among U.S. adolescents, adults, and elderly persons. This

insufficiency may be attributable to lifestyle reasons (e.g., school starting times or shift work) or to primary sleep disorders (e.g., insomnia, restless leg syndrome, disturbances of circadian rhythm).

Chronically inadequate sleep, defined as fewer than about 9 hours for children and adolescents and fewer than 8 hours each day for adults, often is associated with sleepiness during waking hours and, in susceptible individuals, may be related to specific behavioral risk factors such as irritability, hostility, exhaustion, and depression. It is possible that loss of sleep also may directly influence the autonomic nervous system and contribute to risk for cardiovascular events or pulmonary diseases. However, such specific relationships and mechanisms involved are not known.

Recent reports indicate that disrupted sleep is a critical factor in the enhanced risk of sudden death for patients with heart failure and may be critical for many patients with CHD. These findings suggest that treatment of CHD can be improved by using cardiac medications that do not disrupt sleep and by treating sleep disruption that results from heart failure and other cardiovascular conditions.

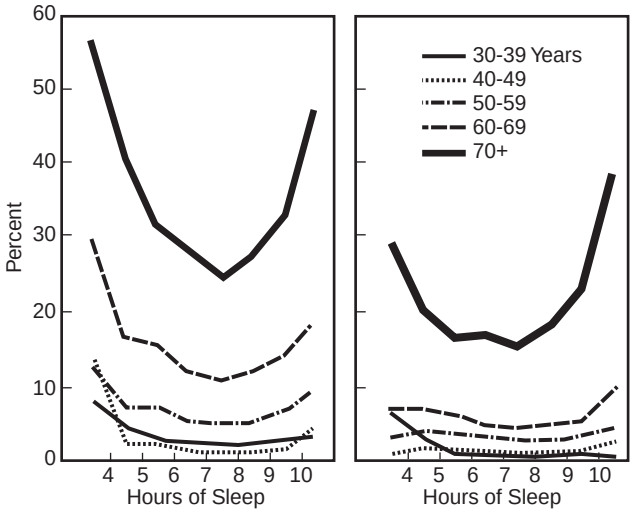


**Figure 12.** Percent of men (left) and women (right) who were dead at six-year follow-up for each reported sleep duration. Adapted and reprinted with permission from Kripke DF, Simons RN, Garfinkel L, and Hammond EC: Short and long sleep and sleeping pills: Is increased mortality associated? Arch Gen Psychiatry 1979;36(1):103-116.

*Excessive sleep*. Excessive sleep, or hypersomnolence, may be a marker of increased mortality risk. Figure 12 illustrates the importance of the length of sleep by summarizing data which support the longstanding observation that increased mortality is associated with extremes in reported sleep length.

## *Obstructive Sleep Apnea Syndrome*

Sleep is directly implicated in a set of breathing disorders of which obstructive sleep apnea syndrome (OSAS) is the primary example. When a patient with OSAS falls asleep, full or partial closure of the throat obstructs airflow; this blockage clears only when the patient arouses. A patient with OSAS may endure hundreds of stoppages and arousals nightly, which affect the heart, blood vessels, and lungs.

Among adults, the major risk factors for OSAS are, in order, obesity, male sex, and increased age. Smoking also contributes to risk. Among children, sleep apnea is associated more commonly with enlarged tonsils and adenoids.

Obstructive sleep apnea syndrome is among the most prevalent of all sleep disorders. It affects about 10 million American adults, but a great majority of them do not know they have it. The behavioral and health consequences of OSAS are many and often include longstanding daytime sleepiness, cognitive impairments, and depressed mood. Children with OSAS experience problems ranging from bed-wetting to disruptions of behavior and learning. Adults with OSAS report memory problems, tiredness, reduced energy, lowered libido, and poor functioning at work. These problems can be severe enough to be life-

threatening such as when sleepiness interferes with driving. Individuals who have OSAS but are not being treated for the condition reportedly have a high rate of driving accidents.

Obstructive sleep apnea syndrome also is associated with various cardiovascular disorders. Sleep apnea is a risk factor for systemic hypertension and stroke, probably because of reflex activation of the sympathetic nervous system, which is associated with impaired delivery of oxygen in the bloodstream because of obstructed airflow during sleep. Pulmonary hypertension and cardiac arrhythmias frequently accompany the stoppages in breathing, and the abrupt arousals that terminate these pauses are associated with wide variations in systemic blood pressure. Sleep apnea also is strongly associated with MI. In one study, cardiac patients in the highest quartile of severity of apnea had a 23-fold higher risk for MI than patients in the lowest quartile.

Each year in the United States, OSAS causes about 120,000 cardiovascular events (MI, stroke) and may be responsible for 20,000 deaths from CVD. The prevalence of OSAS differs between genders and age groups; among U.S. adults, 4 percent of men and 2 percent of women are estimated to have clinically significant OSAS (i.e., more than 15 obstructive events per hour of sleep plus excessive sleepiness). In general, breathing irregularities become common in older men and women, and sleep-disordered breathing reportedly occurs in as many as 25 to 40 percent of all persons above age 65. Although OSAS also is found in children, its prevalence in infants, children, and adolescents has not been evaluated with sound epidemiological methods. Increasing evidence further indicates that OSAS frequently occurs among multiple family members. For example, 8 percent of adults with OSAS have children with the disorder.

### *Other Sleep Disorders*

Compared with OSAS, much less is known about the epidemiology and treatment of related sleep and breathing disorders. These include sleep-disordered breathing associated with aging, sleep-related upper airway resistance (UAR) syndrome, and sleep-state exacerbation of other breathing disorders such as COPD. Sleep, particularly REM sleep, may exacerbate COPD, and sleep fragmentation and insomnia are common complaints among patients with this disease.

Other sleep disorders that affect the cardiorespiratory system include central sleep apnea syndrome, central alveolar hypoventilation syndrome, altitude insomnia, REM-sleep-related sinus arrest, primary snoring, infant sleep apnea, and congenital central hypoventilation syndrome. Equally important are the effects of natural sleep processes on patients who have preexisting diseases such as ischemic heart disease, MI, heart failure, and long-QT interval, an abnormality of the heart's neural conduction system which may increase an individual's susceptibility to arrhythmia.

### *Research Opportunities*

The symptoms and mortality associated with several cardiovascular and pulmonary disorders have definite diurnal patterns, such as the increase in MI, sudden death, and ischemia during early morning hours and the increased mortality from asthma between 2:00 and 4:00 a.m. The mechanisms underlying these diurnal patterns are only partly understood and need to be further clarified.

In addition, the relationship of sleep deprivation to the causes and consequences of stress is not described well. In fact, sleep loss generally is overlooked when stress-related variables are assessed. The influence of sleep deprivation on the emergence of anger, hostility, exhaustion, or

depressed mood and its contribution to increased risk for cardiovascular events are largely unknown. Chronic and acute sleep deprivation may be useful models for examining the physiological mechanisms that underlie stress and CVD. For example, alterations in specific brain regions and neurochemical systems may link sleep disorders, stress, and the end points of CVD.

Research suggests that both genetic and environmental factors may be responsible for the aggregation of sleep-related breathing disorders within families. These factors, however, have not been elucidated fully. Investigations of their effects are crucial and may provide the means to identify at-risk individuals early so that timely behavioral interventions can be applied to ameliorate or even preclude development of these disorders.

Another important area of investigation is identification and examination of the site(s) in the central nervous system that account for the surges in activity of the cardiac sympathetic nervous system during REM sleep. By understanding the mechanisms involved in these surges, investigators may be able to devise strategies for curtailing ischemic attacks and life-threatening arrhythmias. Investigations of neural mechanisms also need to be included in studies of REM-sleep-related changes in respiratory dynamics. Similar studies could illuminate the basis for the impressive alterations of cardiopulmonary dynamics induced by abrupt arousals from sleep.

The effects of sleep-disordered breathing on perfusion of the myocardium and electrical stability of the heart also need to be clarified. Research strongly implicates OSAS in nocturnal cardiac arrhythmias and MI and in daytime systemic hypertension. However, whether OSAS increases the risk of sudden death in patients with ischemic heart disease is not clear. If researchers find that OSAS does increase the risk of sudden death in these patients, the mechanism(s) that account for this increased risk will need to be defined.

Studies also are needed to establish the usefulness of routine monitoring of nocturnal oxygen saturation in cardiac patients to identify patients whose lives are threatened by OSAS. Systems for monitoring sleep at home are now available and can be used to study the effects of sleep disruption on various disease states in cardiac patients. Some sleep recorders have motion sensors that enable researchers to precisely monitor an individual's activity levels and postural changes and the effects of waking. The ability to monitor sleep at home may accelerate identification of the destabilizing mechanisms of sleep and arousal in cardiac patients.

### *Recommendations*

Recommendations for behavioral research on the effects of sleep disorders on heart and lung diseases are:

1. Investigate circadian, sleep, and behavioral mechanisms that influence diurnal variations in the morbidity and mortality from CVD and pulmonary diseases.
2. Identify the effects of chronic and acute loss of sleep on responses to stress and risks for acute and chronic CVD.
3. Elucidate the relative effects of genetic and environmental influences on sleep apnea syndromes.
4. Identify the neural mechanisms responsible for surges in activity of the sympathetic nervous system during REM sleep and in response to abrupt arousals from sleep.
5. Determine the mechanisms for the effects of sleep apnea on perfusion of the myocardium and electrical stability of the heart.

National Heart,
Lung, and
Blood Institute
Report
of the
Task Force on
Behavioral Research in
Cardiovascular, Lung,
and Blood Health and Disease

# II. Behavioral Interventions: Prevention and Management of Disease

# II. Behavioral Interventions: Prevention and Management of Disease

In Part II, the Task Force on Behavioral Research in Cardiovascular, Lung, and Blood Health and Disease reviews the status of research on behavioral interventions to prevent or help manage heart, lung, and blood diseases and sleep disorders. Many of the topics discussed pertain to the behavioral risk factors identified in Part I that predispose individuals to heart and lung diseases. The Task Force focuses on social and behavioral interventions to prevent the onset of disease (primary prevention) as well as the progression of disease (secondary prevention).

Behavioral interventions are strategies that help individuals, groups, and communities to modify behaviors that cause or contribute to disease and to adopt behaviors that prevent or improve the management of disease. These strategies include, but are not limited to, the following activities:

- Provision of persuasive health-promotion information
- Initiation of group and individual programs for changing health behaviors such as cigarette smoking, physical inactivity, or unhealthy diet
- Education of patients and health care providers regarding new skills for improving adherence to treatments and interventions and the sustainability of positive behavioral changes.

As noted in Part I, dramatic changes in lifestyle have occurred in the United States in recent years. These changes are cited as an important contributor to the decline in cardiovascular disease (CVD) mortality and the increase in life expectancy for middle-aged persons in this country. In this regard, during the past 20 years, notable progress has been made in developing and applying behavioral approaches to health promotion and to the prevention and control of CVD. Moreover, behavioral interventions have already become an integral component of patient care for asthma and other lung diseases. By comparison, behavioral research is just beginning in the areas of blood diseases and the prevention and control of sleep disorders. As research defines the behavioral and biomedical risk factors for these conditions, it is important that this knowledge be translated into interventions for health promotion and disease prevention.

Part II is divided into three major sections as follows:

- Behavioral Interventions for Risk Factors
- Behavioral Issues in the Management of Disease
- Improving Outcomes: Cross-Cutting Issues

In the first section, the Task Force highlights recent advances in interventions that target key risk factors for heart, lung, and blood diseases, including cigarette smoking, physical inactivity, adverse diet, obesity, and alcohol abuse. For some of these risk factors (e.g., cigarette smoking), interventions have been successful both for primary prevention (i.e., preventing the initiation of smoking) and for secondary prevention (i.e., achieving smoking cessation).

As discussed in Part I, psychosocial factors (e.g., depression, hostility, social isolation, job

strain) also increase risk for CVD. These risk factors are important, but few interventions have been directed toward *their primary prevention* or toward primary prevention of CVD by their modification. Most intervention research in this area has focused on modifying psychosocial risk factors in patients who have coronary heart disease (CHD). Therefore, recent research advances in this area are summarized under Coronary Heart Disease, under Behavioral Issues in the Management of Disease. In this section, successful behavioral interventions for preventing and treating specific diseases are highlighted. In addition, the Task Force reviews important behavioral factors relevant to the treatment of sleep disorders and to the donation and use of blood and blood products.

In the third and final section, the Task Force summarizes the behavioral aspects of two cross-cutting issues that affect the management of disease: adherence to health care regimens and quality-of-life outcomes. To derive benefit from treatment, patients must adhere to the therapies prescribed. In addition, in many cases, quality of life can be an outcome as important to patients as morbidity and mortality.

## Behavioral Interventions for Risk Factors

The status of research on behavioral interventions to reduce individuals' risk for CVD is addressed in this section under the following five topics: smoking, physical inactivity, diet, obesity, and alcohol abuse. The Task Force highlights successful primary and secondary prevention efforts and delineates specific research opportunities and recommendations for the future.

### Smoking

The dramatic decline in smoking rates in the United States throughout the past 35 years is one of the great success stories of changing risky health behaviors. In 1962, before publication of the *Surgeon General's Report on Smoking and Health*, more than 42 percent of the U.S. population smoked cigarettes regularly. In 1997, fewer than 26 percent of Americans smoke.

Behavioral research and interventions based on this research have facilitated this dramatic change. The broad array of activities targeted against smoking have included prevention programs in schools, mass-media communications, training for health care providers, research on the effects of nicotine, and specific smoking-cessation interventions. Public service agencies, such as the American Cancer Society and the American Lung Association, and Federal and local health agencies have applied the results of behavioral and social research broadly to the development and initiation of community education and action programs, as well as public policies to reduce tobacco use, particularly among young persons.

This progress is both exciting and gratifying. However, cigarette smoking is still the greatest single cause of preventable deaths in the United States. Disturbingly, the decline in the prevalence of smoking is slowing, and smoking among some teenage groups has recently increased. Figure 13 shows the trend in prevalence of smoking among Californians between 16 and 18 years old. These prevalence data focusing on the young indicate that smoking will continue to be a major public health problem for years to come.

#### *Primary Prevention of Smoking*

More effective primary prevention efforts—that is, preventing individuals from beginning to smoke—are key to reducing total tobacco use. Evidence indicates that approximately one-half of all dependent smokers started smoking by age 15, and almost all started by age 19. Of the nearly half of high school smokers who say they expect to quit smoking within 5 years, most are still smoking, and with greater frequency when contacted 5 years later.

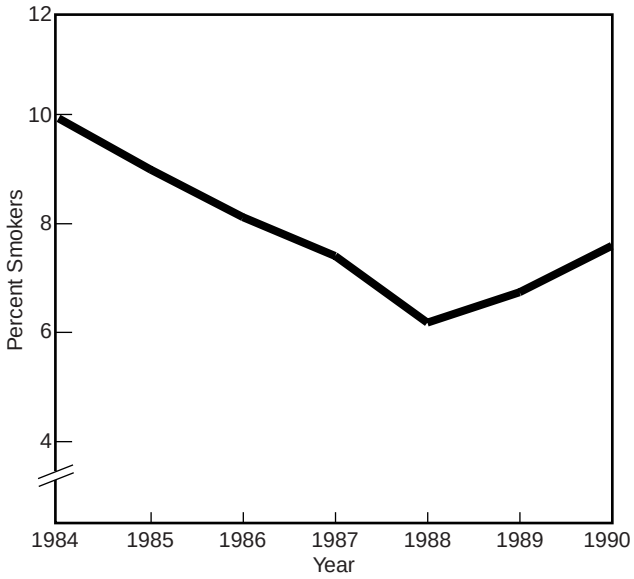


**Figure 13.** Trend in smoking prevalence among 16- to 18-year old Californians. Adapted and reprinted with the permission of Pierce JP, Evans N, Farkas AJ, Cavin SW, Berry C, Kramer M, Kealey S, Rosbrook B, Choi W, and Kaplan RM: Tobacco use in California. An evaluation of the tobacco control program, 1989-1993. La Jolla, California: University of California, San Diego; 1994.

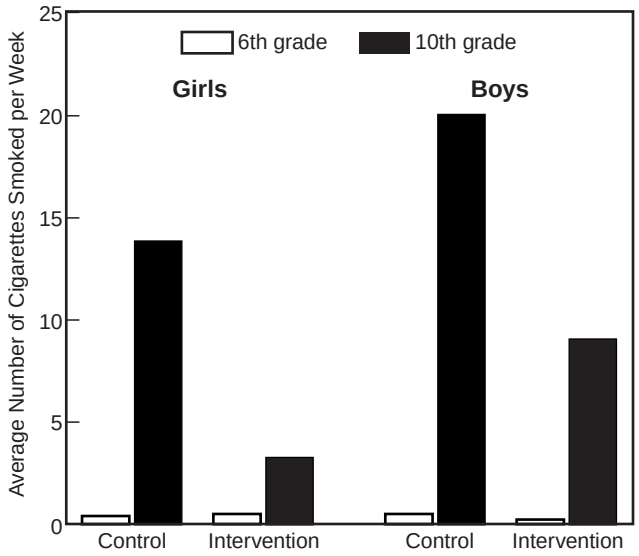


**Figure 14.** Change in smoking patterns between 6th and 10th grade in a cohort of students exposed to the Minnesota Heart Health school-based smoking prevention intervention compared to students in control schools. Adapted and reprinted with permission from Luepker RV and Perry CL: The Minnesota Heart Health Program. Education for youth and parents. Ann NY Acad Sci 1991;623:314-321.

Teenagers seriously misunderstand the risks of becoming dependent on nicotine when they begin to experiment with smoking. More than one-half of all high school students who smoke are dependent on nicotine, and almost 90 percent have withdrawal symptoms when they try to quit smoking. For these reasons, primary prevention must be focused on children of elementary and middle-school ages.

Many different prevention efforts have been undertaken. These include school-based clinical trials and community studies conducted in California, Minnesota, Texas, and Vermont, and in Canada. Figure 14 summarizes the results of a school-based smoking-prevention program that used adolescent peer leaders to teach refusal skills to seventh graders for overcoming peer and psychosocial environmental pressures to begin smoking. This intervention significantly reduced the adoption of smoking among both boys and girls who participated in the program compared with those who did not. A number of these intervention studies demonstrate modest, early success in preventing smoking initiation. Although encouraging, those studies using more rigorous methodologies have tended to demonstrate somewhat weaker effects.

At least two lessons from behavioral research on primary prevention of smoking are useful for future efforts:

- More positive results appear to be obtained when prevention efforts are conducted within the context of other supportive activities in the larger community. For example, the prevalence of smoking tends to be lowest in communities that have restrictive policies for smoking. Public policy initiatives that restrict youths' access to cigarettes may enhance the effectiveness of primary prevention efforts by fostering an environment that is more supportive of nonsmoking behavior.

- Children's risk for tobacco use is higher when they have coexisting problems with other drugs, depression, family disruption, or failure at school. To be most effective, efforts to prevent smoking must be integrated into broader efforts to identify and help high-risk children.

Because teenagers often become addicted to nicotine by the end of their teen years, interventions also are needed to promote smoking *cessation* among young people. Researchers, however, have given very little attention to this important group of smokers. In some surveys, many—if not most—of the teenagers and young adults who were dependent smokers stated that they would not have started smoking if they could choose again. Because of the short amount of time that these individuals have been smoking, with the appropriate intervention they may be more amenable to quitting smoking than healthy adults who are dependent smokers.

## *Interventions to Stop Smoking*

Although about 46 million Americans still smoke, almost as many are former smokers. By the time people reach age 65, most of those who have ever smoked have also successfully quit smoking. Many of those who quit are motivated by symptoms of disease.

The number of Americans who are exsmokers underscores the tremendous effect of improved interventions for smoking, enlightened public policy, and changes in society's acceptance of smoking. Much of the attention on smoking has now shifted to motivating more smokers to quit. Increased recognition of the personal health risks of smoking, the hazards of environmental tobacco smoke, the threat of smoking to an unborn child, and the addictive nature of nicotine supports these efforts.

The immediate and long-term benefits of quitting smoking are dramatic. Smokers who quit before age 50 halve their risk of dying in the next 15 years compared with smokers who do not quit by age 50. Smokers who quit early in their smoking career and smokers who quit in their mid-60s also significantly reduce their risk for heart disease, stroke, and smoking-related cancers.

Behavioral researchers have contributed significantly to understanding factors associated with smoking cessation and to identifying the most successful intervention strategies for achieving smoking cessation. The results of their efforts are summarized below.

*Predictors of smoking cessation.* By understanding who is most likely to quit smoking, and who is not, behavioral researchers can identify potentially important barriers and promoters of smoking cessation. These "predictors" can then be addressed in effective interventions against smoking. In general, epidemiological and intervention studies show that smokers who are most likely to quit smoking successfully have higher incomes, are better educated, are older, are less dependent on nicotine, or have acute health problems. Studies of smoking cessation among women and minorities indicate that gender and ethnicity may also pose unique barriers.

During the past 15 years behavioral researchers have focused considerable attention on the effects of nicotine addiction on quitting attempts and on the maintenance of smoking cessation. Many studies show a relationship between individuals' levels of smoking (i.e., number of cigarettes a day) and their likelihood of maintaining cessation. Smokers who smoke the least number of cigarettes a day are most likely to quit successfully.

Other indices of smoking behavior have been combined and used as a means to assess an individual's degree of addiction. Because the level of nicotine addiction is an important predictor of cessation, behavioral scientists have studied the effect of nicotine replacement therapies as an aid to smoking cessation (see below).

Two other predictors of smoking cessation are smokers' level of confidence in their abilities to succeed in quitting smoking and their readiness to attempt cessation. Models of smoking behavior that incorporate these predictors have influenced the direction of recent research. These models suggest that the most effective interventions are those designed to increase the smoker's confidence in being able to quit, and those tailored to the smoker's level of readiness to quit. Efforts to motivate smokers to move to the next stage of readiness also may be an important goal for smoking cessation interventions.

*Smoking cessation strategies*. Researchers have extensively explored structured interventions to help smokers quit and to prevent relapse. Because the risk of smoking relapse is high for recent quitters, prevention of relapse is a primary emphasis in all smoking-intervention programs.

Smokers relapse for many reasons. Individuals who relapse soon after quitting smoking may be responding to the effects of nicotine withdrawal. Those who relapse after extended cessation (a few weeks or more) are more likely responding to behavioral factors such as psychological stress, concerns about weight gain, and failure to cope with cues associated in the past with smoking (e.g., drinking alcohol).

Many of the successful cessation programs attempt to prevent relapse through the use of social support, cognitive and behavioral strategies, attention to weight, stress management, and exercise. Multisession, multimodal, cessation programs for groups typically yield 1-year cessation rates of 20 to 25 percent after a single attempt to quit. These rates compare favorably with the expected cessation rate (5 percent or less) for smokers who receive no help.

Recently developed group cessation programs emphasize adjunctive treatment for smokers who are likely to experience specific problems associated with cessation (e.g., smokers who have a history of major depression, anxiety, or alcohol abuse). These programs were developed in response to research findings showing that the probability of smoking relapse, like smoking status itself, is not random but is distributed among specific subgroups of smokers. The results indicate that these group programs enhance cessation and that the key element may be greater intensity of therapeutic contact.

Complementary to these specialized interventions are lower-cost efforts to increase cessation. Most smokers who attempt to quit are able to quit on their own without the help of a formal program or cessation aids. However, studies suggest that smokers' initiation of cessation and avoidance of relapse are influenced by a number of psychosocial and environmental factors. These factors include increased cigarette taxes; mass-media messages; smoke-free worksites and public settings; medical advice; and pressure, support, and modeling from nonsmoker or exsmoker friends, coworkers, and family members.

Less-intensive and lower-cost education and support interventions delivered by mail or phone also can promote cessation and reduce relapse, as shown by studies comparing these interventions with no contact. In general, intensive interventions involving frequent contact yield higher success rates than minimal, self-directed strategies such as use of self-help materials, brief telephone contacts with counselors, or exposure to media-based communications. However, because the advantage gained from the higher quit rates may be offset by the considerably higher cost of intensive programs, providers may choose to reserve intensive interventions for smokers at particularly high risk (e.g., those with smoking-related diseases).

Medical care settings offer an obvious opportunity for smoking-cessation interventions. Indeed, tertiary prevention studies provide some of the strongest evidence for the health benefits of cessation (e.g., reduced risk of recurrent MI in

exsmokers as compared with continuing smokers). These studies show that a physician's strong message to quit will increase patients' quit rates from approximately 5 percent to 10 percent and, in some cases, as much as 15 percent. Clinical trials that included smoking-cessation interventions, such as NHLBI's Lung Health Study and the Multiple Risk Factor Intervention Trial, show high and sustained quit rates (almost 40 percent after 1 year). They also show that high-risk smokers (e.g., smokers with heart and lung diseases) can benefit from intensive behavioral programs utilizing nicotine replacement.

Other research shows that the integration of smoking-cessation programs into routine medical care increases the rates of smoking cessation and reduces smoking relapse in a broad range of patients, including pregnant smokers, dental patients, and patients hospitalized for CHD. However, research also shows that physicians continue to neglect to counsel their patients regularly and effectively about smoking cessation. Physicians' time constraints, lack of counseling skills, and perceptions of the ineffectiveness of counseling efforts may account for their failure to counsel patients.

Enlisting physicians and other health care providers to refer smokers to smoking-cessation programs and to reinforce cessation efforts may be a more realistic strategy given the limits of managed care. The development and evaluation of programs to train health professionals to take a more active role in supporting smoking cessation is needed.

Focusing on the addictive aspects of smoking behavior, researchers have also examined the value of pharmacological aids for quitting smoking. This research has resulted in development of new and effective aids for promoting and maintaining smoking cessation. The most widely used and validated of these pharmacological approaches is nicotine replacement therapy using chewing gum or transdermal patch. Both methods are designed to lessen withdrawal symptoms and to control cravings for cigarettes in an effort to prevent relapse.

The safety and efficacy of nicotine polacrilex gum and transdermal nicotine patches have been evaluated extensively both in structured programs and among self-quitters. These studies clearly establish that, when used correctly, the addition of nicotine replacement therapy to a cessation effort nearly doubles the success rate for smoking cessation. More recently, studies show that two alternate forms of nicotine replacement, nicotine nasal spray and a nicotine inhaler, are safe and efficacious. Other promising pharmacological aids for smoking cessation, including antidepressants and anxiolytics, are also being explored.

Often overlooked during the promotion of new medications, however, is the need for adjunctive, complementary behavioral counseling. For smoking cessation, many studies show that counseling significantly enhances the efficacy of nicotine replacement. Some studies even indicate that, without behavioral counseling, the effect of nicotine gum may be no better than a placebo. Failure to obtain adequate behavioral counseling when using nicotine replacement is likely to become a greater problem because nicotine gum and the transdermal patch, the two most popular treatments, are now available without prescription; individuals do not have to contact a health care provider to obtain them.

Tobacco smoking, like many other drug dependencies, is strongly influenced by behavioral factors that cannot be addressed adequately by medication alone. Moreover, many patients do not receive appropriate instructions for using the medications prescribed, which further reduces the likelihood that the agents will be effective. Brief and effective counseling methods must be developed and used with specific medications for tobacco dependence. In addition, these methods need to be incorporated into the services provided by rapidly changing, managed-care settings.

### *Research Opportunities*

Preventing the onset of smoking is key to reducing the number of adults addicted to smoking and the long-term health costs associated with smoking. Even though most children are exposed to some type of drug and tobacco prevention program in school, the prevalence of smoking has increased among teenagers. Recent prevention initiatives are aimed at reducing the availability of cigarettes to young people. These community-wide restrictions offer an important opportunity for strengthening the antismoking messages of school-based prevention programs.

Teenagers who smoke are likely to become addicted and suffer withdrawal symptoms when they try to quit. Because many teenagers and young adult smokers express regret that they ever started smoking, teenagers and young adults may be a particularly critical group for preventive intervention. However, very few smoking-cessation programs specifically target younger smokers. Because teen smokers are younger and because the factors that help maintain their smoking (e.g., importance of self-image, susceptibility to targeted advertising, social influences) may differ from those that are important for older smokers, the behavioral interventions used with younger smokers may need to be designed differently than those used for adult smokers. The potential of such interventions is high given that young smokers may be better able to quit than their adult counterparts.

The vast majority of smokers who quit smoking are able to quit by themselves without the help of a formal smoking-cessation program or nicotine replacement therapy. The decision-making of self-quitters to quit smoking and the reasons for their success in quitting, often after several quit attempts, are not well understood. Further knowledge about these processes could inform public health education efforts to encourage more self-quitters.

Although the advice of physicians is an effective means for encouraging individuals to quit smoking, physicians do not routinely or strongly advise patients to quit. Definitive educational and institutional strategies are needed to encourage physicians either to provide effective counseling or to refer patients to cessation programs. Because increasing numbers of Americans are receiving their health care from managed-care organizations, the counseling efforts of, or referrals by, other health care providers (e.g., nurses, respiratory therapists, dentists) also should be examined.

Because of nicotine's critical effects in reinforcing tobacco use and initiating dependence, the development of medications to help with smoking cessation is a promising avenue of research that, undoubtedly, will continue to develop. However, even with the latest medications, the rates of smoking cessation are still low. These lower-than-expected success rates result from several causes, including a failure to address the behavioral aspects of nicotine addiction, a failure to instruct patients properly on the use of medications, and the cost of medications, which is usually paid by patients out of pocket and, therefore, may sometimes result in inadequate duration or dosages.

Greater attention needs to be given to the effective integration of behavioral counseling with medication. Success rates of medications are often significantly improved with the addition of behavioral interventions. A better understanding of behavioral factors that encourage individuals to continue smoking (e.g., conditioned associations with nicotine intake) is needed to achieve long-term smoking cessation, particularly after medications are withdrawn.

The prevalence of smoking continues to be higher for lower socioeconomic classes, some ethnic groups, and individuals who are predisposed to mental health problems (e.g., those who have a history of major depression or of abuse of alcohol or other drugs) than for other segments of

the population. This pattern suggests that differences in susceptibility to behavioral and/or biological factors affect the adoption and maintenance of smoking. Treatment for these groups and individuals will continue to be difficult until researchers obtain more information on how these cultural, ethnic, biological, and behavioral differences influence smoking and smoking cessation.

### *Recommendations*

Recommendations for behavioral research on interventions for smoking are:

1. Identify smoking prevention programs that are (a) directed at preventing individuals' transition from experimenting with cigarettes to regular smoking, (b) have a longer-lasting effect, and (c) are integrated better with communities' broader antismoking efforts.
2. Identify ways to intervene more effectively among teenagers and young adults who smoke regularly.
3. Assess the effectiveness of low-cost environmental interventions (e.g., mass-media messages, restrictions on cigarette purchases and smoking places) to increase individuals' motivation to quit smoking.
4. Identify educational and institutional strategies for improving and encouraging smoking-cessation counseling by physicians and other health care providers.
5. Evaluate the effectiveness of behavioral interventions combined with nicotine replacement therapy and other emerging pharmacological treatments for smoking.
6. Evaluate smoking prevention and cessation approaches for various racial, ethnic, and income groups. Assess, in particular, whether general or targeted interventions (e.g., for men or women, ethnic groups, individuals with a history of psychological problems) are more effective for these groups.

## Physical Inactivity

The negative effects of physical inactivity are well documented. Interventions to reduce physical inactivity and to promote exercise can prevent or delay the onset of cardiovascular and pulmonary diseases and can improve the functioning and quality of life for individuals who already have these diseases. Two aspects of physical inactivity are pertinent for Part II: primary prevention of diseases or conditions associated with inactivity, and exercise training to reduce the risks of morbidity and mortality in individuals who already have disease. Research progress is being made on both fronts.

*Benefits of exercise*. Aerobic exercise training is now recognized as an important intervention strategy for preventing CHD and for treating and rehabilitating patients who have CHD, chronic obstructive pulmonary diseases (COPD), and other pulmonary disorders such as asthma and cystic fibrosis (CF). Healthy individuals, as well as patients who have cardiopulmonary diseases, including heart failure, can improve their exercise performance via regular exercise training.

Exercise training increases maximum cardiac output and the exercising muscles' ability to extract oxygen from the blood. Training also improves hemodynamic, metabolic, neurohumoral, and respiratory functions. Because of these improvements, exercise is important for individuals at risk of initial or recurrent heart disease.

Typically, the effects of exercise training become apparent within 6 to 12 weeks. The timing and nature of these effects depend on various factors, which include the person's age, health and disease status, and intensity of training. The optimal exercise intensity (i.e., the vigorousness of the

exercise) is usually a level exceeding 40 to 50 percent of an individual's exercise capacity.

*Exercise for elderly persons*. Recently, researchers have used exercise interventions for elderly persons more extensively than in the past. For these persons, aerobic exercise and strength training reduce the loss of lean body mass that occurs with aging and help maintain individuals' functional abilities. In addition, regular exercise of moderate intensity improves older adults' levels of fitness and HDL cholesterol. The length of time needed to achieve the cholesterol effects, however, may be longer for elderly persons than for younger populations. Achieving sustained participation in an exercise program is therefore an important aspect of interventions for older adults.

One particularly effective strategy for achieving their adherence to exercise is supervised home-based exercise (see figure 15). Home-based training was associated with significantly greater improvements in HDL cholesterol levels than was participation in a group exercise program at the senior center.

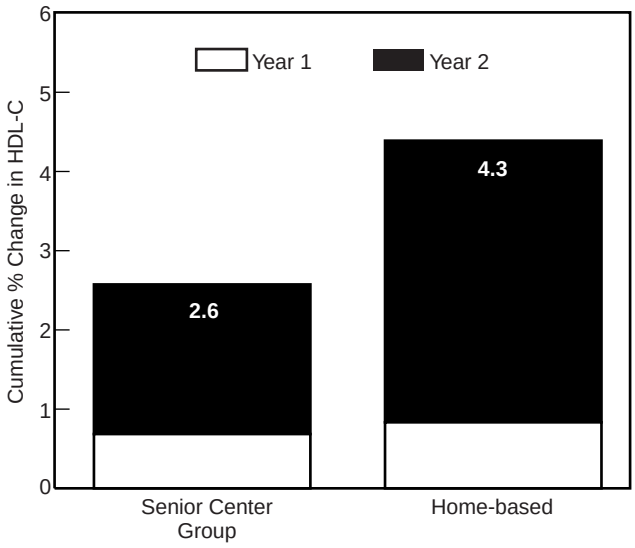


**Figure 15.** Cumulative percent increase in HDL cholesterol after 1 and 2 years of moderate exercise for older adults in senior center compared with those in a supervised home-based environment. Adapted and reprinted with the permission from King AC, Haskell WL, Young DR, Oka RK, and Stefanick ML. Long-term effects of varying intensities and formats of physical activity on participation rates, fitness, and lipoproteins in men and women aged 50 to 65 years. Circulation 1995;91(10):2596-2604.

*Factors predicting exercise activity*. Several psychosocial and other environmental factors affect individuals' adoption of exercise habits. These include personal motivation, social support, and a safe environment for exercising. Research indicates that certain groups, such as blue-collar workers, smokers, and older or overweight individuals, are less likely to be active when these factors are lacking.

Familial factors also affect individuals' exercise activity. Studies show that children are five times as likely to be active when both parents are active as when they are inactive. Most of this similarity between parents' and children's physical activity appears to relate to environmental (both psychosocial and physical) influences, but approximately 30 percent of the variability in family activity levels may relate to genetic factors.

These findings have important implications for intervention. They suggest that both environmental and, potentially, genetic influences must be considered. For example, interventions to promote physical activity might include modifying the physical or social environment so that it is safe and supportive of exercising, identifying persons who have a genetic vulnerability to physical inactivity, and beginning interventions among children at an early age.

*Maintaining exercise behavior.* Ensuring patients' adherence to physical activity over time is just as important as the initiation of an exercise program. Adherence has proven to be challenging for many individuals and, therefore, is receiving increased research attention. More than one-half of all individuals who begin an exercise program relapse or stop the exercise program within 6 months. Reducing this high rate of relapse is necessary because the physiological and psychological benefits of exercise, which are so important

for good health, cannot be maintained if exercise is not continued over time.

## *Promoting Physical Activity: Primary Prevention*

Programs to increase physical activity and prevent conditions associated with inactivity, including CHD, generally have yielded positive results, producing significant increases in activity. In these interventions, emphasis is placed on participant involvement in setting goals; developing a written contract that outlines activities for reaching these goals; having participants monitor their own progress; and establishing a network of other individuals who support, encourage, and praise or reinforce increased activity. Participants are trained in skills to prevent relapse and to establish these important social networks.

In some health-promotion interventions, a recommendation to increase physical activity is only one of several recommendations for behavior change. When interventions for several behavorial risk factors are combined, it is difficult to determine the amount of change resulting from increase in physical activity per se. This problem has arisen in some of the more innovative and large projects that include efforts to increase the level of physical activity in entire communities.

*Community-wide efforts*. Two examples of large, community-wide studies are an intervention in Pawtucket, Rhode Island, and a program conducted in Missouri. In the Pawtucket intervention, emphasis was given to changing policy and the physical environment in partnership with the city government. In collaboration with the city's Department of Parks and Recreation, researchers were instrumental in establishing cardiovascular fitness trials in the two city parks. The results of this intervention indicated that it increased the physical activity level in the community.

Community-wide change also was documented in the similar but lower-cost program in Missouri, which emphasized the formation of walking clubs, walking trials, and special events to promote physical activity. The results of this study indicated that physical inactivity declined significantly in the communities that participated, but increased during the same period in the communities that did not participate.

*Interventions at the worksite*. In addition to these large projects, researchers have conducted physical-activity interventions at worksites and school settings, where many people can be reached on a sustained basis. These sites offer employees or students access to exercise facilities and often include supportive social networks that can be enlisted to encourage physical activity.

One example is the Live for Life intervention sponsored by Johnson and Johnson. In this intervention, employees at four sites received health newsletters and participated in exercise programs, physical-activity contests, and lifestyle seminars. Most of the participants were white-collar workers. At the end of 2 years, 30 percent of the men and 20 percent of the women who participated reported that they had initiated a vigorous exercise program compared with 19 percent of men and 7 percent of women in three comparison sites that did not receive the intervention.

To extend the benefits of physical activity to its blue-collar workers, many of whom are sedentary, Johnson and Johnson initiated a multiple worksite intervention. In this program, researchers compared one-on-one counseling and outreach that targeted high-risk employees (while still reaching all general employees) with two less-intensive interventions (provision of a fitness facility and conduct of a company-wide exercise campaign). The results of this study indicated strongly that one-on-one counseling involving discussion of

employees' motivations and barriers to the initiation of exercise was the most effective approach.

*School-based programs*. School-based programs provide some of the best evidence for the effectiveness of interventions to increase physical activity. These programs consistently have enhanced participants' rates of physical activity, particularly when combined with the school's physical and health education curricula.

One example is the Stanford Adolescent Heart Health Program. This classroom-based program involved almost 1,500 10th graders from four high schools. Two schools received the intervention and two comparable schools did not. The intervention focused on physical activity as one of three CVD risk factors. After 2 months, students from the intervention schools showed significantly greater increases in physical activity than students from control schools.

Another study, the Child and Adolescent Trial for Cardiovascular Health, showed similar results. Almost 3,500 students in 96 elementary schools participated. The intervention included a physical-education program as one of four components. After 2.5 years, students participating in the intervention increased both their levels of moderate-to-vigorous physical activity and their vigorous physical activity in physical-education classes, compared with students in the control schools.

Most school-based interventions to increase physical activity have been implemented in elementary schools. Few such studies have been conducted among students in middle schools or high schools. In addition, long-term follow-up data are not available for many of the programs conducted in elementary schools. Rapid declines in physical activity are often observed during adolescence, particularly among girls. To prevent this decline, new interventions need to be designed specifically for adolescents.

One study demonstrates that increasing the physical activity of adolescents is possible and can lead to beneficial health effects. In this study, researchers evaluated three long-term approaches to physical activity among obese children given a control diet. Two of the approaches included moderate exercise combined with a structured aerobics program or a freely chosen exercise activity integrated into the child's lifestyle. The third approach involved calisthenics that required considerably less expenditure of energy. Figure 16 shows that over a sustained period, moderate exercise ("aerobics" and "lifestyle" in the figure) combined with diet, is superior to low-level calisthenics for maintaining long-term weight loss in obese children.

There are many challenges ahead for research in exercise promotion in primary prevention. These include maintaining the positive effects of interventions over time among groups where success has been achieved, and increasing the levels of

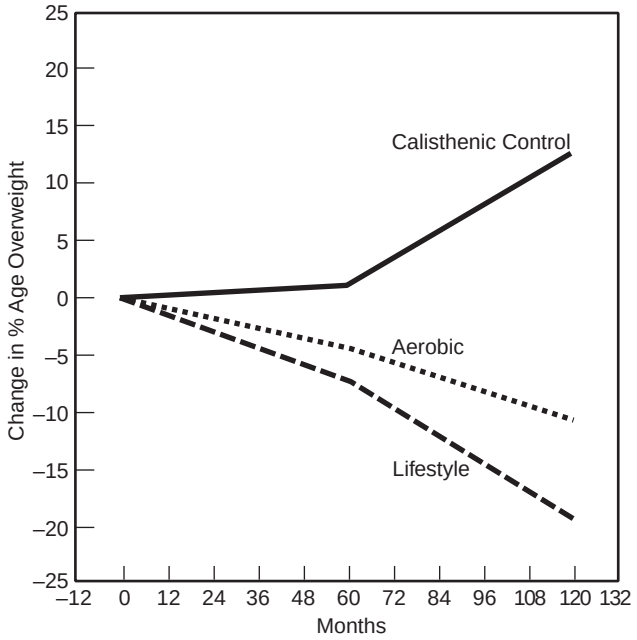


**Figure 16.** Change in percentage overweight after 5 and 10 years of follow-up for obese children randomly assigned to 1 of 3 interventions. Adapted and printed with permission from Epstein LH, Valoski A, Wing RR, and McCurley J. Ten-year outcomes of behavioral family-based treatment for childhood obesity. Health Psychol 1994;13(5):373-383.

physical activity among young people, especially as they approach late adolescence.

## *Exercise Training: Secondary Prevention*

Exercise training benefits patients who have CHD. Besides the effects noted at the beginning of this section, exercise training improves symptoms of angina pectoris in these patients. For patients who have left ventricular (LV) dysfunction, exercise training also can reduce their symptoms of heart failure.

Most important, a meta-analysis of more than 12 randomized controlled trials of patients with CHD showed that exercise rehabilitation reduced the number of deaths among patients by 15 to 25 percent after 3 years. This benefit is comparable to the reductions in mortality obtained among post-myocardial infarction (MI) patients who are pharmacologically treated with beta-adrenergic blockers and among patients who have LV systolic dysfunction and are treated with angiotensin-converting enzyme inhibitors.

The reasons for the reduced risk of mortality associated with exercise in these patients are not known. Exercise rehabilitation may affect certain risk factors for CHD (e.g., improve blood pressure and lipid levels, reduce cigarette smoking, reduce psychological stress). It may also reduce blood clotting time and increase the thresholds for triggers of acute cardiac events (e.g., strenuous physical activity, psychological stress).

Despite these benefits, fewer than 20 percent of the CHD patients who are eligible for exercise rehabilitation participate in these programs. Most of the programs are offered in hospitals, the traditional setting for outpatient cardiac rehabilitation. A typical program lasts for 12 weeks and is available to patients who have had an MI, coronary artery bypass surgery, or percutaneous transluminal coronary angioplasty. Appropriate medical supervision is provided, and electrocardiographic monitoring may be used for high-risk patients.

Other settings for group-based cardiac rehabilitation include universities and community-based organizations, such as the YMCA. For individuals at low and moderate risk of a recurring CHD event, home-based programs have been effective. These programs improve patients' functional capacities and reduce their CHD risk factors. Home-based programs also may be an appropriate alternative for patients who either cannot or prefer not to access more formal services.

## *Research Opportunities*

Recent recommendations for physical exercise emphasize accumulating at least 30 minutes of activity on most days of the week. The greatest effect in reducing mortality, however, appears to occur with the shift from a totally sedentary lifestyle to one of modest activity. Because 25 percent of Americans do not engage in any physical activity, strategies that promote exercise need to be developed for the general population (e.g., in schools or workplaces), for individuals at high risk for CVD, or for those already experiencing cardiovascular problems such as hypertension.

Increased physical activity among elderly persons may help them maintain their functional abilities and reduce risk of morbidity and mortality from cardiovascular and pulmonary diseases. The type and amount of activity that will maximize these benefits need to be determined, and strategies that encourage elderly persons to adopt and maintain recommended activity levels need to be evaluated.

Levels of physical activity typically decrease between childhood and adulthood, and marked decreases occur during adolescence and young adulthood. The developmental periods when individuals decrease their levels of activity need

to be specified so that researchers can develop interventions to reduce or prevent these declines.

Recently, researchers have focused not only on physical activity, but also on sedentary activity. During the past 10 to 20 years, the amount of time that individuals spend in sedentary activities (e.g., watching television) has increased markedly. This increase in sedentary activity may be one reason for the increased prevalence of obesity observed in the United States. Research shows that overweight children spend a disproportionate amount of their leisure time in sedentary activities.

Development of innovative strategies for increasing the motivation of sedentary children and adults to reduce their sedentary activities would be very useful. A recent study indicated, for example, that an intervention focused on decreasing sedentary activity among overweight children may be more effective for weight loss than an intervention focused on increasing physical activity.

Individuals frequently state that they do not exercise or are not able to maintain an exercise program because it is inconvenient or because they are concerned about safety (e.g., when jogging outdoors). By altering the physical environment, such as creating onsite exercise facilities or biking and walking paths, communities and workplaces can encourage individuals to adopt and maintain regular exercise regimens. The value and effectiveness of different environmental changes in promoting exercise within communities and workplaces need to be evaluated.

### *Recommendations*

Recommendations for behavioral research on interventions to increase physical activity are:

1. Assess the effectiveness of individual and community-based interventions (e.g., in schools, at worksites) for promoting diverse populations' adoption and long-term maintenance of the levels of physical activity that are most effective for reducing morbidity and mortality from CHD.
2. Identify ways to increase physical activity among elderly persons to help them maintain their functional status and reduce the potential morbidity and mortality from CHD.
3. Identify key times (e.g., adolescence, young adulthood, older ages) when individuals shift from higher to lower levels of physical activity, and develop interventions to prevent these shifts.
4. Develop strategies to decrease sedentary behavior among children and adults, and compare the effectiveness of efforts to decrease sedentary activity with that of efforts to increase physical activity in terms of their relative impact on long-term exercise behaviors and clinical outcomes.
5. Assess the effectiveness of psychosocial and other environmental changes (e.g., development of bike paths) for increasing the level of physical activity.

## Diet

Studies conducted in hospital metabolic wards clearly demonstrate that a decreased intake of saturated fat and dietary cholesterol can lower serum cholesterol levels. Based on this evidence, behavioral researchers have undertaken many studies of diet modification in noninstitutionalized, free-living adults. The aim of these studies is to reduce cholesterol levels and risk for CHD.

Researchers have pursued two approaches for noninstitutionalized populations: intensive, individualized interventions (e.g., for individuals at high risk of CHD) and population-based programs that are based in the community, school, or workplace. The results of this research are summarized below.

## *Individualized Interventions*

Intensive, individualized interventions to reduce fat intake have been targeted at unselected individuals with a normal risk of CHD (e.g., Women's Health Trial), persons at high risk for CHD (e.g., Multiple Risk Factor Intervention Trial, Oslo Primary Prevention Trial), and persons with documented CHD (e.g., St. Thomas Atherosclerosis Regression Study Lifestyle Heart Trial). In general, these studies show that a decreased fat intake reduces serum cholesterol levels by 5 to 17 percent. The results of several of these studies, especially the more intensive interventions for high-risk individuals, equal the results expected from studies conducted in metabolic wards. In addition, the results indicate that the effects of a dietary intervention are greatest when participants also lose weight, and that HDL cholesterol levels can be maintained by participants' loss of weight and increased exercise.

Research also shows that a very-low-fat diet (i.e., less than 10 percent of calories from fat) results in regression of angiographically documented CAD when included in an intensive intervention that involves exercise, smoking cessation, social support, and stress management. The effectiveness of this intervention indicates that making dramatic changes in the diet (reducing fat to as low as 10 percent) may be an appropriate goal for some patients with CAD. Patients' adherence is important, however. The effects of this intervention on stenosis of the coronary arteries were related to the participants' adherence to the lifestyle-modification program (see figure 17).

Of the numerous angiographic trials conducted to evaluate the effects of lipid-lowering drugs on regression of atherosclerotic plaques, only three included diet modification or diet modification with lifestyle change. In these three studies, the effects of dietary interventions were comparable to the effects achieved with lipid-lowering drugs.

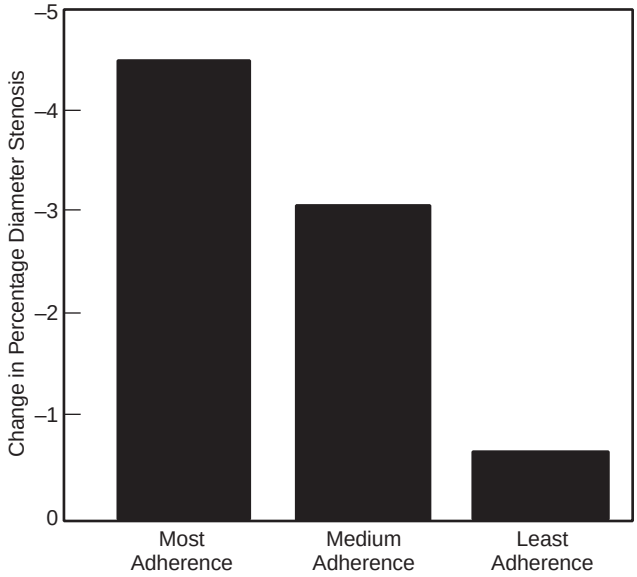


**Figure 17.** Relationship between overall adherence to low-fat vegetarian diet, moderate exercise, smoking cessation, support group participation, and stress management and change in percentage diameter stenosis after 12 months in patients with angiographically documented coronary artery disease. Adapted and reprinted with permission from Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, McLanahan SM, Kirkeeide RL, Brand RJ, and Gould KL: Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. Lancet 1990;336(8708)129-133.

Family interventions may also be especially useful because the risk factors for CHD tend to cluster in families and track from childhood to adulthood. Evidence indicates that the clustering of CHD risk factors is due to both genetics and shared environment (including diet). Therefore, researchers are developing behavioral interventions that specifically target hypercholesterolemic children and their parents.

The major challenge for dietary interventions is maintaining the changes made in eating behavior over time. Encouraging spousal support and maintaining frequent contact with patients help maximize patients' adherence to a dietary regimen. Also, involving entire families in an intervention may help establish permanent changes among children. Studies also show that making program regimens highly prescriptive and structured promotes adherence.

For treatment of hyperlipidemia, dietary interventions are the first approach used, and medications are added only if lipid levels remain elevated. If drug treatment is initiated first, patients' adherence to a low-fat eating regimen may decline, and their overall long-term improvement may be less than the improvement possible with pharmacological therapy combined with a low-fat diet.

## *Population-Based Strategies*

Population-based interventions to prevent CHD that include dietary strategies are designed to increase awareness of the risk factors for CHD and to produce changes in these risk factors. These community-level interventions, however, have been less effective in accomplishing these goals than intensive, individualized approaches.

Three major community-based studies are noteworthy: the Pawtucket Heart Health Project (Rhode Island), the Stanford Five-City Project (California), and the Minnesota Heart Health Program (Minnesota). All of these studies included reduced fat intake as a goal. Although the studies achieved this goal and a reduction in serum cholesterol levels, their results reflected changes that were also observed in the general population within the communities, rather than evidence for the effectiveness of the specific intervention strategy.

Interventions at worksites and at points of purchase (e.g., grocery stores) to improve knowledge about the relationship between diet and health have been successful in reducing serum cholesterol levels and have been modestly successful in improving knowledge. School-based programs have been successful in modifying the sodium and fat content of school meals prepared by dieticians.

The results of several ongoing studies to increase young children's consumption of fruits and vegetables suggest that the food preferences of children and the availability of foods must be changed in order to increase the children's intake of fruits and vegetables. In one study, the consumption of these food items was influenced markedly by reducing their cost and increasing the variety of foods offered. These findings suggest that manipulations of the environment may be more effective for changing eating behaviors than educational interventions.

Researchers are also exploring cost-effective approaches that deliver dietary interventions in physicians' offices and health care maintenance organizations. Studies in these settings show that minimal interventions (e.g., phone calls or mailings to patients, referrals of patients to nutrition professionals) can have positive effects.

## *Research Opportunities*

Dietary strategies that are most effective for modifying the risk factors for CHD warrant further investigation. Studies should include the following: (a) improving understanding of the types of foods that should be consumed or avoided for greatest health benefit, and (b) evaluation of strategies for effecting behavioral changes.

Strategies for promoting long-term changes in dietary behavior also need to be identified. Studies of the relative contribution of biological and behavioral adaptations to these long-term changes (e.g., in patients with different types of hyperlipidemia) will be particularly useful. Because of increased use of medications to treat hyperlipidemia, the effects of this treatment on patients' adherence to a dietary regimen need to be understood, and ways to maximize their long-term adherence to a combined regimen of diet and medication need to be identified.

Efforts also are needed to supplement community-based interventions with other approaches, such as modifying the cost and availability of healthful foods served in schools, worksites, and other community settings. These additional efforts are likely to enhance the modest effects of these

interventions in reducing fat intake and serum cholesterol levels.

Cost-effective approaches specifically need to be developed and evaluated for modifying the dietary intake and cholesterol levels of individuals at high risk of CHD. This research, which will be important for the evolving managed-care environment, should be aimed at identifying the most effective approaches, and at assessing the role of physicians, other health care professionals, and nonprofessionals (e.g., peer counselors) in implementing these approaches.

Studies of the interaction between diet and the genetic aspects of disease are also needed. These studies offer an opportunity for defining specific dietary interventions for individuals with different lipid disorders (e.g., types of hyperlipidemia). These studies are now possible because of the ability to identify genetic polymorphisms associated with different lipid disorders.

### *Recommendations*

Recommendations for behavioral research on dietary interventions are:

1. Determine the dietary components that should be recommended to reduce the risk for CHD, and identify effective approaches for encouraging individuals to adopt the recommended diet.
2. Investigate behavioral strategies that may promote long-term adherence to a diet that is low in saturated fats and cholesterol for the general population and for individuals taking lipid-lowering medications.
3. Evaluate the effect of community-based behavioral strategies (e.g., modifying the cost and availability of low-fat foods) on patterns of dietary consumption and levels of cholesterol.
4. Develop cost-effective approaches to be used in managed-care settings for modifying the diets of individuals at high risk for CHD.
5. Study the interaction of genetic and behavioral (dietary) factors for the prevention and treatment of lipid disorders.

## Obesity

Research on interventions for the national problem of obesity is aimed at preventing individuals in the general population from becoming overweight and treating individuals who are already overweight. As noted in Part I, one out of every three Americans is overweight, and prevention of obesity could save $50 billion to $70 billion each year in health care costs. Another $33 billion is spent each year in the United States on weight-reduction products, including diet foods and drinks.

### *Primary Prevention of Obesity*

Interventions to prevent obesity, which have been focused on communities, worksites, and schools, have had little effect on individuals' body weights. In the three community-based efforts mentioned previously (Pawtucket Heart Health Project, Stanford Five-City Project, and Minnesota Heart Health Program), weight control was included as a means of lowering individuals' cholesterol and blood pressure levels. Prevention of weight gain and treatment of obesity were both included in these interventions.

Analyses of the cohorts participating in these studies showed no effect of the interventions on individuals' body mass index. Cross-sectional analyses, however, showed some benefit in the Stanford and Pawtucket programs. Worksite interventions have had similar, limited effects on reducing body weight.

No major studies have been conducted to prevent weight gain in children or adults who are at high risk for gaining weight or becoming obese. Information on the ages when primary prevention could be particularly appropriate is available, but researchers have made little effort to focus on these time periods. Research exploring possible causes of weight again (e.g., decreased physical activity, pregnancy, menopause, smoking cessation, biological factors, stress) is also sparse.

Success in treating children who are already overweight deserves to be highlighted. If left untreated, these children become overweight adults. Several controlled studies have been conducted with overweight children 8 to 12 years of age. These studies show that by participating in weight-loss programs that include diet, exercise, and behavior modification and that involve the overweight parent, children can successfully reduce their degree of overweight *and* maintain this achievement for 10 years after the intervention. Treatment of overweight adults, however, has been far less successful than treatment of overweight children.

## *Weight-Loss Strategies*

The recommended treatment for individuals who are already mildly to moderately obese is a behavioral program that includes diet, exercise, and training in behavioral techniques. Individuals participating in these interventions lose an average of 8.9 kg during a 20-week program, but then tend to regain a third of the weight they had lost initially at the end of 1 year. Few studies, however, have followed participants longer than 1 year. Better maintenance of weight loss over longer periods of time is a challenge that needs to be addressed by further research.

Figure 18 shows that long-term maintenance programs involving several management strategies are more successful in helping moderately obese individuals maintain weight loss than single-

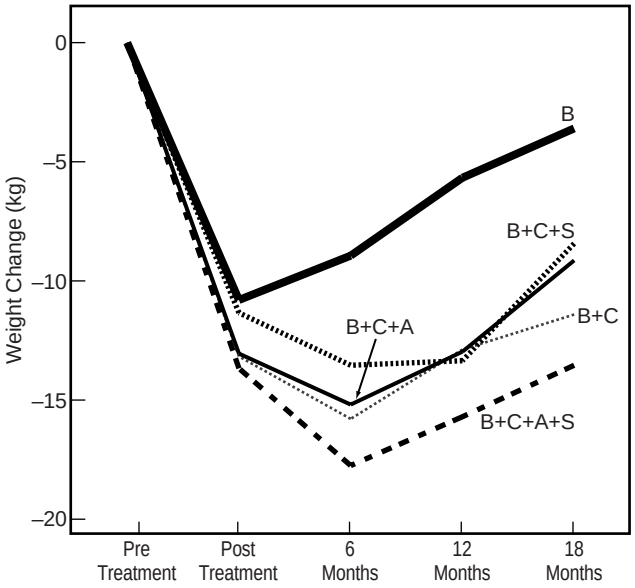


**Figure 18.** Effect of maintenance programs compared with behavior therapy (B) alone on the long-term management of obesity. Note: Treatment programs include C = Posttreatment therapist contact; A = aerobic exercise maintenance program; S = social influence maintenance program. Adapted and reprinted with permission from Perri MG, McAllister DA, Gange JJ, Jordan RC, McAdoo WG, and Nezu AM: Effects of four maintenance programs on the long-term management of obesity. J Consult Clin Psychol 1988;56(4):529-534.

treatment programs relying on behavioral therapy alone.

Better maintenance of weight loss is obtained in programs that include more frequent contact with participants, a combination of diet and exercise, and behavioral strategies such as self-monitoring and prevention of relapse. Very-low-calorie diets (i.e., less than 800 kcal per day) result in greater initial weight loss, but effect no long-term improvements. Some participants in treatment programs achieve much greater weight losses than others, but predicting who will succeed at weight loss or long-term maintenance is not yet possible. Studies show, however, that the persons most likely to succeed continue to record their diet and exercise regimens and continue to exercise and eat a healthy diet.

Weight losses obtained in treatment programs, although modest, are effective in lowering blood

pressure levels and reducing risk factors for CHD. If participants achieve and maintain their weight loss, they will also maintain improvements in these risk factors.

Pharmacological approaches for treating obesity are being developed. Currently, most of the medications act by decreasing dietary intake. Drug treatments for obesity appear to be most effective when included in a broader program of diet, exercise, and behavior modification. The greatest effect of these medications on body weight occurs at 6 months, and some participants respond to the drugs more than others.

However, in the few studies lasting at least 1 year, the effects of medications on body weight were only minimally superior to the effects of interventions without medication. In addition, medications must be used for a long time because individuals regain their weight rapidly after the medications are discontinued. Because of the potential serious side effects of the medications that are available and because long-term data on their effects are limited, use of medications cannot be recommended without caution.

Surgery is an option for patients who are morbidly obese. Surgical procedures are used to create a smaller stomach pouch or to cause malabsorption, and these procedures are often combined. In approximately 50 percent of the patients treated, the procedures result in a loss of more than 50 percent of the patient's initial weight.

### *Research Opportunities*

More effective long-term treatments for obesity are urgently needed. Research efforts should be devoted to understanding why initially successful efforts at weight loss are later abandoned. The difficulty of producing long-term changes in eating and exercise behaviors may be a factor. Clues to successful long-term weight loss may be uncovered by carefully studying persons who have successfully lost weight.

Despite much research on the behavioral treatment of obesity, little is known about the type of diet that should be recommended, the type and amount of exercise needed, and the most effective use of pharmacological treatments. Whether preferences for high-fat foods and sedentary activities need to be modified is not clear, nor is the most effective approach for changing these preferences known.

Much information is already available about the risk factors for obesity. This information will be complemented by further genetic studies. Known risk factors include a family history of obesity, gestational diabetes in the mother, low socioeconomic status, and low metabolic rate.

The behavioral and physiological changes that occur during high-risk periods for weight gain (e.g., between 25 and 34 years of age, following smoking cessation) need to be clarified. This information could then be used to design intensive, individualized interventions to prevent weight gain and future obesity in individuals at high risk for gaining weight. The other predictors of weight gain, including stress and pregnancy, also need to be evaluated to determine the best approaches for apprising individuals that they are at risk and to develop cost-effective prevention strategies.

The overweight American population includes many groups that could benefit from targeted treatment strategies. Because obesity disproportionately affects minorities and persons of low socioeconomic status, more effective approaches are especially needed for preventing and treating obesity in these populations. Racial and ethnic differences in metabolic and behavioral factors related to obesity and in the effect of obesity on risk for CHD should be examined.

No prospective, controlled study has been conducted to investigate the effect of weight loss on obesity-related morbidity (e.g., diabetes, CHD, cancer) and mortality, despite compelling evidence

that obesity is associated with subsequent morbidity and mortality. Many studies show that weight loss lowers CHD risk factors, but this effect has not been demonstrated in a clinical trial. Because of the prevalence of obesity among Americans and the substantial information on the relationship between obesity and morbidity and mortality from CVD, a rigorous study should be launched to obtain the data needed to support a major national campaign to reduce Americans' body weights.

### *Recommendations*

Recommendations for behavioral interventions to prevent or treat obesity are:

1. Identify the factors important for maintaining long-term weight loss. Determine why individuals who are initially successful in losing weight later regain weight.
2. Develop new approaches for treating individuals who are overweight. Identify the most effective ways to change eating and exercise behaviors and to combine behavioral and pharmacological interventions.
3. Identify key time periods and individuals at risk for obesity, and elucidate ways for intervening against major weight gains to prevent obesity in individuals at high risk for it.
4. Develop treatment and prevention approaches for specific groups of overweight persons such as minority women and individuals of low socioeconomic status.
5. Determine whether weight loss decreases morbidity and mortality from CVD in overweight individuals.

## Alcohol Abuse

Use or abuse of alcohol has been linked to a number of CVD risk factors and disorders. For example, cross-sectional and prospective studies have established that alcohol intake affects blood pressure levels. Use of alcohol accounts for more than 10 percent of the hypertension observed in men—an effect that is as strong or stronger than the effect of salt intake. In addition, increased intake of alcohol may occur with other behavioral risk factors for CVD, such as hostility and depression, and alcohol may have a particularly pronounced effect on the blood pressure levels of persons who have high-stress jobs.

Use of alcohol also has many detrimental health effects. For example, heavy alcohol consumption may lead to acute disturbances of cardiac rhythm in the absence of other signs of heart disease. Long-term abuse of alcohol is also associated with sudden cardiac death. After abstinence, risk of death is reduced in patients with cardiomyopathies.

### *Effects of Interventions*

Many of the detrimental effects of alcohol use can be reduced or reversed by stopping alcohol intake. For example, abstinence reduces the risk of death in patients with cardiomyopathies, and long-term withdrawal from alcohol use can significantly reduce blood pressure levels in normotensive and hypertensive individuals. The combination of alcohol withdrawal and restricted caloric intake may additionally reduce both blood pressure and triglyceride levels. All these results suggest that prevention and treatment of alcohol abuse can reduce cardiovascular morbidity and mortality significantly.

Most intervention studies to reduce or eliminate use of alcohol have been limited to individuals who consume more than six drinks a day. The effects of these interventions, however, could benefit other individuals who initially consume lesser amounts.

### *Preventing Relapse*

Various counseling interventions for problem drinking have been used for decades, but their efficacy has only recently been clearly demonstrated. Similar to individuals who are treated for smoking and use of other drugs, most individuals who complete treatment for alcohol abuse relapse within several years. Maintaining abstinence from alcohol after achieving initial cessation is a critical problem.

Frequently, heavy use of alcohol is associated with other behaviors such as smoking and adverse diet. The existence of these multiple risk factors complicates efforts to intervene with these patients. Only limited knowledge exists about possible approaches to making lifestyle changes that address alcohol withdrawal and abstinence as well as the "standard" risk factors for CVD (e.g., smoking, hypertension, physical inactivity).

Recently, counseling has been focused on changing specific behaviors associated with alcohol use. For example, a skills-training approach has been used to teach alternative behaviors for coping with specific situations that are likely to elicit urges to drink. This approach can reduce the likelihood of alcohol consumption in these situations.

Development of effective pharmacological interventions for alcohol abuse also has been a prominent research objective. Available treatments include disulfiram, naltrexone, anxiolytics, and selective serotonin reuptake inhibitors. Some of these, however, interact undesirably with cardiac medications.

Abuse of multiple drugs also is extremely common among individuals who abuse alcohol. Many alcoholics, therefore, require interventions for several drug abuse problems. Whether abuse of all other drugs and all CVD risk factors should be treated simultaneously with alcohol abuse or whether, and in what order, these problems should be treated separately is not known. Effective treatment for alcohol use and abuse, using various modalities, must be integrated with treatment for existing cardiovascular conditions and other behavioral risk factors.

### *Research Opportunities*

More information is needed about the effectiveness of alcohol withdrawal on blood pressure levels and other CVD risk factors and conditions. It is not clear which individuals would benefit most from intervention and which strategies would be most effective. Possible suitable candidates for alcohol withdrawal programs might include individuals with other psychosocial risk factors for CVD (e.g., a high-stress occupation, mood disorders).

With the continued development of effective pharmacological therapies for alcohol abuse, there will be an increasing challenge to integrate appropriate biological therapies and behavioral interventions for alcohol abuse with treatment of CVD.

Rates of relapse continue to be high among heavy users of alcohol, and greater efforts are needed to develop effective approaches for preventing relapse. This challenge pertains not only to alcohol use, but also to all behavioral risk factors for CVD. Recent reviews suggest that the cardiovascular benefits of preventing relapse emerge gradually and may not be observed immediately after intervening. This finding indicates that efforts to modify alcohol use and to reduce other CVD risk factors should be complementary. Additional research is needed to improve understanding of the relationship between changes in alcohol use and in other CVD risk factors, including the interactions between the biological and psychosocial factors involved.

### *Recommendations*

Recommendations for behavioral interventions to prevent or treat alcohol abuse are:

1. Encourage short- and long-term studies of the effects of alcohol withdrawal on blood pressure levels and other CVD risk factors and conditions to determine which individuals benefit most from the intervention and how best to treat other psychosocial risk factors in patients with CVD.
2. Evaluate the effectiveness of intervention approaches that include multiple components, such as combined use of pharmacological therapy and behavioral interventions.
3. Expand use of maintenance or relapse-prevention approaches in programs that integrate treatment of alcohol use with treatment of other CVD risk factors.

## Behavioral Issues in the Management of Disease

The association of behavior with cardiovascular and pulmonary diseases is well described in Part I of this report. In the present section, the Task Force addresses behavioral aspects of interventions to improve the management of CHD, chronic lung diseases, sleep disorders, blood diseases, and the nation's blood supply and usage. Research on interventions for both primary and secondary prevention is considered.

### Coronary Heart Disease

Coronary heart disease is the leading cause of death and disability in the United States. As we described in Part I, a significant proportion of CHD is caused or exacerbated by behavioral factors, including high-risk behaviors (e.g., smoking, diet, physical inactivity) and psychosocial risk factors (e.g., social isolation, depression, hostility). High blood pressure is also a significant and modifiable risk factor for CHD. The major behavioral risk factors associated with hypertension include obesity, intake of salt and alcohol, and exposure to chronic stress.

Interventions to alter these risk factors can lower blood pressure levels and the risk of recurrent disease in persons who have established CHD. These interventions also may aid in preventing the development of CHD in healthy individuals.

#### *Primary Prevention*

Behavioral research on primary prevention interventions to alter risk behaviors associated with the development of CHD has been considerable. These interventions, targeted to specific risk factors, include, for example, smoking cessation, diet modification, and exercise promotion.

In addition to this risk-specific research, an important model of primary prevention has emerged during the past decade that involves modifying multiple risk factor behaviors within an entire community by educational and environmental interventions. The first generation of these studies has been completed, and their results have been published. The studies include the three large demonstration projects cited earlier: the Pawtucket Heart Health Project, the Stanford Five-City Project, and the Minnesota Heart Health Program. As noted previously, because of the strong general trends toward favorable changes in risk factors and health behaviors, these large demonstration projects did not yield clear evidence that the interventions resulted in reduced overall measures of CHD risk (see the sections on Diet and on Obesity under Risk Factor Interventions).

In these studies, some program components were evaluated independently, however, and were found to be effective. These included innovations such as (a) contests and competitions to encourage participation in programs for smoking cessation, weight control, and physical activity and (b) point-of-purchase messages in grocery stores and restaurants.

Smaller "communities" also have been productive arenas for delivering interventions targeting multiple risk factors. Worksites, schools, churches, and community centers offer the advantages of a shared social environment and group cohesiveness. Minority, cultural, and other groups also constitute important social structures where health promotion programs can have significant effects. These naturally occurring social groups offer opportunities for conducting nutritional interventions, implementing health-oriented policies such as restrictions on smoking, and sharing information through communication channels such as newsletters or group meetings.

Several programs at worksites and schools have resulted in changes in participants' risk factors for CHD. Individuals who have participated in intensive interventions within these settings have improved their nutritional habits, lost weight, or reduced their cigarette smoking. Few programs have demonstrated positive effects on an entire social group such as a company workforce. Studies are just beginning to evaluate the impact of interventions aimed at improving individuals' ability to cope with stress. These studies include those examining worksite stress programs and their effects on psychosocial, hemodynamic, and neuroendocrine indicators of stress.

## *Secondary Prevention*

Improved survival rates for individuals with initial manifestations of CHD have resulted in a large number of adults at risk for increasing disability due to their existing disease. An estimated 13.5 million Americans have angina pectoris or a history of acute MI. Another 4.7 million have heart failure, and more than 500,000 undergo major heart procedures (e.g., coronary artery bypass surgery, percutaneous transluminal coronary angioplasty) each year.

Several randomized clinical trials have included behavioral interventions to ameliorate the effect of risk factors on the prognosis of patients with CHD. Overall, the results of these trials indicate that behavioral interventions to reduce recurrence of CHD are very promising. Indeed, one quantitative review of psychosocial intervention studies conducted in over 2,000 CHD patients concluded that these interventions reduce morbidity and mortality above and beyond standard cardiac rehabilitation regimens.

Studies show that interventions to modify psychosocial risk factors, including stress, improve risk profiles and quality of life for cardiac patients. Preliminary evidence also indicates that an intensive behavioral program that combines stress management with dietary modification and exercise can promote the regression of coronary atherosclerosis.

In one randomized clinical trial, the Recurrent Coronary Prevention Project, researchers evaluated the effect of a behavioral intervention to reduce stress on the prognosis of patients with CHD. The intervention consisted of a number of behavioral strategies (i.e., learning to identify stressful situations, to modify habitual responses to these situations, and to relax) administered in a group setting. The group of patients participating in the intervention experienced nearly a 50 percent reduction in the recurrence of a CHD event, compared with the group of patients that did not participate in the intervention and received usual care.

Another recent study demonstrated that stress management and exercise interventions reduced the occurrence of myocardial ischemia, and that these interventions lowered the risk of other cardiac events as well. These benefits, compared to usual care controls are shown in figure 19. In this study, 107 heart disease patients were assigned to a 4-month program of either stress management or exercise training. A usual care comparison group served as a control. Stress management was also associated with reduced ischemia both during daily life and during laboratory mental stress testing.

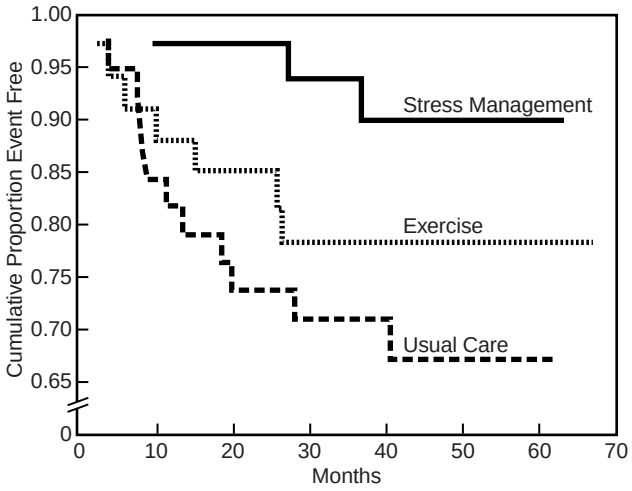


**Figure 19.** Time-to-event curves for exercise, stress management, and usual care interventions in cardiac patients with ischemia. Reprinted with permission from Blumenthal JA, Jiang W, Babyak MA, Krantz DS, Frid DJ, Coleman RE, Waugh R, Hanson M, Appelbaum M, O'Connor C, and Morris JJ: Stress management and exercise training in cardiac patients with myocardial ischemia. Arch Intern Med 1997;157(19):2213-2223.

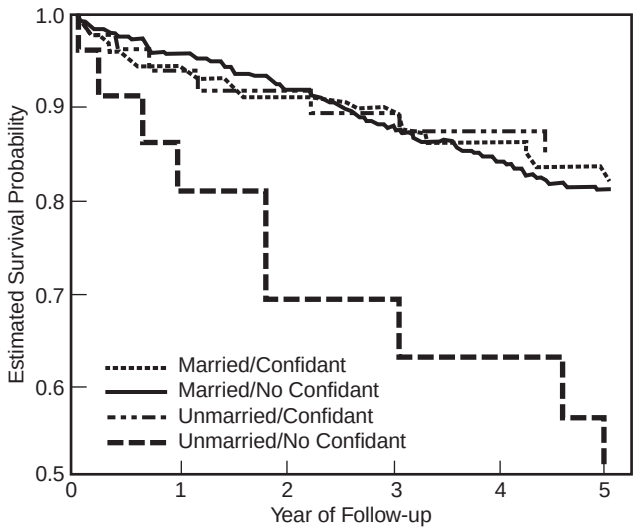


**Figure 20.** Survival curves for patients with significant coronary artery disease subgrouped by marital status and presence of a close confidant. Reprinted with permission from Williams RB, Barefoot JC, Califf RM, Haney TL, Saunders WB, Pryor DB, Hlatky MA, Siegler IC, and Mark DB. Prognostic importance of social and economic resources among medically treated patients with angiographically documented coronary artery disease. JAMA 1992;267(4):520-524.

Reducing a patient's social isolation may also reduce morbidity. Epidemiological research shows that patients with documented CAD who are extremely socially isolated (i.e., unmarried and lacking a close confidant) experience a 5-year mortality rate that is three times higher than the mortality rate among patients who are not so socially isolated (see figure 20).

A clinical trial conducted in Montreal also indicates that providing male CHD patients with social support in the form of a nurse who helps them deal with problems that arise may improve their prognosis; however, this outcome was not replicated in a recently completed, randomized trial. Other studies demonstrate that giving patients support (e.g., through group meetings and skills training in communication, assertion, and conflict resolution) helps them establish more supportive relationships and improves their prognosis for CHD. As yet, researchers have not identified how these benefits are achieved by these types of interventions. The effectiveness of the interventions for different types of patients, lengths of treatment, and specific medical diagnoses also needs to be defined.

Reducing depression also may reduce morbidity from CHD. As demonstrated by large clinical trials, cognitive behavior therapy and pharmacological therapy are effective treatments for depression and, when combined, appear to be especially effective for reducing the recurrence of depression. Trials of secondary prevention that include psychotherapy and pharmacological therapy to treat depression in CHD patients are under way.

*Multifactorial interventions*. Efforts to improve serum lipid levels and other risk factors for CHD include the use of lipid-lowering drugs, education, counseling, behavioral and psychosocial strategies, and lifestyle interventions. In some studies, researchers have targeted multiple risk factors and have included multiple interventions. The effects have been positive in these studies but need to be examined further.

An increasing number of clinical trials demonstrate that the use of lipid-lowering drugs to reduce serum lipid levels in CHD patients significantly slows or reverses atherosclerosis and decreases the number of fatal and nonfatal reinfarctions in these patients. The research literature also documents significant benefits from interventions that combine education about risk factors, counseling, and, in some cases, behavioral strategies. These combined interventions have improved the risk factor profiles (smoking, physical activity, serum lipid levels, and weight) of CHD patients. In addition, several randomized trials of educational and behavioral interventions targeting multiple risk factors have reduced total mortality in these patients. The relative contributions of lipid-lowering drugs and of lifestyle changes to these positive outcomes have not been delineated, however. This information has not been obtainable because of the design of the studies conducted.

Interventions that reduce serum lipid levels by strict adherence to low-fat diets, sometimes in combination with other approaches such as exercise and stress management, also slow or reverse the development of atherosclerotic plaques. The effects of these interventions are similar in magnitude to the effects achieved with the use of lipid-lowering drugs. These results are impressive, but because the studies were small, the results need to be replicated to confirm whether these types of lifestyle interventions can yield benefits similar to those achieved with lipid-lowering drugs.

The goal of this research is important, especially because a large proportion of the population cannot or will not take medications to lower their lipid levels. Indeed, persuasive evidence indicates that patients' adherence to drug regimens is as difficult as their adherence to lifestyle changes.

Because the evidence for the benefits of psychosocial interventions, education, and behavioral strategies is strong, these interventions are recommended for the management of patients with CHD. However, national data indicate that few of these patients participate in these types of interventions. Continued efforts are needed to evaluate the efficacy of these approaches and to establish methods for increasing the participation of CHD patients in these programs.

### *Research Opportunities*

Interventions to improve the psychosocial risk factors of patients with CHD need to be evaluated in secondary prevention studies using a randomized clinical trials methodology. These types of studies rely on smaller sample sizes than large, community-based efforts in primary prevention and take advantage of the enhanced motivation of patients with evidence of an increased risk for CHD. Based on the results of preliminary studies, these trials should test the efficacy of interventions that incorporate, for example, various combinations of cognitive behavioral approaches, training in coping skills, and pharmacological treatment as indicated.

Evaluations of the effect of psychosocial and comprehensive behavioral interventions that integrate stress management, dietary modification, and exercise on the secondary prevention of CHD are lacking. Studies of these effects in women and minority groups, in particular, have not been conducted.

Alternative intervention strategies may need to be developed and tailored to optimize the benefits for different sociocultural and demographic groups. Such strategies should take into account differences in risk of disease, mechanisms of an intervention's effect, and impediments to achieving adherence and long-term maintenance of behavior change. These differences may affect the emphasis needed in each intervention and should be investigated.

The development and validation of technology for evaluating surrogate end points (e.g.,

angiograms, measures of myocardial perfusion or contractile function) enable researchers to assess the effects of treatment for CHD more rapidly and at less cost than was previously possible. These methods need to be applied to evaluating the efficacy of lifestyle changes. Clinical trials to assess the effect of lifestyle interventions should include examination of the changes in psychosocial risk factors, smoking, physical activity, serum lipid levels, and central nervous system responses to stress. By studying these changes simultaneously, researchers can clarify the importance of interventions' components and thereby improve their cost-effectiveness.

The large, community-based demonstration projects referenced earlier experienced difficulties in evaluating their success partly because of ongoing favorable changes in risk factors and health behaviors among the general population. However, not all communities and sociocultural groups have made these changes to the same degree. In fact, CHD mortality and morbidity differentials between low- and high-socioeconomic-status groups have widened. Investigations of the potential of community and group interventions to decrease risk factors and to reduce the effect of disease on low-income, socially disadvantaged, and minority groups are therefore increasingly important.

As noted, studies show that psychosocial factors increase an individual's risk for CHD and that modification of these factors reduces the risk for progression or recurrence of disease in persons who already have CHD. Examination of the effects of interventions to prevent the onset of psychosocial risk factors is therefore timely. These interventions should build on the strategies and findings of current trials of patients with CHD. The outcomes of these studies could include changes in psychosocial risk factors or changes in related risk factors (e.g., diet, smoking, neuroendocrine reactions to stress) that may be pathways for the increased risk from psychosocial factors.

### *Recommendations*

Recommendations for research on behavioral interventions to improve the management of CHD are:

1. Evaluate the effect of psychosocial and behavioral interventions to decrease psychosocial risk factors in adults with CHD. Examine the effects of these interventions on health behaviors and CHD end points (e.g., angiographic evidence of CHD).
2. Evaluate the effect of psychosocial and lifestyle interventions tailored for women and for low-income and minority persons who have CHD.
3. Evaluate the effect of lifestyle interventions on the risk factors for and manifestations of CHD.
4. Conduct pilot, feasibility, and targeted intervention studies of new models for community and other group-based programs for reduction of CHD risk factors in disadvantaged, minority, and low-socioeconomic-status groups.
5. Conduct preliminary studies to examine the feasibility of interventions for primary prevention of psychosocial risk factors (e.g., depression, stress, social isolation) for CHD.

## Chronic Lung Diseases

Chronic lung diseases affect 29 million Americans and a significant amount of behavioral research has addressed issues of disease management for COPD, asthma, and tuberculosis. Researchers have focused on improving the ability of patients, families, and health professionals to manage these diseases. Much more limited but promising research has addressed behavioral issues in managing CF.

Restrictive airway diseases (e.g., sarcoidosis, bronchiolitis), which limit airway expansion and may obliterate airway elasticity, are also significant health problems. However, the behavioral factors associated with these disorders have not been examined. Occupational lung diseases, including white lung, black lung, occupational asthma, and asbestosis, are also serious conditions, but they have also been given little attention and deserve further study.

The status of behavioral research on asthma, COPD, CF, and tuberculosis is summarized below. Research opportunities and recommendations follow.

## *Asthma*

Asthma is an inflammatory obstructive airway disease characterized by acute episodes of bronchial spasm. Morbidity and mortality from asthma have increased during the past 20 years and appear to be disproportionately high among minority populations. The reasons for these differences in morbidity and mortality are not clear, but they may be due to race, culture, social factors, income level, physical environment, or access to quality health care. Gender differences in causes and patterns of symptoms and in self-management have also been evident in recent studies.

Asthma is prevalent across the lifespan; however, the relevant issues in managing asthma vary for different ages and stages of development. These issues include avoiding and controlling allergens and triggers of asthma, self-monitoring of symptoms and airway flow, and appropriately managing acute symptoms. Asthma is a chronic disease that includes periods of acute symptoms. Because patients' adherence to preventive medications is often poor, promoting adherence is an important objective of all interventions to improve self-management of the disease.

*Asthma self-management.* A growing body of research addressing these issues suggests that adults and parents of children with asthma can learn to improve their management techniques and realize greater control over the disruption asthma causes. Researchers have demonstrated that self-management education offered in the clinic and other settings can improve outcomes, including control of symptoms, correct metered-dose inhaler use, better environmental control, and reduced health care costs. As shown in figure 21, asthma self-management education has also been found to reduce the number of hospitalizations for asthma. Limited work, however, has focused efforts on the self-management education of patients with a history of extensive health care use, and found it to reduce subsequent overuse of health services. In addition, little is known about the ability of such interventions to sustain asthma self-management over time. National guidelines have been established for the management of asthma (by the National Asthma Education and Prevention Program—NAEPP) that place a strong emphasis

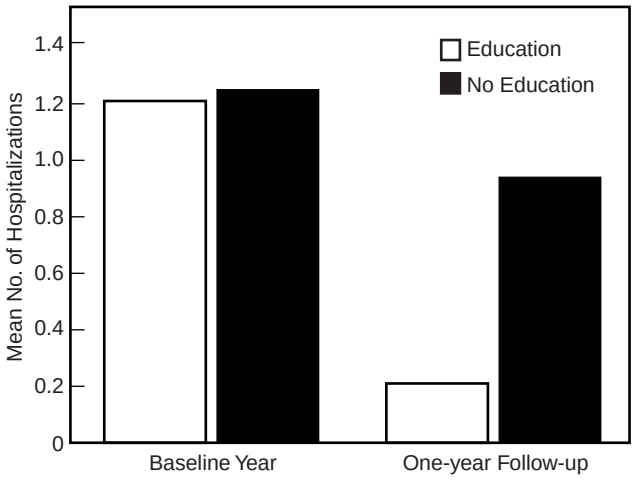


**Figure 21.** Effect of asthma self-management education on hospitalizations of low-income children who had one or more hospitalizations during the baseline year. Adapted and reprinted with permission from Clark MN, Feldman CH, Evans D, Levison MJ, Wasilewski Y, and Mellins RB. The impact of health education on frequency and cost of health care use by low-income children with asthma. J Allergy Clin Immuno 1986;78(1):108-115.

on incorporating asthma self-management education into regular clinical care. However, little research has examined what impact these guidelines have had on the quality of asthma care and education in this country.

Social, cultural, and economic factors have been shown to affect both the way in which asthmatics manage their disease and how individuals in the patient's social environment assist in or deter the use of effective strategies. For example, studies of low-income, minority asthmatic children suggest that interventions to improve family management skills and problem-solving related to disease may influence health care utilization and asthma self-management.

The amount of distress a patient feels and the amount of social support available to the patient have been shown to predict emergency department visits. Recent findings also suggest the likelihood that slow-onset, fatal asthma can be predicted, in part, by the social–psychological profile of the patient, specifically, being unable to self-manage because of poor social support, social isolation, or pressing psychological or social problems. The clinician's ability to communicate and teach has also been shown to influence patient self-management behavior. The need for clinicians to understand patients' perspectives, to be able to create partnerships with patients to co-manage the disease, and to provide optimum therapeutic regimens are highlighted in the NAEPP guidelines.

*Peak-flow monitoring and symptom perception*. Peak-flow monitoring (PFM) is a strategy for self-monitoring of airway obstruction using an inexpensive home meter. It allows persons with asthma to identify potentially dangerous airflow obstruction, often before they are symptomatic. Use of PFM has become more common. However, evaluation of educational interventions comparing patient use of PFM to patient monitoring of symptoms alone (including cough, wheeze, shortness of breath, sleep disturbances, school and work interruptions) has not been conclusive. Some studies show no better outcomes for individuals using PFM than for those using conventional symptom monitoring. Other studies suggest that using PFM may have value in reducing days lost from work, symptoms, and urgent care visits.

Recent research has shown that some children and adults with asthma have poor ability to judge their own level of airway obstruction. This insensitivity to increased airflow obstruction may place them at risk of delaying treatment and suffering dangerous asthma episodes. Peak flow monitoring may be a promising strategy for management of these individuals.

## *Chronic Obstructive Pulmonary Diseases*

Chronic obstructive pulmonary diseases, which include chronic bronchitis and emphysema, are the fourth leading cause of death in America. Chronic, severe shortness of breath and disability characterize these progressive, obstructive lung diseases, which generally affect middle-aged and older adults. Because cigarette smoking directly causes most COPD, this disease is usually preventable. Research on smoking, such as the Lung Health Study, shows that early interventions to stop smoking can prevent progression of COPD.

Researchers have addressed several behavioral issues pertaining to COPD. These include patients' reduced functional ability and quality of life, inadequate diet, poor adherence, and impaired cognition. Because of the severe disability and limitation of activities that can result as COPD advances, investigators have examined the value of behaviorally oriented rehabilitation programs. This research shows that pulmonary rehabilitation programs combining self-management education and exercise training can improve patients' exercise capacity and overall quality of life. The benefits of these programs include improved exercise treadmill performance, increased capacity

for work, better understanding of disease, increased physical activity and workdays, reduced dyspnea, and improved psychological profile. These benefits, however, tend to diminish after 1 to 2 years, and further research is needed to determine how to sustain the gains achieved.

Recent findings also show that persons with COPD often have nutritional deficiencies because of an inadequate diet. In response to these findings, rehabilitation approaches currently include an evaluation of the patient's diet, nutritional supplements, and behavioral counseling about their diet.

In some individuals, progressive COPD is associated with cognitive impairment—an outcome that may stem from chronic hypoxia. Although the extent to which this impairment can interfere with self-management of the disease or rehabilitation is not known, some evidence indicates that long-term oxygen therapy may attenuate the declines in cognition that occur with COPD.

## *Cystic Fibrosis*

Cystic fibrosis is a progressive, genetically determined obstructive lung disease. Until recently, it was inevitably fatal in the teenage years, but new treatments are now extending the life of these patients into adulthood. The disease is characterized by a wide variety of systemic effects, including mucous obstructions of the airways, chronic cough, and nutritional malabsorption.

Behavioral issues in this disorder relate to patients' self-management of the disease, the impact of CF on the family and patient, and adherence to therapy. The treatments for CF are complex and difficult, and include complicated pharmacological regimens, exercise, nutritional supplements, postural drainage, and special diets.

Several studies have identified potential problems associated with the self-management of CF and have suggested several areas for research emphasis. These areas for emphasis include patients' problems with self-care, decision-making, and home care. Parents of CF patients report several important areas of concern, disruption of family life, and difficulties managing at home. Indeed, fear, anxiety, and stress may be more salient concerns for CF patients and their families than for patients with other chronic diseases. The coping strategies of CF patients also are likely to be somewhat different. These problems and concerns have increased as the life expectancy of CF patients has been extended.

A limited number of behavioral interventions have been undertaken to improve the management of CF. Some of these, which are aimed at maintaining patients' weights and adherence to therapy, have shown promising results lasting up to 9 months. However, these studies did not include a comparison population, and the results are therefore limited.

Other research suggests that survival of CF patients is enhanced by physical activity. Studies are under way to determine whether interventions to increase exercise among these patients improve their health outcomes.

## *Tuberculosis*

Tuberculosis is a chronic infectious disease that is the most common chronic lung disease in the world. The incidence of tuberculosis has increased dramatically in the United States during the past 20 years, largely because of its association with HIV and acquired immunodeficiency syndrome (AIDS).

Treatments for tuberculosis and preventive therapies for individuals at high risk of this disease are highly effective, but they require the patients' commitment to many weeks of treatment. In addition, patients must modify some of their other behaviors, including their alcohol consumption. Because of the requirements of treatment, poor

adherence to therapy is widespread among individuals who have, or are at risk for, tuberculosis. Adherence is a particular concern with this disease because tuberculosis is most common among low-income, indigent populations with high rates of illicit drug use who are not likely to adhere to therapy.

Despite these challenges, however, researchers have dramatically improved patients' adherence to therapy for tuberculosis by using a strategy known as directly observed therapy. With this strategy, each dose of treatment is delivered by a health care provider and its consumption is directly observed.

### *Research Opportunities*

The management of lung diseases poses different issues and concerns for different population groups, depending on the patient's age, gender, culture, and socioeconomic level. These differences need to be assessed, and interventions that are tailored for specific groups and reflect lifespan factors need to be evaluated, especially for populations at high risk of lung disease.

As noted, asthmatics vary in their ability to perceive airway obstruction, and the poor perception of symptoms may be a risk factor for dangerous exacerbations of the disease. Research is needed to determine the feasibility of training asthmatics to improve their perception and monitoring of symptoms and to clarify the value of this training for enhancing the management of asthma. Training efforts to improve the perception and self-monitoring of symptoms also need to be evaluated as a component of asthma management programs.

Short-term studies suggest that self-management programs for patients with lung disease improve their disease outcomes, including their control of symptoms, quality of life, correct use of metered-dose inhaler, and health care costs. Ways to maintain the gains of self-management education and physical training need to be identified for different lung diseases.

The role of health care providers in teaching and otherwise encouraging patients' self-management of lung diseases is not well understood. Ways to educate and support health care providers in using effective techniques for patient–provider communication and in educating patients in self-management strategies for lung disease need to be identified.

As noted, no controlled studies have been conducted to examine the long-term effectiveness of using PFM at home to manage asthma. The effectiveness and sustainability of this strategy and the appropriate candidates for self-monitoring need to be determined.

Adherence to preventive therapies for asthma and to treatments for COPD, CF, and sarcoidosis is a significant issue in managing lung diseases. Different approaches for encouraging and assessing adherence to medical regimens and for enabling patients to adjust (i.e., self-regulate) medications at home to meet changing situations need to be compared.

Enhancing the quality of life of patients with CF also is hampered by the nature of the medical regimen in this disease. In addition, patients' frequent symptoms, delayed sexual development, and reaction to others' designation of them as terminally ill may significantly compromise their functioning. Controlled studies of the effect of CF on patients' and families' quality of life and of innovative self-management interventions to improve their quality of life would clarify key issues for managing the disease.

No studies have been conducted to examine the psychosocial factors involved in sarcoidosis. Sarcoidosis is the most common of the fibrotic lung diseases. According to best estimates, it affects 5 in 100,000 whites and 40 in 100,000

blacks in the United States, and it disproportionately affects black women. Sarcoidosis may result in shortness of breath, fatigue, pain, facial disfiguration, disability, and, in some cases, death. The magnitude of the effect of this common disease on individuals' quality of life and the psychosocial issues in managing this disease have not been extensively evaluated.

### *Recommendations*

Recommendations for behavioral research on interventions for lung disease are:

1. Identify social, cultural, and gender influences on the self-management of lung diseases and the effectiveness and efficacy of programs tailored for specific populations.
2. Evaluate symptom-perception training as a strategy for enhancing the management of asthma.
3. Develop self-management strategies for sustaining the gains achieved from self-management education and physical training for different lung diseases.
4. Identify innovative and effective strategies for educating and supporting health care providers in patient–provider communication and in developing self-management strategies for their patients with lung disease.
5. Evaluate the effectiveness and sustainability of PFM for managing asthma, and identify appropriate candidates for this self-monitoring strategy.
6. Compare different approaches for encouraging and assessing adherence to medical regimens and evaluate the feasibility of patients' adjustment of medications at home (self-regulation) to meet changing situations.
7. Conduct controlled studies of the effect of CF on patients' and families' quality of life, and develop innovative self-management interventions to improve their quality of life.
8. Evaluate the effect of sarcoidosis on patients' quality of life, and elucidate the psychosocial issues involved in managing this disease.

## Sleep Disorders

Several types of sleep disorders are associated with cardiopulmonary conditions. One of the most prevalent and serious these sleep disorders is obstructive sleep apnea syndrome (OSAS). As noted in Part I, OSAS has many behavioral and health consequences, including increased risk for hypertension, stroke, and MI.

The major symptoms of OSAS are snoring and excessive daytime sleepiness, and many patients with severe disease suffer morbid sleepiness (that is, sleepiness associated with profound behavioral impairment). Reliable and accurate laboratory assessments of OSAS have established that sleepiness does not result only from decreased oxygen to the brain, which does occur, but also from the severe fragmentation of sleep. Many treatments for OSAS reduce snoring and even prevent oxygen deficiency, but they do not stop sleep disruptions. Thus, the development of effective interventions to prevent the onset of this syndrome is important.

A number of factors enhance the risk for OSAS and other related disorders. Obesity is the main factor, and others include male gender, middle age, and cigarette smoking. Regular use of alcohol or hypnotic drugs may also be a factor. In addition, the incidence of OSAS may be increased markedly among individuals in certain occupations, such as long-haul truck drivers, probably because of their sedentary lifestyles, which increase the risk for obesity and other factors.

Research indicates that OSAS aggregates in families. Recent studies of families show that race and ethnicity also are associated with increased risk for OSAS. For example, new data show that blacks are at increased risk for OSAS at younger ages than nonblacks. Whether the racial or ethnic differences in risk result from the structure of airways, inherent differences in respiratory control, cultural attitudes toward weight and snoring, or other factors has not been established.

By identifying groups at risk for OSAS, appropriate primary prevention or early intervention approaches may be developed. Researchers have recommended weight loss, for example, as a primary prevention strategy for patients who are prone to develop obesity, such as those with Prader-Willi Syndrome. These patients are at risk for OSAS.

Recent advances have been made in treating OSAS and other sleep-related breathing disorders. The earliest treatments were surgical; for example, chronic tracheostomy was used to create a permanent opening in the throat that could be closed during waking hours and opened during sleep to bypass the airway obstruction. Nonsurgical approaches also can be very effective when patients adhere to these treatments.

*Continuous positive airway pressure*. The most common nonsurgical approach to treating OSAS is continuous positive airway pressure (CPAP). This approach is used to "splint" open a patient's upper airway with a stream of air that is applied continuously through the patient's nose. Patients' adherence to this treatment varies, however. Most reports indicate that patients use CPAP significantly fewer hours each night and fewer nights each week than is recommended or prescribed. Indeed, data from several studies show that patients' adherence to this treatment regimen is at least 50 percent less than is prescribed. Yet, even a single night without CPAP results in significant sleep disturbance and daytime sleepiness for these patients. Understanding the importance of CPAP treatment and enhancing adherence are therefore critical.

Recent data indicate that patients who have been treated with CPAP for several years have higher long-term adherence rates than those who have been treated for less time, but interventions to improve adherence have not been examined systematically in controlled studies of adult patients or children.

*Other interventions*. Besides CPAP, dental and other oral and nasal appliances, as well as positional devices, are available for treating OSAS. The efficacy of these approaches, however, has not been established.

For secondary prevention of OSAS, weight loss is variably effective. Several small interventions have been successful in weaning patients from CPAP therapy after they have lost significant weight by behavioral or surgical means. A weight loss of several kilograms has been shown to reduce sleep-related respiratory disturbances, including sleep apnea and snoring, in some patients. Combined weight loss and CPAP also reduces the rates of hypertension among OSAS patients more substantially than CPAP without weight loss.

Besides weight loss, smoking cessation could be of some benefit for OSAS patients. This possibility, however, has not been tested in any trials of smoking cessation among OSAS patients.

## *Research Opportunities*

Intervention strategies that promote good nutrition and exercise, and that prevent obesity, smoking, and alcoholism are important for the primary prevention of OSAS and other sleep-related breathing disorders. Identification of genetically susceptible groups (e.g., children of OSAS patients) is a first step in developing specific primary prevention programs for these

groups. Targeting specific occupational groups for primary prevention efforts also may be warranted.

Decisions about treatment (who, when, how) are some of the most difficult issues faced by clinicians who work with these disorders. For patients who have a serious sleep disorder that is life-threatening, these decisions are relatively clear-cut and the patients are treated promptly and vigorously. However, few data are available to help in determining which of many treatments to recommend (e.g., surgery, nasal decongestants, behavioral management) for a specific patient with a chronic sleep disorder.

For example, physicians currently treat OSAS differently depending on the age of the patient. Physicians' first choice for adults is often CPAP, but their first choice for children may be surgery; their choice for elderly persons may be no treatment at all. For OSAS, these differences in treatment need to be assessed in relation to their efficacy, their success over time, and the progression or recurrence of the disorder.

Although adherence to CPAP is low, the consequences of incomplete adherence are not well defined, and few approaches for improving patients' use of CPAP have been tested. The barriers to treatment (e.g., cost, understanding of the need for treatment, excessive sleepiness, interference with nighttime routines, travel, family attitudes, cultural biases) need to be evaluated more aggressively.

Upper-airway resistance syndrome (UAR) is a newly identified sleep disorder that involves serious sleep disruption and symptoms of breathing disruption during sleep that are less obvious than OSAS. The syndrome may be quite common and is dangerous because of the daytime consequences of greatly fragmented sleep; its seriousness in terms of cardiorespiratory risks is perhaps of less concern than these behavioral impairments.

The excessive daytime sleepiness that occurs with UAR is similar to that with OSAS. However, very little is known about this syndrome. The risks for it, or for OSAS, among young children in particular, are not known. Yet, early interventions with young children may be particularly useful for preventing the later problems that can arise with both of these disorders.

The effect of OSAS on an individual's quality of life has not been well studied either. Excessive sleepiness clearly leads to many secondary problems that compromise a person's quality of life. In addition, depression is a significant comorbid feature of OSAS, but the effects of successfully treating mood disorders in patients with OSAS have not been evaluated.

Greater understanding also is needed of the implications of the higher incidence of OSAS in certain occupational groups. OSAS among long-haul truckers may pose serious risks to public safety, as well as to the health, well-being, and employment of the drivers. Other data, from studies of patients with OSAS, show that they are more likely to be involved in motor-vehicle accidents than patients without OSAS, but the level of the disorder that causes increased accident rates is not known.

The public safety aspects of OSAS may be a potential barrier to having individuals with OSAS seek treatment. Individuals who snore may not seek treatment for snoring if identification of OSAS can result in the loss of their driving licenses or jobs. Such barriers are indicative of the complex, difficult, and grave issues involved in treating patients with OSAS.

### *Recommendations*

Recommendations for behavioral research on interventions for sleep disorders are:

1. Evaluate the efficacy of interventions to prevent the development of risk factors for OSAS in children of patients who have OSAS or in other groups at high risk for sleep-related breathing disorders.

2. Assess the natural history of OSAS and the efficacy of treatments for OSAS during several life stages (from infants to elderly persons). Clarify, in particular, the short-term neurobehavioral outcomes (e.g., reversible, mild sleepiness), the long-term neurobehavioral outcomes (e.g., developmental delays, learning deficits, accidents), and the rates of progression or recurrence of the disorder.

3. Evaluate barriers to CPAP treatment and develop programs that sufficiently enhance adherence to this treatment to gain adequate therapeutic efficacy. Determine the neurobehavioral consequences (e.g., neurological deficits) and pathophysiological mechanisms (e.g., repetitive arousals, hypoxemia, hypercapnia) associated with untreated or inadequately treated OSAS and UAR.

4. Determine the relationship of age-related increases in the prevalence of sleep-disordered breathing to behavioral or functional outcomes, and identify the most appropriate interventions for each age group.

5. Examine the effect of OSAS and treatment for OSAS on patients' quality of life.

6. Determine the level of sleep-disordered breathing associated with a risk of motor-vehicle accidents. Develop and test interventions that target lifestyle and other factors associated with sleep-disordered breathing as an occupational disease.

## Blood Diseases

The NHLBI is responsible for the study and treatment of blood diseases and for research to maintain the safety and adequacy of the blood supply. Behavioral science is germane to each of these areas of scientific and clinical activity. For example, individuals with sickle cell disease, thalassemia disorders, and hemophilia are identified in early childhood; these are all conditions with debilitating symptoms that pose significant challenges to normal development, family functioning, and psychosocial adjustment. Behavioral interventions to enhance adherence to medical therapies, especially by the young, are also essential if benefits of contemporary therapeutic regimens are to be realized. Behavioral scientists have the expertise to contribute significantly to our understanding of the many psychosocial considerations relevant to these diseases and to the development of effective medical strategies and interventions to enhance quality of life. Because behavioral research is only just beginning to explore this area of opportunity, this section, unlike others in the report, points primarily to the future and outlines recommendations regarding the several potential roles to be played by the behavioral sciences in contemporary research on blood diseases.

### *Sickle Cell Disease*

Sickle cell disease, a significant health problem, affects about 1 in 500 American blacks and a lesser number of individuals of Mediterranean, Near Eastern, and East Indian origin. This disease is a group of genetic blood disorders characterized by the predominance of sickle-shaped hemoglobin. The most common manifestation of sickle cell disease after infancy is periodic and recurrent episodes of pain that occur throughout life.

Other complications of sickle cell disease include gallstones and leg ulcers, as well as life-threatening conditions such as acute chest syndrome (lung involvement) and stroke. Older children and adolescents may experience delayed growth and development, which have important psychosocial consequences. And infants, who must take penicillin daily, must be monitored

carefully to avoid death from infectious complications.

Individuals who have sickle cell disease confront major challenges throughout their lives and have to balance the adverse consequences of their disease against their career, family, and quality-of-life goals. The clinical severity of the disease varies widely. Some persons manage the disease remarkably well, whereas others face chronic, severe problems. In general, the pain that occurs with sickle cell disease can be managed at home, but emergency treatment and hospitalization often are needed to give intravenous fluids and to manage narcotic medications.

Behavioral researchers have begun to explore four major aspects of sickle cell disease, as follows: (a) the psychological consequences of living with the disease, which include depression, cognitive effects, and social and family problems; (b) behaviors associated with the precipitation or exacerbation of pain episodes; (c) behavioral and psychosocial factors that interfere with pain management; and (d) behavioral and psychosocial interventions for treating pain episodes and managing the disease and its complications. The potential for contributing important information on each of these topics is considerable.

*Prevention and management of pain.* Scientists who have been studying sickle cell disease have focused on a set of factors associated with the precipitation of episodic pain. These pain triggers include dehydration, temperature changes, infection, and excessive exercise. Behavioral researchers could contribute to the primary prevention of pain (e.g., by improving patients' management of these triggers and their adherence to treatment) and of other complications from sickle cell disease.

Prevention programs could be developed, for example, to train children to maintain high levels of fluid intake or to teach parents and patients to recognize signs of early infection and seek immediate treatment. Such programs could help prevent life-threatening medical complications.

Behavioral researchers also could identify barriers to effective pain management such as poor access to care for younger patients from lower socioeconomic groups. As barriers are identified, researchers could develop and test interventions for overcoming these barriers and enhancing patients' quality of life. In addition, behavioral research could clarify issues arising with long-term transfusions for sickle cell disease patients who have had a stroke (see the problems associated with iron-chelation therapy, discussed below in the section on Thalassemia Disorders).

*Psychosocial complications.* Sickle cell disease poses significant stress and psychological distress for patients and their families. Up to 50 percent of children, adolescents, and adults with sickle cell disease have depression, anxiety, or other psychological problems, and many adults are not able to work and fulfill their family responsibilities. The potential for complications of sickle cell disease poses additional stress. These complications include cognitive problems or deficits such as memory loss and, among young children, a high risk of cerebrovascular infarction or stroke, which occurs in up to 10 percent of these patients.

Until recently, scientists assumed that patients who had the most severe sickle cell disease were at the greatest risk for developing behavioral problems. However, research now indicates that these problems (e.g., family conflicts, poor coping strategies, daily stress, related psychosocial difficulties in adjusting to the disease) are associated less strongly with the severity of disease than with distress, use of health care services, and frequency of pain. These findings are important because they suggest that behavioral and psychosocial interventions for individuals and families affected by sickle cell disease may help prevent and treat pain episodes and enhance overall management of this condition.

## *Thalassemia Disorders*

Thalassemia disorders such as Cooley's anemia are genetic blood diseases that mainly affect people of Mediterranean, Middle Eastern, African, Southeast Asian, Asiatic, Chinese, and Indian origin. These diseases result in inadequate production of hemoglobin, which causes severe anemia beginning shortly after birth.

Most individuals with thalassemia disorders need frequent blood transfusions throughout their entire lives. In addition, the excess iron received from transfused blood must be removed to minimize toxicity to their tissues and organ systems and to ensure their survival. For this treatment, patients receive a chelating drug that is administered intravenously by ambulatory pump for about 10 hours every day. This iron-chelation therapy is effective, but it is also inconvenient, uncomfortable, and expensive.

Twenty years ago, patients who had thalassemia disorders rarely survived beyond adolescence. Because of medical advances, however, patients now live longer to face increasing psychosocial difficulties that are secondary to their disease and the invasive treatment needed to manage the disease. Ensuring adherence to the daily requirement for iron-chelation therapy is a significant problem. Fifty percent of the adolescents who need this therapy do not adhere to the treatment, and their nonadherence can lead to congestive heart failure or iron-induced damage to other organs.

A 1995 NHLBI report, *Cooley's Anemia: Progress in Biology and Medicine*, highlighted the paucity of assessment and intervention research on the psychosocial needs of patients and their families who are coping with thalassemia disorders. Behavioral research on these disorders could contribute to improved management of them by (a) documenting the psychological consequences of living with thalassemia and (b) identifying behavioral and psychosocial factors such as discomfort, inconvenience, and distress that interfere with adherence to iron-chelation therapy and other treatment regimens. The goal of this research is to develop interventions to improve adherence to treatment and to enhance the coping skills of persons who are living with thalassemia.

## *Hemophilia*

Hemophilia is a rare, sex-linked genetic disorder that causes prolonged bleeding because of clotting factors that are missing in the blood. This disorder occurs in approximately 1 in 5,000 live male births. Major complications of hemophilia arise because of prolonged bleeding episodes, which can occur spontaneously in severe hemophiliacs, or from trauma in all hemophiliacs. These bleeding episodes could be life-threatening and are marked by pain and irreversible damage to the individual's joints.

Recent advances have significantly increased the life expectancy of hemophiliacs. The availability of factor concentrates, which are used to treat bleeding episodes promptly, now make treatment at home possible. This treatment includes physical therapy as well as infusions of concentrates. Because of the increasing complexity and time needed for treatments, however, patients' nonadherence has become a significant problem.

Another concern has been the shortened life expectancy of older hemophiliacs who were exposed to HIV through treatment. Concentrates that were manufactured from pooled plasma before 1985 were not sufficiently screened, allowing transmission of HIV infection among hemophiliacs. Since 1985, however, blood donors have been screened for HIV infection and new purification methods have been used. Since this time, no cases of HIV transmission from donor-screened, purified factor concentrates have been documented in the United States.

The availability of recombinant factor VIII and recombinant factor IX provides an extra measure

of protection against possible HIV infection. Reducing the risk of HIV transmission to sexual partners of hemophiliacs who are positive for HIV infection, however, is an important topic for behavioral research.

Additional research is also needed on other behavioral aspects of hemophilia. Behavioral researchers could contribute significantly to the management of hemophilia by (a) identifying behavioral predictors of traumas that result in increased bleeding episodes; (b) documenting the psychological consequences of living with hemophilia (including prevention of HIV transmission) and the effects of hemophilia on families; (c) identifying behavioral and psychosocial factors that compromise adherence to treatment that involves periodic replacement of blood clotting factors; and (d) exploring the contributions of behavioral and psychosocial interventions, including physical activity, to the management of hemophilia by preventing trauma, improving adherence, and enhancing pain management.

### *Research Opportunities*

Behavioral factors are an important aspect of blood diseases and the psychological sequelae that can alter the course of these diseases. Although treatment for these diseases has advanced significantly, the critical issues of adherence and the effect of treatments on the quality of life of patients and their families have largely been unexplored.

The importance of behavioral factors in blood diseases has been documented, but behavioral scientists are not as active in research on blood diseases as is needed. Behavioral science and behavioral scientists must be integrated into ongoing and new research efforts to improve understanding, treatment, and management of the major blood diseases.

Descriptive studies of individuals with sickle cell disease indicate that living with this disease can be accompanied by significant adverse consequences, including severe depression, cognitive deficits, and family problems. These consequences cause major problems for managing the disease and increasing patients' use of health care services. The studies underscore the need for interventions that enhance patients' abilities to cope with sickle cell disease, prevent and treat adverse episodes of symptoms, control pain, and improve management of the disease.

Because improved management of inherited blood diseases has extended patients' lives, new issues related to employment, education, marriage, and childbearing have arisen. Behavioral research can improve understanding of these adult-life issues. Additional behavioral research is needed to evaluate the quality of life of patients and their families and to identify the factors that affect individuals' adaptive or maladaptive psychosocial and behavioral adjustment.

Improving adherence to medical treatment for sickle cell disease and thalassemia disorders is a major challenge. As noted, many patients, particularly adolescents, do not adhere adequately to iron-chelation therapy. Similarly, parents may fail to administer the antibiotics prescribed to prevent potentially fatal infections in infants and young children with sickle cell disease. The behavioral factors associated with this nonadherence to treatment need to be identified. Based on this research, interventions could be designed to improve adherence and thereby decrease the morbidity and mortality associated with sickle cell disease and thalassemia disorders.

Optimal management of hemophilia involves frequent infusion of replacement factor and use of adjunctive physical therapy. Behavioral researchers can clarify the factors that impede an individual's adjustment to management and treatment of hemophilia. This research would yield essential information for developing behavioral interventions to improve patients' coping strategies and adherence to treatment.

Chronic, inherited blood diseases can influence the development of children's peer and social relationships. Family members, including parents, siblings, and partners and children of adults with these diseases, also may have problems adjusting to these diseases. Behavioral researchers could elucidate the important variables pertaining to overall family functioning and formation of peer relationships.

### *Recommendations*

Recommendations for behavioral interventions to improve the management of blood diseases are:

1. Include behavioral scientists as integral members of research and clinical teams studying and treating blood diseases.
2. Identify the psychosocial factors associated with adverse medical (including psychological) consequences of living with sickle cell disease, such as pain, depression, cognitive deficits, and family problems. Design behavioral interventions for patients and families to prevent and treat the debilitating psychological consequences of sickle cell disease, and evaluate the effects of these interventions on the management and medical outcomes of this disease.
3. Determine the relationship of behavioral and psychological factors to adverse medical consequences and management (e.g., by iron-chelation therapy) of thalassemia disorders. Develop and test behavioral interventions to help persons with thalassemia disorders cope with the challenges of maintaining their lifestyles (e.g., in relation to employment, education, marriage, childbearing).
4. Determine the factors associated with nonadherence to treatment for blood diseases, including nonadherence to the preventive use of penicillin for children with sickle cell disease and of iron-chelation therapy for thalassemia disorders and sickle cell disease. Design interventions to improve adherence to medical treatments for these conditions.
5. Identify behavioral and psychosocial factors associated with patients' positive adjustment to hemophilia throughout their lifespans, and develop behavioral interventions to improve patients' adherence to medical regimens.
6. Conduct prospective studies to determine the factors involved in establishing adaptive and maladaptive relationships with peers and ensuring the overall functioning of families of patients with blood diseases. Develop appropriate interventions for improving patients' family and social adjustments.

## Blood Supply and Usage

Before the mid-1980s, the amount of blood donated and the number of units of whole blood or packed red cells that were transfused continually increased. Since then, however, the rate of increase of both donations and transfusions has slowed and, between 1989 and 1994, the rate declined. Figure 22 shows the decrease in the number of units donated, especially in 1994, and of the number of units transfused (used)—changes that presumably reflect concerns about the danger of transmitting viruses in donated blood. To reduce the risk of infection, many patients elected to donate their own blood for later use (autologous, or self, donation) or for use by their family and friends.

In recent years the "cushion" between the collection and usage of blood has decreased, placing the nation's supply of blood in jeopardy. The erosion of this cushion reflects losses in the donor pool because of the improved testing of donated blood and the careful screening of donor's

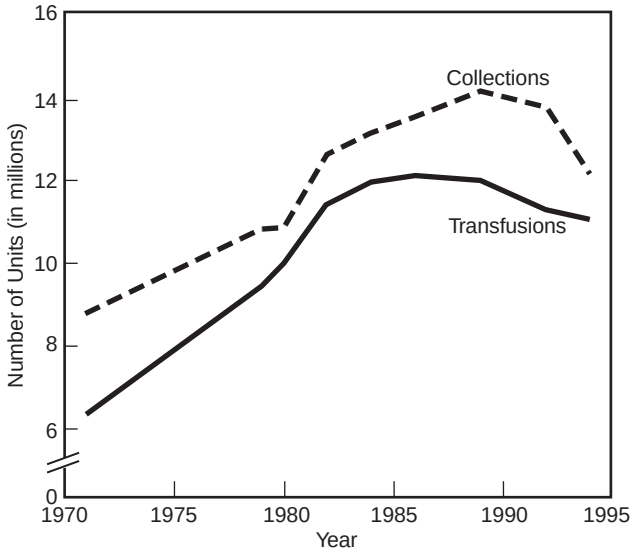


**Figure 22.** Trends in donation and usage of blood in the U.S., 1971-1994. Drawn with permission from data supplied by Surgenor DM.

medical information. When a donor's blood tests positive for infection, the donor is excluded, resulting in more shortages of general and type-specific blood for many geographic areas. The safety and adequacy of the nation's blood supply thus involve behavioral issues.

## *Donor Motivation and Screening*

The availability of an adequate blood supply depends on the behavior of blood donors. With few exceptions, the organizations that collect blood recruit donors by strategies that have changed only slightly over the past 20 years or more. These strategies must be updated. Systematic behavioral research to develop strategies for increasing blood donations has been minimal.

Surveys of blood donation have yielded data on the demographics of current donors and have indicated potential areas of study to improve recruitment strategies. Statistics indicate, for example, that the average annual number of donations per donor is about 1.6 to 1.8 and that many donors give blood only once a year. In addition, fewer minorities donate blood than is anticipated based on their representation in the population. Whether their opportunities for giving blood are limited or whether other factors are involved is not clear. The regulations governing blood donation allow a donor to give blood every 8 weeks if the donor is healthy and not anemic.

Procedures for handling donors who have an infectious disease are well established. When a donor's blood tests positive for an infectious disease, the donor's blood is rejected and the donor is advised of this fact and is often counseled about receiving treatment for the disease. Donors who are positive for HIV antibodies are usually referred for further medical care.

A donor's blood also is rejected if it tests positive for hepatitis C or human T-cell lymphotrophic virus (HTLV-I and HTLV-II). However, information on the follow-up of these donors and on their response is much more limited. The natural history of HTLV infection and its implication for donors with HTLV are also unclear. Clarification of these issues is important and may alter the screening of donors.

## *Transfusion Medicine*

Transfusion medicine is a science discipline that includes research on the collection, processing, storage, administration, and postinfusion follow-up of all blood elements. The blood elements include liquid plasma, all of the mostly trace proteins dissolved in this liquid, and all of the cells that circulate in the bloodstream, including precursor cells that reside mostly in bone marrow.

The most commonly transfused blood component is a unit of red blood cells that has much of the plasma removed. The red blood cells transport oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs. The cells are transfused to anemic patients who are not able to make their own red blood cells or to make them fast enough to meet their bodies' needs. Transfusion of red blood cells often is prescribed for patients who are bleeding.

Other blood components that are transfused include plasma, which is usually frozen soon after it is collected to preserve fragile proteins in the plasma, and platelets. Platelets can be harvested from individuals' whole-blood donations, and four to eight platelet "units" can be combined for a therapeutic infusion. Enough platelets for a therapeutic dose also can be obtained (by apheresis) from a single donation.

Many clinicians believe that single-donor platelets are better than platelets that are harvested and pooled from random whole-blood donations. Pooled platelets expose recipients to more donors, thus increasing the risk of transfusion-transmitted diseases. Use of single-donor platelets is much more costly, but limits recipients' exposure to platelet antigens and these diseases.

Like any therapeutic drug or procedure, transfusion of blood or its components can have side effects. The expected therapeutic results must be weighed against the potential side effects when deciding whether to use blood transfusions. In each instance, scientific knowledge must be tempered by clinical judgment.

During the past few years, blood transfusion has become increasingly safe. At the same time, the potential for side effects has received greater attention, and blood and blood components have been used more judiciously. The possibility of contracting AIDS from transfused, donated blood is now almost unmeasurably rare. Many of the unwanted potential side effects from blood transfusion can be eliminated if prospective patients donate their own blood for later autologous transfusion. Usually, only red blood cells can be used for these transfusions; the cells have a shelf life of up to 42 days, whereas platelets have a shelf life of only 5 days.

Current audits of blood usage suggest that overall levels of use are appropriate and that instances of overutilization or underutilization are few. Improved education of physicians about the use of blood transfusions and more cautious use of transfused blood because of the fear of AIDS probably account for this appropriate level of use.

Use of specific donations, however, varies. Use of autologous blood, for example, has increased significantly in the past 10 years, but still varies substantially between hospitals and geographic areas. Further study and documentation of the behavior of physicians in promoting and using autologous transfusions are therefore needed. Audits also indicate that transfusion of single-donor platelets has increased markedly. In addition, although the rate of plasma transfusion has not changed in more than 10 years, evidence suggests that use of plasma often is inappropriate.

### *Research Opportunities*

Studies show that a small proportion of donors do not report at-risk behavior and do not correctly report the possibility of infectious disease, especially HIV infection. Behavioral researchers could help determine the reasons for this failure in communication and design strategies to improve donors' reporting. Their reporting is complicated by the fact that donors who have at-risk behaviors may be in a "window of infection"—the period when positive antibodies are not discernible in their blood.

Behavioral scientists should be more involved in designing and evaluating strategies to recruit and retain donors, increase the average annual donation of each donor, and enhance recruitment of blood donors from minority groups. Their expertise would contribute significantly to these efforts.

As noted, donors who are positive for viral and other infectious agents on screening tests are informed of their status. This information may cause them significant distress. Behavioral scientists who have expertise in stress and psychological reactions to negative or indeterminate information can help design studies to evaluate the nature and scope of the problems that may arise

when donors receive unexpected, negative information. They can devise ways to help donors better understand and cope with this information and thus minimize potential adverse reactions from donors and their family members and friends.

To prevent use of inappropriate transfusion methods and strategies, new approaches are needed to encourage physicians to give careful consideration to minimizing the transfusion of specific blood components (e.g., plasma or platelets).

### *Recommendations*

Recommendations for behavioral interventions to improve management of the nation's blood supply and usage are:

1. Devise strategies to identify donors who have at-risk behaviors that could affect the quality of the blood or blood components they donate.
2. Develop and evaluate various strategies for recruiting and retaining donors and for increasing annual donations from eligible individuals. Examine the barriers to donation by members of ethnic groups who are underrepresented in the donor pool, and devise and test interventions to increase their participation and donations.
3. Design and evaluate behavioral interventions to minimize potential adverse reactions of donors and their families when screening tests show that the donors are positive for viral and other infectious agents. Develop and test strategies that blood bank personnel could use to inform these donors fully about their results in a manner that minimizes anxiety and stress for the donor.
4. Examine the factors associated with inappropriate transfusion practices (overutilization or underutilization), and design and evaluate programs to motivate physicians to adhere to current guidelines for blood transfusion.

## Improving Outcomes: Cross-Cutting Issues

Two issues that cut across all behavioral interventions to improve the management of heart, lung, and blood diseases and sleep disorders are adherence to therapy and quality of life. Behavioral research on these issues is described below.

### Adherence to Therapy

The success of medical treatments depends on the ability of clinicians and patients to agree on optimal therapeutic regimens tailored to patients' special needs. Considerable negotiation may be needed between physicians and patients to determine the medicines that will work and treatment schedule that the patients will follow. This partnership between providers and patients is especially important when treating chronic diseases, since the context for managing the disease changes frequently and the medical regimens must be fine-tuned over time.

Behavioral studies demonstrate that patients often do not adhere to the treatments recommended and that their nonadherence is common for all types of regimens and diseases, including life-threatening illnesses. Thirty percent to 70 percent of patients may not adhere completely to the treatments recommended, and more than 80 percent may fail to adhere to difficult behavioral prescriptions such as the recommendation to stop smoking.

Failing to take medications is the best-known example of nonadherence, but other behaviors may constitute partial adherence or nonadherence as

well. For example, patients may not follow recommended treatments by not using a ventilator mask in the workplace, irregularly using iron-chelation therapy for thalassemia, not completing chest physiotherapy for CF, continuing to smoke after a heart attack, dropping out of a cardiac rehabilitation program, only partially adhering to a lipid-lowering diet, or keeping a cat in a household even though they are asthmatic.

Poor adherence to therapy can have significant negative consequences for the patient's health and for the health care system. A patient's nonadherence to a prescribed treatment can result in failed treatment; unnecessary and dangerous intensification of treatment; costly diagnostic evaluations, complications, and hospitalizations; and death. In a research study, patients' nonadherence to the treatment protocol may seriously compromise the validity of the results of the study and make detection of treatment effects difficult. If adherence to medications cannot be assessed accurately in these studies, researchers will not be able to evaluate precise dose–response relationships and the safety of a treatment.

*Measuring adherence*. Too often, patients' poor adherence is not identified because clinicians and researchers do not measure adherence adequately. Behavioral researchers have developed a number of strategies for assessing a patient's adherence. These include self-report (including daily diaries, questionnaires, and interviews); clinical judgment; biochemical assays; measurements of medications used; review of a pharmacy's database of filled prescriptions; and electronic monitoring.

In general, studies of the reliability and validity of these different strategies suggest that adherence is often overestimated because of "demand" characteristics (implicit and explicit perceptual cues that communicate expectations to patients) during traditional assessments that ask patients about their behavior, and because of the limitations of patients' memories. In addition, patterns of partial adherence often cannot be detected with these strategies, except for electronic monitoring.

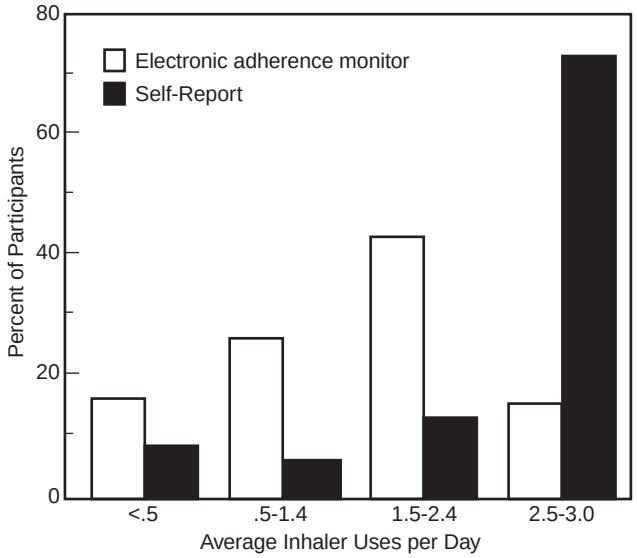


**Figure 23.** Average self-reported daily use and average electronically-recorded use of inhalers among adult participants in a COPD clinical trial who were instructed to use the inhaler 3 times per day. Reprinted with the permission from Rand CS, Wise RA, Nides M, Simmons MS, Bleecker ER, Kusek JW, Li VC, and Tashkin DP: Metered-dosed inhaler adherence in a clinical trial. Am Rev Respir Dis 1992;146:1559-1564.

Some data also suggest that different measurement methods may yield different predictors of adherence. For example, the predictors identified by patients' self-reports may differ from those identified by electronic monitoring. Figure 23, taken from NHLBI's Lung Health Study, demonstrates the importance of accurately measuring patients' adherence during a clinical trial. In this study, adherence to the use of an inhaler was measured by self-report and by an electronic monitor. As reported in many studies, patients' self-reports significantly overestimate adherence to medications, and electronic monitoring offers new possibilities for accurately measuring adherence patterns.

The availability and expansion of databases from patients in managed-care settings, improved self-report instruments, and the increased usage of

electronic monitoring devices will enable researchers and clinicians to accurately measure and promote patients' adherence to treatment.

*Predictors of adherence.* Because adherence is fundamentally important to the achievement and evaluation of treatment outcomes, many behavioral studies have been focused on predictors of adherence. These studies indicate that patients' characteristics (e.g., gender, ethnicity, personality, income, education) are not important predictors of adherence. Rather, the most important predictor of adherence is the nature of the prescribed therapy.

Patients adhere best to therapies that are simple, are easy to follow, are clearly beneficial in reducing pain or symptoms, involve little change in lifestyle, and are limited in duration. Patients adhere poorly when the duration of therapy is long, the treatment is preventive, the benefits are not evident, the disease is asymptomatic, or the regimen is complex. Psychological distress, more serious psychological problems or substance abuse also may interfere with patients' ability to adhere to therapy.

A small but increasing number of studies suggest that a patient's initial adherence is an important predictor of the patient's subsequent adherence. In addition, the relationship between a patient and a provider affects the patient's adherence; better communication and patients' satisfaction with the care provided are associated with improved adherence.

The adherence of pediatric patients is a special problem. Whereas adults' adherence to therapy generally involves only patients and health care providers, children's adherence is necessarily a family affair. In the family setting, adherence to therapy has been associated with the family's cohesion and communication, the family's health beliefs, and, for ethnic or immigrant populations, the family's level of acculturation (i.e., its acceptance of Western beliefs and practices).

Family conflict and poor family communication often contribute to poor adherence, particularly among adolescents. As with adults, children's nonadherence relates to poor communication with health care providers. How children learn responsibility for their treatment regimens as they grow up is an area of growing research interest. Little is known about how parents teach medication use, the best age for assuming responsibility, and the impact of this transfer of responsibility on adherence.

*Improving adherence*. Based on studies of the predictors of adherence, behavioral researchers have developed strategies for improving adherence among pediatric and adult patients. Interventions have significantly enhanced patients' adherence to medication regimens and to smoking-cessation and weight-control programs. Multimodal interventions typically include a number of specific strategies, such as reinforcement, providing environmental cues (e.g., pairing the use of an inhaler with the act of toothbrushing) to remind or prompt individuals to take their mediation, and use of self- or other (e.g., electronic) monitoring.

Direct observation of therapy (i.e., providers' observation of each dose taken) has also been shown to improve adherence. However, this labor-intensive strategy is generally practical only when the probability of nonadherence is very high and when the public health consequences of nonadherence are serious. Direct observation of therapy has been very effective, for example, for ensuring patients' adherence to treatments for tuberculosis.

In a limited number of studies, electronic monitoring of therapy has improved adherence, for example, to long-term use of inhaled medications. Other strategies that may help improve adherence include interventions to enhance patients' social support networks (e.g., structured group support, spousal or family support, provider support, community support); education of providers to improve their skills in counseling patients on the importance of adherence; and behavioral

approaches to enhance patients' motivations to adhere to treatment.

*Maintaining behavioral changes*. Achieving long-term maintenance of behavioral changes that involve lifestyle is a challenge that is closely related to adherence. Studies show that behavioral changes such as smoking cessation or the adoption of new dietary habits, exercise activity, or other lifestyle changes can be achieved for short periods of time. However, information on ways to maintain these changes for extended periods of time is limited. This dearth of knowledge makes it difficult to design effective interventions that would yield sustained behavioral changes. Whether methods needed to *maintain* behavioral change are fundamentally different from those used to *initiate* such change is not known.

Typically, behavioral interventions involve a period of intensive interaction between patients and providers that includes health education, cognitive and behavioral counseling, or other approaches based on prevailing learning theories or readiness-to-change models. Follow-up with patients is negligible. Thus, while behavior change programs emphasize strategies to initiate changes in lifestyle, far less is known about factors that predict the long-term success of interventions. Similarly, less is known about ways to influence these factors to maintain behavior change.

## *Research Opportunities*

Patients fail to adhere to treatments for many different reasons, and their patterns of nonadherence are many and various. Most of the research on adherence has focused on estimating the extent of nonadherence and identifying factors that are associated with adherence problems. This information could be used to design interventions that are tailored to overcome specific barriers or alter patient nonadherence patterns. The value of such tailored approaches to nonadherence problems in the treatment of heart, lung, and blood diseases as they occur in various populations has yet to be studied. In particular, it is not known under which conditions tailored interventions or more general programs of disease management are more effective in achieving positive health outcomes.

Many managed-care organizations now have the capacity to monitor patients' adherence to the filling of prescriptions, the keeping of medical appointments, and other health care behaviors. These organizations also can monitor the providers' adherence to documenting their counseling sessions or referrals. Structured managed-care settings may offer opportunities for interventions that include feedback on the adherence patterns of both patients and providers. The use of monitoring, feedback, incentives, and disincentives by these organizations might enhance the adherence of both patients and providers.

As noted, the communication between providers and patients is an important aspect of patients' adherence. A provider's skill in assessing adherence and potential barriers to adherence and in conveying concern and empathy is associated with a patient's level of adherence. However, even though adherence is important for achieving successful treatment outcomes, providers receive little or no education to enhance their assessment and counseling skills regarding patients' adherence. Effective primary and continuing education programs need to be developed for clinical disciplines (e.g., exercise physiology, nutrition, respiratory therapy, and health psychology) that can have an effect on patients' adherence to treatment.

Clinical trials of primary and secondary prevention of disease that include both medical and lifestyle interventions offer opportunities for studying the factors that contribute to successful maintenance of behavioral changes. Managed-care organizations offer similar opportunities because they have an integrated structure and internal databases that ease access to patient information and systematic implementation of interventions to promote adherence. Basic and

applied research on the maintenance of behavioral changes should be encouraged in these settings. This research would be difficult to pursue across multiple private practices.

Very few randomized, controlled studies have been conducted to test adherence-promoting interventions or to evaluate the effect of these interventions on relevant clinical outcomes. Well-controlled, randomized studies are needed to examine these issues.

### *Recommendations*

Recommendations for behavioral interventions to improve patients' adherence to therapy are:

1. Determine the benefits of adherence-promoting interventions that are tailored to individuals or to groups (e.g., children with CF) and that address patient-specific barriers and clinical outcomes.
2. Evaluate adherence-promoting interventions within managed-care organizations that use pharmacy and database monitoring as well as incentives and disincentives unique to the clinical setting.
3. Develop and evaluate primary and continuing education programs for clinical disciplines involved in patients' adherence. Target providers' communication and counseling skills on adherence.
4. Identify intervention methods that are specifically designed to foster long-term behavioral changes, and determine the personal and social attributes that contribute to individuals' long-term adoption of healthy lifestyles.
5. Identify cost-effective adherence-promoting interventions and evaluate their usefulness across different clinical and research populations.

## Quality of Life

When measuring outcomes, medical researchers have previously focused almost exclusively on biological end points such as mortality rates and laboratory test results. This information was thought to provide an appropriate and sufficient guide for medical decision-making. Recent changes in health care delivery and a broadened understanding of the experiences of health and disease, however, have begun to direct attention to medical outcomes as they are viewed from the perspectives of patient and society.

Increasingly, physician–patient relationships function as partnerships and health status is now understood to reflect more than the biological processes of disease alone. Illnesses cause different degrees of pain, physical impairment, and anxiety, and medical treatments can both induce a variety of side effects and impose substantial financial burdens on patients. All these factors must also be viewed within the context of a patient's resources, both at the personal and the community levels. As a result, assessment of medical outcomes has expanded to include such factors as self-care functioning, mobility, social interactions, employability, consumption of medical resources and overall life satisfaction.

Health-related quality of life is a broadly defined concept that subsumes many of these newly recognized, patient-centered medical outcomes. Because of the diversity of these outcomes, quality of life lacks a simple definition, but instead encompasses a variety of psychological and behavioral considerations. Among these considerations, the experience of physical pain is naturally important, as are the effects of illness on both mood and satisfaction with one's overall health and sense of well-being.

Another dimension of quality of life is functional status—a patient's ability to perform common daily activities (e.g., self-care, walking,

or preparing a meal) and to integrate these activities in the fulfilment of significant life roles (e.g., occupational, marital, parental). Loss of function may result from a variety of disease manifestations, such as claudication or dyspnea on walking, stroke-related disorientation, or fear of unpredictable ischemic events and life-threatening arrhythmias, etc.

*Measuring quality of life*. Because individuals respond differently to the same illness and may voice different values about the most significant functional capacities, quality of life is usually conceptualized as inherently subjective and multidimensional. However, in some contexts quality of life may be measured more quantitatively. For cost-benefit analyses, for example, a numerical value is assigned to each health state and functional outcome in an attempt to quantify the net impact of a disease or an intervention on quality of life. In a "utility" rating scale, for instance, this is often accomplished by asking groups or individuals to make choices between hypothetical health scenarios that are associated with different potential outcomes. Prototypically, such choices balance changes in disability and discomfort ensuing from different treatment regimens. Such models have been helpful in prioritizing health care services.

The domains of quality of life that are commonly measured include physical, emotional, cognitive, occupational, and social–interpersonal functioning. These can be assessed by a variety of self- or interviewer-administered questionnaires. Although the development and use of these instruments is relatively recent, they have significantly advanced the evaluation of quality of life among patients with heart, lung, and blood diseases.

*Recent findings*. Research has shown that health-related quality of life is an independent predictor of various medical outcomes, including mortality. Several multidimensional scales have also been shown to distinguish between diagnostic groups, yielding relatively distinct "profiles" of various chronic diseases. While COPD patients obviously suffer from exercise intolerance, for example, they also experience adverse effects in the realms of social functioning and mental health. Similarly, persons surviving a recent MI report dramatic declines in physical and role functioning, even in the absence of persistent pain.

Because some chronic diseases such as asthma and hypertension often cause only sporadic or mild symptoms, the quality of life of patients with these diseases is difficult to determine from biological measurements alone. Research based on patients' self-reports, for example, shows that impotence is more common among men who have high blood pressure than among men with normal blood pressure, even before antihypertensive medications are prescribed. Using standard neuropsychological tests, it has also been shown that hypertensive individuals who are not treated for their hypertension experience a variety of subtle changes in cognitive functioning, including deficits in attention, learning, memory, mental flexibility, and abstract reasoning.

An increasing number of studies also document patients' changes in health-related quality of life in response to medical and surgical treatments. With respect to the treatment of hypertension, randomized studies comparing the effects of antihypertensive medications show that diuretics cause more sexual dysfunction than do other drugs. In most other respects, however, antihypertensives do not reduce patients' quality of life and there are no appreciable differences among the major drug classes.

In evaluating the treatment of CAD, the first major study of bypass surgery suggested that medical and surgical interventions affect mortality similarly, but that physical functioning (e.g., exercise tolerance) is improved most by bypass surgery. In patients with single-vessel CAD, angioplasty appears to improve exercise tolerance, as well as self-reported physical functioning and

psychological well-being, when compared to treatment with antianginal medications. Other data indicate that bypass surgery and coronary angioplasty are associated with similar rates of recurrent MI and mortality, but that performance of daily activities is benefited better by surgical intervention. On the other hand, cardiac surgery causes a spectrum of central nervous system dysfunction that is both acute and, in some patients, persistent. The most common effects are relatively subtle deterioration in attention, memory, and mental speed.

Studies of patients with COPD demonstrate that standard pulmonary indices of disease severity correlate only weakly with patients' exercise tolerance, dyspnea, and overall quality of life. Thus, biological measurements of pulmonary function correlate poorly with patients' symptomatology. Similarly, in studies evaluating treatments for chronic lung disease, quality-of-life assessments do not always agree with other medical outcomes. For example, a quality-of-life scale to evaluate dyspnea may indicate a treatment benefit that is not apparent by spirometry or by the patient's arterial blood gas values. On the other hand, treatment intervention may enhance a patient's medical prognosis but not improve functional capacities important to the patient or overall life satisfaction.

Although little research has yet been conducted on quality of life in patients with chronic blood disorders, there is evidence that erythropoietin improves both physical and psychosocial functioning of patients with anemia induced by renal failure. Clearly, the pain, discomfort, and challenging regimens associated with the management of other blood disorders are also likely to have an impact on quality of life that needs to be better understood.

In summary, behavioral research on quality of life has improved understanding of the effect of heart, lung, and blood diseases on patients' lives. This research has increased awareness that quality-of-life outcomes cannot be deduced simply by measuring the physiological aspects of disease and that the efficacy of treatments must be viewed from the wider perspectives of patients' subjective well-being and their abilities to function well in the major activities of life.

### *Research Opportunities*

A wide variety of quality-of-life measures have been developed and tested. Some of these measures are general and applicable to a wide variety of diseases. An advantage of these generic measures is that they can be used for comparisons across illnesses and for population monitoring. However, these general measures may not be useful for discerning some of the subtle effects of specific diseases and their treatments. Specific, disease-targeted measures have therefore also been developed. The relative advantages and disadvantages of generic and targeted measures need to be evaluated further.

Although many quality-of-life measures have been thoroughly evaluated, the psychometric properties (e.g., reliability, validity) of others remain to be established. Patients' responses to questionnaires assessing their subjective states of well-being may be influenced by reporting biases, personality and characteristics of individuals that are unrelated to health status. Also, patients' frameworks for evaluating their quality of life with progressively disabling diseases may change over time; this "response shift" complicates measurement and interpretation of the patients' responses. Measures that capture patients' subjective experiences of health and well-being need further development to document their independence from reporting bias and their responsiveness to change.

Quality-of-life measures are now commonly used in evaluating medical and surgical treatments. These measures document the effects of treatments on quality-of-life profiles or on years of life adjusted for quality of life. Generic quality-of-life measures, however, have rarely been used to

evaluate behavioral interventions. Use of instruments to measure quality of life in research on behavioral interventions should therefore be encouraged.

Medical, surgical, and behavioral interventions all use resources and all are designed to improve patients' quality of life and to extend their life expectancy. There is some evidence that certain behavioral interventions can produce health benefits at a lower cost than do other health care interventions. Further research is needed to compare the relative cost and utility of behavioral interventions versus medical and surgical treatments for the same medical conditions.

### *Recommendations*

Recommendations for behavioral research on quality of life are:

1. Evaluate the relative merit of disease-specific and generic measures of quality of life for predicting behavioral and clinical outcomes in diverse populations.
2. Establish the psychometric properties (e.g., reliability and validity) of measures used to assess perceived well-being and functional health status.
3. Evaluate the effects of behavioral interventions on the health-related quality of life of patients treated for heart, lung, and blood diseases, and sleep disorders.
4. Compare the relative cost and utility of behavioral interventions versus medical and surgical treatments for the same condition.

National Heart,
Lung, and
Blood Institute
Report
of the
Task Force on
Behavioral Research in
Cardiovascular, Lung,
and Blood Health and Disease

# Appendixes

# Bibliography

The following references are intended as broad resources for individuals interested in the current status of behavioral research in cardiovascular, lung, and blood health and disease. The list is not intended to be comprehensive or to reflect important contributions from individual studies, but rather, to cite the sources used in the figures and to provide relevant information from related documents and official reports and other pertinent articles and recent reviews. The sources are listed alphabetically within each group.

## Sources Cited in Figures

A Strategic Plan for the Office of Behavioral and Social Sciences Research at the National Institutes of Health. NIH Publication No. 97-4237.

Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al: A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336(16):1117-1124.

Blumenthal JA, Jiang W, Babyak MA, Krantz DS, Frid DJ, Coleman RE, et al: Stress management and exercise training in cardiac patients with myocardial ischemia. Arch Intern Med 1997;157(19):2213-2223.

Clark MN, Feldman CH, Evans D, Levison MJ, Wasilewski Y, Mellins RB: The impact of health education on frequency and cost of health care use by low-income children with asthma. J Allergy Clin Immuno 1986;78(1)108-115.

Epstein LH, Valoski A, Wing RR, McCurley, J: Ten-year outcomes of behavioral family-based treatment for childhood obesity. Health Psychol 1994; 13(5)373-383.

Frasure-Smith N, Lesperance MD, Talajic M: Depression following myocardial infarction: impact on 6-month survival. JAMA 1993;270(15):1819-1825.

House JS, Landis KR, Umberson D: Social relationships and health. Science 1988;241: 540-545.

Kamarck TW, Everson SA, Kaplan GA, Manuck SB, Jennings JR, Salonen R, et al: Exaggerated blood pressure responses during mental stress are associated with enhanced carotid atherosclerosis in middle-aged Finnish men: findings from the Kuopio Ischemic Heart Disease Study. Circulation 1997;96(11):3842-3848.

Kaplan JR, Adams MR, Anthony MS, Morgan TM, Manuck SB, Clarkson TB: Dominant social status and contraceptive hormone treatment inhibit atherogenesis in premenopausal monkeys. Arterioscler Thromb Vasc Biol 1995;15(12):2094-2100.

Kawachi I, Sparrow D, Spiro A, Vokonas P, Weiss ST: A prospective study of anger and coronary heart disease: The Normative Aging Study. Circulation 1996;94(9)2090-2095.

King AC, Haskell WL, Young DR, Oka RK, Stefanick M: Long-term effects of varying intensities and formats of physical activity on participation rates, fitness, and lipoproteins in men and women aged 50 to 65 years. Circulation 1995;91(10):2596-2604.

Krantz DS, Kop WJ, Santiago HT, Gottdiener JS: Mental stress as a trigger of myocardial ischemia and infarction. Cardiol Clin 1996;14(2):217-287.

Kripke DF, Simons RN, Garfinkel L, Hammond EC: Short and long sleep and sleeping pills: Is increased mortality associated? Arch Gen Psychiatry 1979;36(1):103-116.

Luepker RV, Perry CL: The Minnesota Heart Health Program. Education for youth and parents. Ann NY Acad Sci 1991;623:314-321.

Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, et al: Can lifestyle changes reverse coronary heart disease? The lifestyle heart trial. Lancet 1990;336:129-133.

Perri MG, McAllister DA, Gange JJ, Jordan RC, McAdoo WG, Nezu AM: Effects of four maintenance programs on the long-term management of obesity. J Consult Clin Psychol 1988;56(4):529-534.

Pierce JP, Evans N, Farkas AJ, Cavin SW, Berry C, Kramer M, et al: Tobacco use in California. An evaluation of the tobacco control program, 1989-1993. La Jolla, California: University of California, San Diego; 1994.

Rand CS, Wise RA, Nides M, Simmons MS, Bleecker ER, Kusek JW, et al: Metered-dose inhaler adherence in a clinical trial. Am Rev Respir Dis 1992;146:1559-1564.

Stepney R: Smoking behavior. A psychology of the cigarette habit. Brit J Dis Chest 1980; 74(4):325-344.

Verdecchia P, Porcellati C, Schillaci G, Borgioni C, Cucci A, Battistelli M, et al: Ambulatory blood pressure: an independent predictor of prognosis in essential hypertension. Hypertension 1994;24(6): 793-801.

Williams RB, Barefoot JC, Califf RM, Haney TL, Saunders WB, Pryor DB, et al: Prognostic importance of social and economic resources among medically treated patients with angiographically documented coronary artery disease. JAMA 1992;267(4)520-524.

Yeung AC, Vekshtein VI, Krantz DS, Vita JA, Ryan TJ, Ganz P, et al: The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. N Engl J Med 1991;325(22):1551-1556.

## Related Documents and Official Reports

Agency for Health Care Policy and Research. Cardiac Rehabilitation. Clinical Practice Guideline No. 17. Rockville, MD. AHCPR Publ No. 96-0672, October 1995.

Agency for Health Care Policy and Research. Smoking Cessation: Clinical Practice Guideline No. 18. Washington, DC. AHCRP Publ No. 96-0692, 1996.

Effects of alcohol on health and body systems. In Eighth Special Report to the U.S. Congress on Alcohol and Health From the Secretary of Health and Human Services September 1993. US Department of Health and Human Services, Public Health Service, NIH, NIAAA. NIH Publ No. 94-3699, 1994.

The Handbook of Health Behavior Change, edited by SA Shumaker, EB Schron, JK Ockene. New York: Springer Publishing Co, Inc, 1990.

The Health Consequences of Smoking and Nicotine Addiction. A Report of the Surgeon General. Washington DC, GPO. DHHS Publ No. 88-8406, 1988.

Obesity. Workshop III. From AHA Prevention Conference III. Behavior Change and Compliance: Keys to Improving Cardiovascular Health. Circulation 1993;88(3):1391-1396.

Perioperative red cell transfusion–consensus conference. JAMA 1988;260(18):2700-2703.

Preventive cardiology and its potential influence on the early natural history of adult heart diseases: the Bogalusa Heart Study and the Heart Smart Program. Am J Med Sci 1995;310(Suppl 1): S133-S138.

Towards prevention of obesity: research directions. The National Task Force on Prevention and Treatment of Obesity: Obesity Res 1994;2(6): 571-584.

Understanding and promoting physical activity. In Physical Activity and Health: A Report of the Surgeon General. DHHS, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Heath Promotion, 1996.

Why We Eat What We Eat: The Psychology of Eating, edited by ED Capaldi. Washington DC: American Psychological Association, 1996.

## Other Pertinent Articles and Recent Reviews

Adler NE, Boyce T, Chesney MA, Cohen S, Folkman S, Kahn RL, et al: Socioeconomic status and health. The challenge of the gradient. Am Psychol 1994;49:15-24.

Ancoli-Israel S, Kripke DF, Klauber MR, Fell R, Stepnowsky C, Estline E, et al: Morbidity, mortality and sleep-disordered breathing in community-dwelling elderly. Sleep 1996;19(4): 277-282.

Arnold JM, Sasson Z, Mathias S, Black WR, Gill JB, Higginson L, et al: Impact of medical interventions on quality of life in cardiovascular disease: a consensus viewpoint. Can J Cardiol 1997;13(3):235-236.

Bolton MB, Tilley BC, Kuder J, Reeves T, Schultz LR: The cost and effectiveness of an education program for adults who have asthma. J Gen Intern Med 1991;6(5):401-407.

Bruvold WH: A meta-analysis of adolescent smoking prevention programs. Am J Public Health 1993;83(6):872-880.

Busse WW, Kiecolt-Glaser JK, Coe C, Martin R, Weiss ST, Parker SR: Stress and asthma. Am J Respir Crit Care Med 1995;151:249-252.

DeFronzo RA, Ferrannini E: Insulin Resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care 1991;14:173-194.

Fletcher GF, Balady G, Blair SN, Blumenthal J, Caspersen C, Chaitman B, et al: Statement on exercise: benefits and recommendations for physical activity programs for all Americans. Circulation 1996;94:857-862.

Gaziano JM, Manson JE: Diet and heart disease. The role of fat, alcohol, and antioxidants. Cardiol Clin 1996;14(1):69-83.

Goldman L, Cook EF: The decline in ischemic heart disease mortality rates: an analysis of the comparative effects of medical interventions and changes in lifestyle. Ann Intern Med 1984;101: 825-836.

Guyatt GH, Feeny DH, Patrick DL: Measuring health-related quality of life. Ann Intern Med 1993;118(8):622-629.

Isenberg SA, Lehrer PM, Hochron S: The effects of suggestion and emotional arousal on pulmonary function in asthma: a review and a hypothesis regarding vagal mediation. Psychosom Med 1992;54:192-216.

Jiang W, Babyak M, Krantz DS, Waugh RA, Coleman E, Hanson MM, et al: Mental stress-induced myocardial ischemia and cardiac events. JAMA 1996;275:1651-1656.

Kaplan RM, Sallis JF, Patterson TL: Health and Human Behavior. New York: McGraw Hill, 1993.

Klatsky AL: Alcohol, coronary disease, and hypertension. Annu Rev Med 1996;47:149-160.

Krantz DS, Kop WJ, Gabbay FH, Rozanski A, Barnard M, Klein J, et al: Circadian variation of ambulatory myocardial ischemia: triggering by daily activities and evidence for an endogenous circadian component. Circulation 1996;93(7): 1364-1371.

Lehrer PM, Isenberg S, Hochron SM: Asthma and emotion: a review. J Asthma 1993;30(1)5-21.

Leplege A, Hunt S: The problem of quality of life in medicine. JAMA 1997;278(1):47-50.

Manuck, SB: Cardiovascular reactivity in cardiovascular disease. Int J Behav Med 1994;1:4-31.

Manuck SB, Marsland AL, Kaplan JR, Williams JK: The pathogenicity of behavior and its neuroendocrine mediation: an example from coronary artery disease. Psychosom Med 1996;57:275-283.

McGovern PG, Pankow JS, Shahar E, Doliszny KM, Folsom AR, Blackburn H, et al: Recent trends in acute coronary heart disease: mortality, morbidity, medical care, and risk factors. N Engl J Med 1996;334(14):884-890.

Miller TQ, Smith TW, Turner CW, Guijarro ML, Hallet AJ: Meta-analytic review of research on hostility and physical health. Psychol Bull 1996; 119(2):322-348.

Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Buchard C, et al: Physical activity and public health. JAMA 1995; 273(5):402-407.

Pickering TG, Devereux RB, James GD, Gerin W, Landsbergis P, Schnall PL, et al: Environmental influences on blood pressure and the role of job strain. Hypertension 1996;14(Suppl 5):S179-S186.

Ries AL, Kaplan RM, Limberg TM, Prewitt LM: Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. Ann Intern Med 1995;122(11):823-832.

Schneiderman N, Skyler JS: Insulin metabolism, sympathetic nervous system regulation, and coronary heart disease prevention. In: Behavioral Medicine Approaches to Cardiovascular Disease Prevention, edited by K Orth-Gomer, N Schneiderman. New Jersey: Erlbaum, 1996, pp. 105-133.

Shaten BJ, Kuller LH, Neaton JD: Association between baseline risk factors, cigarette smoking, and CHD mortality after 10.5 years. MRFIT Research Group. Prev Med 1991;20:655-659.

Siwach SB: Alcohol and coronary artery disease. Int J Cardiol 1994;44(2):157-162.

Strobel RJ, Rosen RC: Obesity and weight loss in obstructive sleep apnea: a critical review. Sleep 1996;19(2)104-115.

Thompson RJ, Gil KM, Abrams MR, Phillips G: Stress, coping, and psychological adjustment of adults with sickle cell disease. J Consult Clin Psychol 1992;60:433-440.

Tosteson AN, Weinstein MC, Hunink MG, Mittleman MA, Williams LW, Goldman PA, et al: Cost-effectiveness of populationwide educational approaches to reduce serum cholesterol levels. Circulation 1997;95(1):24-30.

Verrier RL, Nearing BD: T-wave alternans as a harbinger of ischemia-induced sudden cardiac death. In Cardiac Electrophysiology: From Cell to Bedside, edited by DP Zipes, J Jalife. Philadelphia: WB Saunders, 1995.

Williams RB, Chesney MA: Psychosocial factors in established coronary artery disease: the need for research on intervention. JAMA 1993;270(15): 1860-1861.

Wing RR: Changing diet and exercise behaviors in individuals at risk for weight gain. Obes Res 1995;3(Suppl 2):277S-282S.

Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S: The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328(17)1230-1235.

# Abbreviations

| | |
|---|---|
| AIDS | Acquired immunodeficiency syndrome |
| ARIC | Atherosclerosis Risk in Children |
| CAD | Coronary artery disease |
| CARDIA | Coronary Artery Risk Development in Young Adults |
| CF | Cystic fibrosis |
| CHD | Coronary heart disease |
| COPD | Chronic obstructive pulmonary diseases |
| CPAP | Continuous positive airway pressure |
| CVD | Cardiovascular disease(s) |
| HDL | High density lipoprotein |
| HIV | Human immunodeficiency virus |
| HPA | Hypothalamic-pituitary-adrenal |
| HTLV | Human T-cell lymphotrophic virus |
| LDL | Low density lipoprotein |
| LV | Left ventricular |
| MI | Myocardial infarction |
| NAEPP | National Asthma Education and Prevention Program |
| NHLBI | National Heart, Lung, and Blood Institute |
| NIH | National Institutes of Health |
| OSAS | Obstructive sleep apnea syndrome |
| PFM | Peak flow monitoring |
| REM | Rapid eye movement |
| SIDS | Sudden infant death syndrome |
| SUNDS | Sudden unexpected nocturnal death syndrome |
| VLDV | Very low density lipoprotein |
| UAR | Upper-airway resistance |

# Task Force on Behavioral Research

## Cardiovascular, Lung, and Blood Health and Disease

### Chair

Stephen B. Manuck, Ph.D.
Professor
Department of Psychology
University of Pittsburgh

### Subgroup Chairs

#### Behavioral and Social Antecedents of Disease

David S. Krantz, Ph.D.
Professor
Department of Medical and Clinical Psychology
Uniformed Services University of the Health Sciences

#### Behavioral Interventions: Prevention and Management of Disease

Margaret A. Chesney, Ph.D.
Professor
Department of Medicine
University of California, San Francisco

### Rapporteurs:

#### Task Force Report

Thomas Kamarck, Ph.D.
Associate Professor
Department of Psychology
University of Pittsburgh

#### Behavioral Intervention: Prevention and Management of Disease

Cynthia S. Rand, Ph.D.
Associate Professor of Medicine
Division of Pulmonary and Critical Care Medicine
The Johns Hopkins University School of Medicine

### Behavioral Antecedents of Disease

David S. Krantz, Ph.D. (Chair)
Professor
Department of Medical and Clinical Psychology
Uniformed Services University of the Health Sciences

Mary A. Carskadon, Ph.D.
Professor
Department of Psychiatry and Human Behavior
Brown University School of Medicine

Kathleen Light, Ph.D.
Professor
Department of Psychiatry
University of North Carolina at Chapel Hill

Stephen B. Manuck, Ph.D.
Professor
Department of Psychology
University of Pittsburgh

Karen A. Matthews, Ph.D.
Professor
Departments of Psychiatry, Epidemiology, and Psychology
University of Pittsburgh School of Medicine

Thomas Pickering, M.D., D. Phil.
Professor of Medicine
The New York Hospital
Cornell University Medical College

Neil Schneiderman, Ph.D.
Professor of Psychology, Medicine, and Biomedical Engineering
Department of Psychology
University of Miami

Richard L. Verrier, Ph.D.
Co-Director
Institute for Prevention of Cardiovascular Disease
Beth Israel Deaconess Medical Center
Harvard Medical School

### Behavioral Interventions: Prevention and Management of Disease

Margaret A. Chesney, Ph.D. (Chair)
Professor
Department of Medicine
University of California, San Francisco

Mary A. Carskadon, Ph.D.
Professor
Department of Psychiatry and Human Behavior
Brown University School of Medicine

Noreen M. Clark, Ph.D.
Dean and Marshall H. Becker Professor of Public Health
University of Michigan School of Public Health

Karen M. Gil, Ph.D.
Associate Professor
Department of Psychology
University of North Carolina at Chapel Hill

Robert M. Kaplan, Ph.D.
Professor and Interim Chair
Department of Family and Preventive Medicine
University of California, San Diego School of Medicine

Cynthia S. Rand, Ph.D.
Associate Professor of Medicine
Division of Pulmonary and Critical Care Medicine
The Johns Hopkins University School of Medicine

Doris Wethers, M.D.
Director
Comprehensive Sickle Cell Center
St. Luke's Roosevelt Hospital Center

Redford B. Williams, M.D.
Professor of Psychiatry and Behavioral Sciences and Medicine
Department of Psychiatry
Duke University Medical Center

Rena R. Wing, Ph.D.
Professor of Psychiatry and Epidemiology
Department of Psychiatry
University of Pittsburgh School of Medicine

## Consultants

James A. Blumenthal, Ph.D.
Professor
Department of Psychiatry
Duke University Medical Center

Thomas Creer, Ph.D.
Professor
Department of Psychology
Ohio University

Kenneth Perkins, Ph.D.
Professor
Departments of Psychiatry, Epidemiology, and Psychology
University of Pittsburgh School of Medicine

Phyllis L. Pirie, Ph.D.
Professor
Division of Epidemiology
University of Minnesota School of Public Health

## NHLBI Staff

### Coordination:

Barbara Liu, S.M., Coordinator
Deputy Director
Office of Science and Technology

Nancy Eng, Coordinator
Program Analyst
Office of Science and Technology

Judy Corbett
Program Analyst
Office of Science and Technology

### Resource:

Michele Hindi-Alexander, Ph.D.
Health Science Administrator
Division of Lung Diseases

Peter G. Kaufmann, Ph.D.
Leader, Behavioral Medicine Scientific Research Group
Division of Epidemiology and Clinical Applications

Clarice Reid, M.D.
Director
Division of Blood Diseases and Resources

**Discrimination Prohibited:**
Under provisions of applicable public laws enacted by Congress since 1964, no person in the United States shall, on the grounds of race, color, national origin, handicap or age, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any program or activity (or, on the basis of sex, with respect to any education program or activity) receiving Federal financial assistance. In addition, Executive Order 11141 prohibits discrimination on the basis of age by contractors and subcontractors in the performance of Federal contracts, and Executive Order 11246 states that no federally funded contractor may discriminate against any employee or applicant for employment because of race, color, religion, sex, or national origin. Therefore, the National Heart, Lung, and Blood Institute must be operated in compliance with these laws and Executive Orders.