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CHAPTER 9

Social Support and Coronary Heart Disease

Underlying Psychological and Biological Mechanisms

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Social support has been prospectively associated with mortality and implicated in the etiology of coronary heart disease (CHD; see reviews by Berkman, 1985; Broadhead et al., 1983; Cohen, 1988; House, Landis, & Umberson, 1988; Wallston, Alagna, DeVellis, & DeVellis, 1983). Although there has been a tremendous effort to establish a relation between support and CHD, relatively little work has focused on how social support influences CHD pathogenesis. We feel that differentiation between conceptions of social support and specification of pathways through which each type of support influences CHD are requisite for understanding the role of support in the prevention of disease. In service of this goal, we review studies of the role of social support in the etiology of CHD, suggest some distinctions in social support based on existing research, argue for functionally

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distinct stages of CHD pathogenesis, and propose a series of psychological and biological models linking different conceptualizations of social support to CHD. Our discussion is limited to the etiology of disease (onset and progression, but not recovery) and focuses on disease end points (morbidity and mortality) rather than illness behaviors such as symptom reporting and use of medical services.

The major thrust of our argument is that in order to understand the influence of social support on CHD, we must take into account both how we conceptualize social support and the stage of disease under consideration. The development of CHD subsumes numerous stages, each accompanied by a somewhat different set of pathophysiological processes. Conditions that influence coronary artery atherogenesis, for instance, may not be the same as those responsible for the various functional and clinical expressions of CHD. Moreover, various conceptualizations of social networks and supports vary widely, and individual concepts may be plausible predictors of some stages of disease but not of others.

Differentiating Social Support

There is little agreement among the scientific community in regard to a precise definition of social support (Cohen & Syme, 1985; Shumaker & Brownell, 1984; Wilcox & Vernberg, 1985). Moreover, existing studies apply the term to a broad range of conceptualizations of social networks and the functions that they provide. Rather than attempt an all-encompassing definition, we propose broad categorical classifications of the concepts commonly included under the social support rubric, and we define some specific concepts that we feel may be linked with physical disease. Cohen and his colleagues (Cohen & Syme, 1985; Cohen & Wills, 1985) proposed a distinction between *structural* and *functional* support measures. Structural measures describe the existence of and interconnections between social ties; functional measures assess whether interpersonal relationships serve particular functions (e.g., provide affection).

Only a small sample of possible conceptions of social support have been used with any frequency in studies of CHD morbidity and mortality. The most common measure is a structural index of social ties that is often termed *social integration* (SI). A prototypical SI index includes marital status, closeness of family and friends, participation in group activities, and church and religious affiliations. Functional measures used in the physical disease literature include network satisfaction and perceived availability of material aid or psychological support.

Differentiating Stages of CHD

The Natural History of CHD

Available research reveals much about the course of development of coronary disease and about the risk factors that contribute to it. CHD is usually the clinical manifestation of an underlying pathological process, coronary artery atherosclerosis. Atherosclerosis refers to the development of fibrofatty plaques (atheromas) within the inner lining, or intima, of the artery. With the progression of atherosclerosis, plaques frequently change in composition as well as size; other changes include calcification and, later, ulceration and hemorrhage (McGill, 1972). The progressive enlargement and complication of atherosclerotic plaques may narrow the arteries and eventually obstruct blood flow to the heart, resulting in cardiac electrical instability, damage or death of the heart tissue, or both. These sequelae of coronary artery atherosclerosis ultimately affect the ability of the heart to maintain its normal rhythmicity and essential function as a pump. The usual clinical expressions of CHD include angina pectoris and its variants (chest pain, generally resulting from insufficient coronary blood flow), acute myocardial infarction (death of the heart tissue as a result of interrupted coronary blood flow), cardiac arrhythmias (electrical instability) and sudden death (often the consequence of arrhythmia; Sokolow & McIlroy, 1987).

Epidemiological and experimental studies of the origins of CHD have advanced vigorously over the past several decades, and a variety of physiological and environmental variables are clearly of etiological significance. Elevated serum lipid concentrations, arterial hypertension, and cigarette smoking account for much of the geographic distribution of CHD, and within geographic areas, these variables act as risk factors for extent and severity of the disease (Keys et al., 1972; McGill, 1968). There is evidence that the behavioral characteristics of individuals (e.g., coronary-prone behavior) also modulate risk for CHD, as do several attributes of social support summarized elsewhere in this chapter (Manuck, Kaplan, & Matthews, 1986). The mechanism(s) by which psychosocial variables contribute to coronary disease risk remain unclear, however, and (unlike such established risk factors as hypertension and elevated serum lipids) have only recently become a subject of intensive investigation. Nevertheless, a review of the sequence of events leading from development of the atherosclerotic lesion to the clinical manifestations of CHD helps identify a group of biologic processes upon which psychosocial factors could exert significant influence.

Biological Processes underlying CHD

The first lesion usually observed in the arterial intima is the fatty streak (Figure 1). Universally observed in children, such lesions are believed to be reversible and to have no physiological consequences (McGill, 1972). Although the process by which nonreversible, fibrous plaques develop is not known with certainty, injury (or possibly repeated injury) to the endothelial lining of the artery is believed to play an important initiating role (Ross, 1981). Such injury may lead to the local adherence of platelets and subsequent release of mitogenic (growth) substances, an

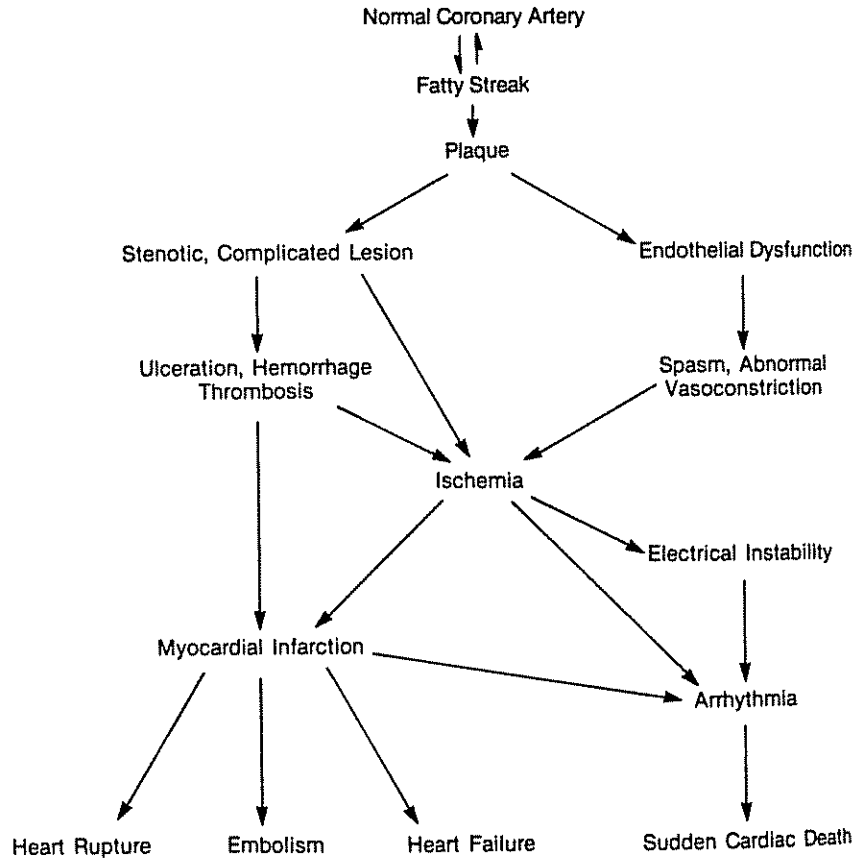

Figure 1. Pathophysiological pathways thought to connect the various processes associated with coronary artery atherogenesis and coronary heart disease.

increased infiltration of lipids into the artery wall, and intimal smooth muscle cell proliferation, all of which are aspects of plaque formation (Davies, 1986; Schwartz, Campbell, & Campbell, 1986).

Once formed, a progressing plaque may interfere with the ability of the artery wall (particularly the endothelial lining) to dilate in response to hemodynamic demands or to the presence of endogenous vasoactive substances. Such vascular dysfunction may result in arterial spasm, possibly contributing to myocardial ischemia—an inadequate supply of oxygen to the muscular tissue of the heart (Furchgott, 1983; Sokolow & McIlroy, 1987). The plaque may also induce aggregation and activation of platelets and the release by platelets of thomboxane A_2, a potent vasoconstrictor (Neri-Serneri et al., 1981). Independently of effects on endothelial or platelet function, the atherosclerotic plaque may progress through various stages of complication. An enlarging plaque can impede blood flow through the artery and thus cause ischemia, especially if myocardial oxygen demand should increase (e.g., during exercise). Finally, the plaque may also hemorrhage within itself (or rupture), resulting in thrombus formation, an interruption of blood flow to the heart, and ischemia (Sokolow & McIlroy, 1987).

Myocardial ischemia can have a number of consequences. If severe, ischemia may result in myocardial infarction and perhaps death of the individual. When death occurs quickly, it is generally because the infarction has triggered a fatal arrhythmia (Segal, Kotler, & Iskandrian, 1985). Post-infarction events include heart failure (impaired ability of the heart to function as a pump because of muscle death), embolization of such organs as the brain or gut (by thrombi found within the left ventricular cavity), and heart rupture. Even if not severe, myocardial ischemia may disrupt the electrical stability of the heart, thereby heightening its vulnerability to arrhythmias (Lown, 1987), which may then be triggered independently of such anatomical events as thrombosis, hemorrhage, and myocardial infarction. Arrhythmias triggered by ischemia-induced electrical instability, often ventricular tachycardia or fibrillation, are believed to be a major cause of sudden cardiac death (SCD; Segal, Kotler, & Iskandrian, 1985).

Research Suggesting a Link between Social Support and the Etiology of Physical Disease

Below we present a select review of the studies linking various conceptions of social support to the etiology of CHD. We focus on conceptions of social support that are examined across several studies.

Mortality Studies

The best documented effects in this literature are the role of social integration (SI) on all-cause mortality. In general, after controlling for traditional risk factors such as blood pressure, cigarette smoking, and serum cholesterol levels, healthy persons with higher SI scores are at lower risk for all-cause mortality than their more isolated counterparts (Berkman & Syme, 1979; House, Robbins, & Metzner, 1982; G. Kaplan, Cohn, Cohen, & Guralnik, 1988; G. Kaplan, Salonen, et al., 1988; Orth-Gomér & Johnson, 1987; Schoenbach, Kaplan, Fredman, & Kleinbaum, 1986; Seeman, Kaplan, Knudsen, Cohen, & Guralnik, 1987; Welin et al., 1985). SI deterioration (loss of network contacts) has also been associated with higher all-cause mortality risk (G. Kaplan & Hahn, 1989). Associations of SI and mortality in this literature are generally weaker for women and nonwhites than for white men (Berkman, 1986). Although there are also data on the role of satisfaction with social support in total mortality, the limited number of studies and lack of conceptual consistency across studies makes it difficult to draw conclusions (see Berkman & Syme, 1979; Blazer, 1982; House et al., 1982).

Data on the role of SI in mortality attributable to CHD are most relevant to this discussion. The studies that provided these data report beneficial effects of SI similar to those found in all-cause analyses (House et al., 1982; G. Kaplan, 1985, for Alameda County data originally reported by Berkman & Syme, 1979; G. Kaplan, Cohn, et al., 1988; G. Kaplan, Salonen, et al., 1988; Orth-Gomér & Johnson, 1987; Orth-Gomér, Undén, & Edwards, 1988; Vogt, Mullooly, Ernst, Pope, & Hollis, 1992). There is also evidence that SI predicts CHD mortality for persons who are unhealthy at the onset of the study—specifically, male survivors of acute myocardial infarction (MI; Ruberman, Weinblatt, Goldberg, & Chaudhary, 1984). These men were followed for 1 to 3 years after their MI. After controlling for traditional risk factors, relatively isolated survivors with low levels of education were found to have more total deaths and more sudden cardiac deaths than their less isolated, more educated counterparts.

Mortality studies of initially healthy persons do not clarify the stage of the disease process at which support acts. Hence greater CHD mortality for those with fewer social contacts may be accounted for by SI influences on the development of early lesions, lesion progression, or functional expressions of CHD such as MI. These studies also fail to indicate when in the course of diagnosed disease death occurs. Some specificity is provided by the single study reporting SI prediction of mortality for persons with serious disease (Ruberman et al., 1984). Because this study predicts CHD mortality after an initial event, it suggests that support plays a role in processes involved in triggering MI, or possibly in processes

leading to alterations in the rate of progression of coronary artery occlusion. These results do not, however, eliminate the possibility of SI influences on early disease onset or progression.

Morbidity Studies

Although there are strong suggestions that various conceptions of social support are associated with the onset of CHD, the results of the morbidity studies are less consistent and generally more difficult to interpret. There is evidence from two studies of Japanese-American men that SI is associated with decreased prevalence of MI, angina pectoris (AP), and total coronary heart disease (Joseph, 1980; Reed, McGee, Yano, & Feinlieb, 1983). A recent study of Swedish men similarly indicates an association between SI and decreased incidence of CHD (Orth-Gomér, Rosengren, & Wilhelmsen, 1993).

Evidence from three angiography studies, however, is less clear. In the first, British valvular heart disease patients who felt they could rely on family and friends were less likely to have histories of hypertension and myocardial infarction, as well as ECG evidence of myocardial infarction (Cooper, Faragher, Bray, & Ramsdale, 1985). Perceptions of support were not, however, related to signs of peripheral vascular disease, mitral valve disease, angina, or number of vessels with significant narrowing. In the second, patients in six San Francisco Bay Area hospitals who reported greater availability of instrumental support or feeling loved had less coronary occlusion than their unsupported counterparts (Seeman & Syme, 1987). Coronary occlusion was unrelated to SI, its structural components, or emotional support from family or friends. In the third study, a group at Duke University found that coronary occlusion was related to less emotional support among Type A individuals, but to more emotional support among Type Bs (Blumenthal et al., 1987). Although Seeman and Syme also tested the Type A behavior pattern by emotional support interaction, they did not find this effect.

Sample biases in angiography studies also suggest cautious interpretation. Because angiography study samples are limited to symptomatic and other high-risk patients, these investigations attempt to discriminate between high-risk persons who have CAD and those who do not, which differs substantially from distinguishing between the diseased and healthy in the general population (Cohen & Matthews, 1987).

One of the studies of CHD in Japanese-American men, the Honolulu Heart Study, examined SI as a predictor of the onset (incidence) of CHD, as well as the concurrent (prevalence) relations between SI and disease (Reed, McGee, & Yano, 1984; Reed et al., 1983). Total CHD rates were higher

among more isolated men when a SI scale developed through factor analysis was used. This effect was accounted for primarily through the prediction of nonfatal MI. This scale was not associated with the incidence of angina or of fatal MI, however, and a conceptually developed SI scale failed to predict any of these outcomes.

Several morbidity studies that examine the possible role of social support as a buffer (or moderator) of the increased risk of CHD associated with high levels of stress are also relevant. Johnson and Hall (1988) found that degree of interaction with coworkers buffered work stress against CHD prevalence for both males and females. Medalie and Goldbourt (1976) found that men who reported that their wives loved and supported them were buffered from the effects of high anxiety on the incidence of angina pectoris. In contrast, the Honolulu Heart Study (Reed et al., 1984) found no stress-buffering effect of an SI-like index for men in predicting CHD incidence.

Psychosocial Models Linking Social Support to CHD

At the most elementary level, it can be posited that social networks and social supports are linked to CHD either through their influence on behavioral patterns that decrease risk for disease or through effects on biological responses that influence disease onset and progression. In the following section, we discuss possible psychological and behavioral pathways through which social networks and supports could influence behavioral and biological risk for CHD.

We alluded earlier to two generic models of the influence of social support on CHD. The *stress-buffering* model proposes that support operates by protecting people from the potentially pathogenic influence of stressful events. The *main effect* model suggests that support has a beneficial influence irrespective of whether persons are under stress. The epidemiological data we reviewed are consistent with research on other health outcomes indicating that social integration is the primary cause of main effects of social support, and perceived availability of support is the primary cause of stress-buffering effects (see Cohen & Wills, 1985; Kessler & McLeod, 1985).

Social Integration and the Main Effect Model

Social integration has been conceptualized by Thoits (1983) as having multiple identities or ties to members of the network with different roles. Summaries of a number of psychological pathways through which social integration may influence the susceptibility to disease follow.

Information-Based Models

Having a wide range of network ties presumably provides multiple sources of information and hence an increased probability of having access to an appropriate information source. Information could influence health-relevant behaviors or help one to avoid stressful or other high-risk situations. For example, network members could provide information regarding access to medical services or regarding the benefits of behaviors that positively influence health and well-being. It is noteworthy, however, that integration in a social network could also operate to the detriment of health: discouraging use of medical services, providing inadequate alternative care, or influencing people to adopt behaviors inimical to health (e.g., McKinlay, 1973; Sanders, 1982; Seeman, Seeman, & Sayles, 1985).

Identity- and Self-Esteem-Based Models

There are several theoretical perspectives suggesting that social integration increases feelings of self-esteem, of self-identity, and of control over one's environment that result in better health. Social integration is presumed to provide a source of generalized positive affect, a sense of predictability and stability in one's life situation, and a recognition of self-worth because of demonstrated ability to meet normative role expectations (Cassel, 1976; Hammer, 1981; Thoits, 1983; Wills, 1985). These positive psychological states are presumed to be facilitative because they lessen psychological despair (Thoits, 1985), result in greater motivation to care for oneself (Cohen & Syme, 1985), or result in a benign neuroendocrine response (Bovard, 1959; Cassel, 1976).

A popular model in this category assumes that it is isolation that causes disease, rather than social integration that enhances health. This approach assumes that isolation increases negative affect and sense of alienation, and decreases a sense of control. Alternatively, one can merely view isolation as a stressor.

Social Influence Models

A socially integrated person is subject to social controls and peer pressures that influence normative health behaviors. To the extent that these pressures promote healthful behaviors (e.g., exercise, better diet, not smoking, moderating alcohol intake), social integration would promote better health. To the extent that normative behaviors within a social network promote behaviors that are deleterious to health, social integration would result in poorer health and well-being.

Tangible Resource-Based Models

A network may operate to prevent disease by providing aid and tangible and economic services that result in better health and better health care for network members. For example, network members could provide food, clothing, and housing that operate to prevent disease and limit exposure to risk factors. Networks may also provide nonprofessional health care that prevents minor illness from developing into more serious disease.

Perceived Social Support and the Stress-Buffering Models

The stress-buffering model posits that support protects persons from the potentially pathogenic influence of stressful events. The following models focus on the *perceived* availability of social support because this conception has been found to result in stress-buffering effects. We (Cohen & McKay, 1984; Cohen & Wills, 1985) have also proposed that stress buffering occurs only when there is a match between the needs elicited by the stressful event and the functions of support that are perceived to be available. For example, having someone who would loan you money may be useful in the event of a temporary job loss but useless when facing the death of a friend. A matching of support with need is implied, although not specified, in many of the models discussed below. We have also argued that certain types of support may be useful in coping with all or many stressors. Specifically, having people to talk to about problems (appraisal support) and having people who make you feel better about yourself (self-esteem support) may be generally useful, because these are coping requirements elicited by most stressors.

All of the stress-buffering models we discuss assume that stress puts persons under risk for CHD. This risk is presumed to occur either because stress triggers neuroendocrine response or arterial flow disturbances, or because behavioral adaptations to stress often include detrimental health practices like smoking and poor diet. Perceived social support operates in these models by decreasing the probability that situations will be appraised as stressful, by directly dampening neuroendocrine responses to stress, or by preventing persons from adopting unhealthy behaviors.

Information-Based Models

Stress may elicit network provision of information about the nature of the potential stressful events or about ways of coping with those events (see discussion of social comparison under stress by Cohen & McKay, 1984; Wills, 1983). To the extent that this information reduces the evaluation of

potential threat or harm in the context of existing coping resources, the event would be appraised as less threatening and/or harmful, and hence the risk of illness would be decreased (Lazarus & Folkman, 1984). It is also likely that in many cases the perception of available support operates *without any actual support being provided*, that is, believing that others will provide needed information if it becomes necessary can similarly result in potentially stressful events being appraised as benign (e.g., Wethington & Kessler, 1986). In both cases, a reduction in stress appraisal would be presumed to reduce negative affect, negative health behaviors, and concomitant physiological reactivity.

Identity- and Self-Esteem-Based Models

These models are minor twists on the information models described above. They suggest that others' willingness to help and/or the enhanced ability to cope that results from receiving help increase feelings of personal control and self-esteem. Such feelings may influence health through increased motivation to perform health behaviors or through suppression of neuroendocrine responses. Again, the mere perception that help is available may similarly trigger these processes.

Social Influence Models

Social controls and peer pressures could influence persons to cope with stressors in particular normative manners. Such influence processes would promote health to the extent that the normative coping behaviors were effective in reducing perceptions of stress, nonadjustive behavioral adaptations, and negative affective responses. Inappropriate norms, however, could lead to less effective coping and hence greater risk of stress-elicited CHD. To the extent that social coping norms were internalized, or that persons expect others to pressure them to cope in a particular manner, the mere perception of availability could influence the stress–disease process in the same manner as actually receiving support.

Tangible Resource-Based Models

Network contribution of aid or of tangible or economic services could reduce the probability of potentially stressful events being appraised as threatening or harmful and hence reduce the behavioral and affective concomitants of such an appraisal. Again, the mere perception of the availability of aid may operate without actual receipt of help. Tangible resources could also help resolve specific tangible problems after a stress appraisal is made.

Biological Models Linking Social Support to CHD

The models discussed above link social support to CHD either through influences on health practices or through neuroendocrine or hemodynamic response. The stress-buffering models generally address how perceived availability of support short-circuits the potential behavioral, hemodynamic, and neuroendocrine pathways that link stress to CHD pathogenesis, and the main effect models suggest direct influences of social integration on behavioral, neuroendocrine, and hemodynamic pathways. We alluded to evidence of increased risk for CHD among those with poor health practices (e.g., smoking), and these risks are discussed in detail elsewhere in this volume (see Chapters 10 and 11). In this section, we address the role that hemodynamic and neuroendocrine alterations accompanying or resulting from behavioral responses to provocative psychosocial stimuli may play in various stages of disease progression.

Central to our analysis is the argument that to understand the role of social support in CHD, it is necessary to consider the temporal courses of both the support concept and the disease stage under investigation. In short, some stages of the development of CHD extend over many years; to influence these stages, a psychosocial factor must endure over a similar period. Other stages of CHD develop very quickly, and as a consequence, a presumption of support endurance is not necessary for support to influence such a stage. In general, we argue that temporally stable concepts of support are plausible predictors of long-term stages of disease development (e.g., lesion formation and progression), and that both stable and unstable support concepts are plausibly involved in short-term stages of disease expression (e.g., myocardial infarction or arrhythmia).

We assume that social integration is a relatively stable support concept because it involves the existence of relationships (e.g., marriage and friendship) that tend to last for prolonged periods. We also assume that perceived availability of support is a relatively unstable concept because it is responsive to changes in the quality of relationships and in social and physical contexts. There is, however, little existing evidence on the stability of these or other social support concepts, and we accept the possibility that these stability assumptions may prove wholly or partly incorrect (see conflicting evidence on the stability of perceived support in Cohen, Sherrod, & Clark, 1986; Sarason, Sarason, & Shearin, 1986). For example, it is likely that the relative stability of support concepts vary across the life course (see Chapters 2 and 11). The correctness of our current assumptions about the stabilities of SI and perceived support, though, is not central to our premise that temporal stability is a key issue in proposing plausible models of the relations between social support and CHD.

Behavioral Stimuli and Coronary Risk

Current speculation regarding the biological mediation of behavioral influences on CHD is of a rather general nature, typically emphasizing the potential effects that acute cardiovascular and neuroendocrine reactions to stress might have on either atherogenesis or the precipitation of acute clinical events (Manuck et al., 1986). This focus on hemodynamic and neuroendocrine parameters derives in large measure from the frequent observation that Type A individuals respond to diverse psychomotor, cognitive, and interpersonal challenges with larger blood pressure and catecholamine reactions than do their more placid Type B counterparts (Houston, 1986; Wright, Contrada, & Glass, 1985). Additionally, there are several reports that patients with histories of angina pectoris or previous infarction show greater blood pressure responses to common laboratory stressors than patients without CHD or nonpatient controls (Corse, Manuck, Cantwell, Giordani, & Matthews, 1982; Dembroski, MacDougall, & Lushene, 1979; Shiffer, Hartley, Schulman, & Abelmann, 1976). In one prospective investigation of initially healthy men, large diastolic blood pressure reactions to cold immersion (the cold pressor test) predicted the 23-year incidence of CHD (Keys et al., 1971). Similarly, studies in cynomolgus monkeys show a significant positive association between the magnitude of animals' heart rate responses to an experimental stressor and extent of diet-induced coronary artery atherosclerosis (Manuck, Kaplan, & Clarkson, 1983, 1985). Together these findings suggest that recurrent episodes of acute cardiovascular and neuroendocrine reactivity evoked by behavioral stimuli may contribute to risk for coronary disease, and that such risk may be greatest among those individuals who exhibit the largest magnitude of psychophysiological response.

It is unclear when in the natural history of coronary disease these stress-induced cardiovascular or neuroendocrine adjustments would most likely contribute to pathogenesis. Nevertheless, it may be useful to consider what role such factors might play at successive stages in disease progression and to summarize the relevant evidence that currently exists.

Influences on Atherogenesis

Early Lesion Development

We hypothesized previously that arterial flow disturbances (turbulence, shear stress) that accompany marked cardiovascular reactions to behavioral stimuli promote injury to arterial endothelium (Manuck et al., 1986). Consistent with this hypothesis are experimental studies showing that exposure to behavioral stressors (e.g., physical restraint, tail shock)

produces several effects compatible with the development of early atherosclerotic lesions; these include structural changes in the arterial intima, subendothelial accumulation of mononuclear leukocytes, and the rapid turnover of endothelial cells in rat aorta (Gordon, Guyton, & Karnovsky, 1981; Hirsch Maksem, & Gagen, 1984). The further observation that beta-adrenergic receptor blockade mitigates both the endothelial changes and hemodynamic responses evoked by stress suggests that behaviorally induced endothelial injury may stem in part from acute cardiovascular adjustments associated with sympathetic nervous system activation (Hirsch et al., 1984). Unfortunately the arterial endothelium is not directly observable or amenable to imaging at the cellular level, and hence the forgoing results of animal experiments are not currently confirmed by in vivo studies of human beings.

Because stress is associated with biological responses that promote the development of early lesions, it is possible that support concepts that buffer stress might also enter into this phase of pathogenesis. This premise, however, is subject to several qualifications. Atherogenesis usually proceeds slowly, with significant lesions developing during early adulthood but generally not culminating in clinical events until the fifth decade of life. In order for a psychosocial factor to influence its development, we must assume either that short-term exposure to the psychosocial factor is sufficient to trigger a biological process with long-term implications or that the psychosocial factor endures and actively influences the pathogenic process over the course of the disease stage. The latter assumption is usually thought to be reasonable for the various behavioral dispositions previously implicated in coronary disease, such as Type A behavior and personality traits relating to hostility and the expression of anger. Hence it can be assumed that in order to buffer the influences of chronic stress or recurring acute stress, one would need to have perceptions of support that endure over many years. Although there is little known about the stability of support concepts, perceived support is generally thought to be only moderately stable and would not meet the above criterion. The implications of this work for social integration are less ambiguous: Because SI is considered quite stable and has been found to be negatively associated with negative affect and psychological distress, we expect that persons with lower SI are at greater risk for early lesion development.

Lesion Progression

Beyond the initiating events in atherogenesis, the progressing lesions of atherosclerosis also appear to be influenced by behavioral factors. For instance, there are now several demonstrations that Type A behavior, as

well as aspects of anger and its expression, are correlated significantly with coronary artery atherosclerosis in patients undergoing diagnostic cineangiography (Dembroski, MacDougall, Williams, Haney, & Blumenthal, 1985; Frank, Heller, Kornfeld, Sporn, & Weiss, 1978; MacDougall, Dembroski, Dimsdale, & Hackett, 1985; Williams et al., 1988; Williams et al., 1980). Yet there is no evidence that these associations are mediated by hemodynamic or neuroendocrine mechanisms. In fact, in the one published study germane to this question, no significant relationship was observed between extent of angiographically documented atherosclerosis and the magnitude of patients' cardiovascular reactions to mental stress (Krantz et al., 1981). Studies employing animal models, in contrast, offer some support for the hypothesis that sympathetic nervous system arousal (or its hemodynamic manifestations) underlie behavioral influences on plaque development. We noted earlier that the coronary atherosclerosis of cholesterol-fed cynomolgus monkeys was found, in two investigations, to be greatest among animals that exhibited the largest cardiac responsivity to a common laboratory stressor (Manuck et al., 1983, 1985). When males of the same species are housed in small social groups subject to periodic reorganization (i.e., an unstable social environment), the more dominant animals develop more extensive coronary atherosclerosis than their less competitive, subordinate counterparts (J. Kaplan, Manuck, Clarkson, Lusso, & Taub, 1982). Moreover, the worsened atherosclerosis of socially dominant monkeys can be prevented by long-term administration of a beta receptor blocking agent (propranolol hydrochloride), further indicating that sympathetic activation contributes to the behavioral exacerbation of atherogenesis in this animal model (J. Kaplan, Manuck, Adams, Weingand, & Clarkson, 1987).

Whether elevations in sympathetic-adrenal medullary activity potentiate atherogenesis through associated cardiovascular adjustments (e.g., turbulence accompanying an increased heart rate and blood pressure) or via effects attributable to increased levels of circulating catecholamines is a matter of some debate. Fluid dynamics are often invoked as contributing factors in atherogenesis because of the nonuniform (or focal) distribution of lesions within arteries. Atherosclerosis tends to predominate within large arteries and in close proximity to bifurcations or bends in the vessels—the same areas where flow disturbances (as might occur under stress) are most readily propagated (Manuck, Muldoon, Kaplan, Adams, & Polefrone, 1989). Elevated catecholamine concentrations have also been implicated in the development of arterial lesions. Such associations could reflect effects directly on the artery wall or influences of the catecholamines on such other pathogenic processes as alterations in lipid metabolism and platelet aggregation (Herd, 1983; Schneiderman, 1977). Other neuroendo-

crine substances may play a role in atherogenesis as well. For instance, the release of corticosteroids is increased under stress. In one investigation with coronary angiography, arterial occlusion was found to be greatest among men having high plasma cortisol concentrations (Troxler, Sprague, Albanese, Fuchs, & Thompson, 1977). The reproductive hormones are similarly reactive to disruptions of the social environment. In animal studies, impaired female reproductive function potentiates atherogenesis. In cynomolgus monkeys, for instance, loss of ovarian function following surgical ovariectomy produces a corresponding loss of female "protection" against diet-induced coronary artery atherosclerosis (Adams, Kaplan, Clarkson, & Koritnik, 1985). Interestingly, social subordination among reproductively intact female cynomolgus monkeys is also associated with impaired ovarian function (as evidenced by anovulation and low luteal-phase progesterone concentrations) and, in the presence of a cholesterol-containing diet, with an increased severity of coronary artery atherosclerosis (Kaplan, Adams, Clarkson, & Koritnik, 1984).

The preceding paragraphs enumerate some of the ways that behavioral variables might foster atherosclerosis. If perceived social supports protect individuals against coronary disease by ameliorating the atherogenic influences of predisposing psychosocial factors (e.g., Type A behavior or stress), this protection might be achieved by modulation of the same hemodynamic or neuroendocrine mechanisms that underlie the behavioral exacerbation of atherosclerosis. To the extent that the direct influence of SI is mediated by decreases in chronic emotional distress, the neuroendocrine mechanisms outlined earlier may similarly provide indirect evidence for the plausibility of the main effects of SI on lesion progression. Because of the stability of SI, we would expect that it could play a role in the long-term development of lesion progression. Again, it is somewhat unclear what duration of stress (or support) exposure is required to influence lesion progression, and hence it is difficult to assess the potential roles of stress and perceived support in these stages.

It should be cautioned that there is still little evidence that behaviorally evoked physiological reactions of any kind, whether cardiovascular or neuroendocrine, contribute to atherogenesis. Additionally, what data do support such an association are derived largely from experimental studies employing animal models.

Functional Expressions of CHD

Several investigators have demonstrated that emotional arousal and exposure to behavioral stressors can provoke transient and often painless (or silent) myocardial ischemia in individuals with existing coronary

artery disease (Sigler, 1967; Taggart, Gibbons, & Somnerville, 1969; Selwyn et al., 1986; Rozanski et al., 1988). It is noteworthy that the ischemia induced by emotional factors typically occurs at substantially lower heart rates than those associated with exercise-induced ischemia in these same individuals (Selwyn et al., 1986; Rozanski et al., 1988; Sung, Wilson, Robinson, Thadani, & Lovallo, 1988). This observation suggests that exercise and emotional factors may produce ischemia by somewhat different mechanisms (Sung et al., 1988). It is most likely that exercise causes ischemia in coronary patients by increasing myocardial oxygen demand to a level that cannot be supplied by the individual's atherosclerosis-laden (and hence occluded or stenotic) arteries (Sokolow & McIlroy, 1987). Emotional arousal or stress, in contrast, may induce coronary artery vasospasm or rapid thrombus formation within the artery, thereby reducing the supply of blood to the myocardium and creating an oxygen deficit (and thus ischemia) in the absence of an increased myocardial oxygen demand (Selwyn et al., 1986; Rozanski et al., 1988). An additional possibility is that behavioral factors raise myocardial oxygen demand beyond the individual's threshold for ischemia, but do so by increasing myocardial *contractility* in the absence of a corresponding rise in heart rate (Sung et al., 1988). Whatever the exact mechanism(s) of behaviorally induced ischemia, this functional manifestation of CHD (unlike patients' underlying atherosclerosis) is highly amenable to investigation because of the wide availability of portable EKG monitoring devices and software for detection of ischemic events, as well as the recent development of instrumentation permitting ambulatory radionuclide ventriculography (for measurement of left ventricular performance).

Myocardial infarction and electrical instability of the heart represent further escalations in CHD severity (Sokolow & McIlroy, 1987). It is generally accepted that thrombosis in a stenotic coronary artery (possibly associated with plaque rupture and hemorrhage) is a major cause of myocardial infarction (Segal et al., 1985; Sokolow & McIlroy, 1987). Although behavioral stimuli have been shown to trigger myocardial ischemia in individuals with existing coronary artery disease, it is not clear that psychosocial factors similarly potentiate the anatomical events immediately preceding myocardial infarction. Rather, it is likely that such events are related more closely to slow developmental processes operating within plaques (Bracket & Powell, 1988). Additionally, the occurrence and timing of heart rupture, myocardial thrombotic embolism, and heart failure (all of which are potential consequences of myocardial infarction and generally result in death) appear to reflect the condition of the anatomical substrate more than they do the prevailing hemodynamic and metabolic (i.e., neurogenic) milieu.

Unlike myocardial infarction, which is usually associated with acute anatomical changes, electrical instability of the heart represents an electrophysiological abnormality (Lown, 1987). This instability predisposes to arrhythmia and SCD (Segal et al., 1985). It is difficult to overestimate the importance of SCD (often defined as death occurring within 24 hours of the onset of initial symptoms), as it accounts for 50% to 65% of all mortality associated with CHD (Sokolow & McIlroy, 1987). The terminal event in most SCD cases is thought to be an arrhythmia that has degenerated to ventricular fibrillation, and a large proportion of SCD appears not to be associated with acute infarction or thrombosis (Friedman et al., 1973; Segal et al., 1985). The hallmark of SCD is its occurrence without warning or prodromal signs; thus there is no history of CHD in approximately half of SCD cases, and most patients having a previous history evidence no signs of worsening prior to their sudden demise (Lown, 1987; Segal et al., 1985).

Although the role of behavioral factors in myocardial infarction remain unclear, there is evidence linking emotional arousal and stress to both electrical instability of the heart and its sequelae, arrhythmia and SCD (Lown, 1987). It should be noted that the most common autopsy finding in cases of SCD is severe, multifocal coronary artery atherosclerosis (Friedman et al., 1973; Segal et al., 1985). This underlying atherosclerosis probably creates the ischemic environment within which electrical instability develops. But although such instability may have an atherosclerotic origin, once present the electrophysiologic abnormality is apparently independent of its anatomical substrate (Lown, 1987).

It has been hypothesized that in the electrically unstable heart, momentary changes in myocardial excitability caused by transient stimuli (e.g., neural traffic triggered by emotional arousal) provoke ventricular fibrillation (Kuller, Talbott, & Robinson, 1987; Lown, 1987; Verrier, 1987). Experimental studies in dogs have shown that various behavioral stimuli (aversive stimulation, avoidance conditioning, and induced rage) reduce thresholds for ventricular fibrillation (Verrier, 1987). Related experimental work indicates that similar behavioral challenges also alter myocardial perfusion, possibly acting as an arrhythmogenic stimulus (Billman & Randall, 1981; Vatner et al., 1971). In human beings, it is known that ventricular premature beats (VPBs) can initiate ventricular fibrillation and that frequent or complex VPBs are associated with an increased risk of SCD (Segal et al., 1985). Importantly, the incidence of VPBs in both cardiac patients and normal individuals can be increased with exposure to a variety of psychological challenges, including standard laboratory stressors, public speaking, and automobile driving (Lown, 1987; Taggart, Carruthers, & Sommerville, 1973; Taggart et al., 1969).

Among epidemiological evidence pertinent to the role of social sup-

ports in SCD are results of the Health Insurance Plan ancillary study of the Beta Blocker Heart Attack Trial (Ruberman et al., 1984). Here, a 3-year follow-up of individuals with previous myocardial infarction and complex VPBs revealed that both stress and isolation were independently related to elevated risk for SCD. A further and particularly striking example of sudden death potentially associated with behaviorally induced arrhythmia is that observed among young male Hmongs (members of a Laotian mountain tribe) who recently emigrated to large cities in the United States. Upward of 100 instances of unexplained nocturnal death have occurred among this population since the early 1980s. These deaths are thought to be the result of ventricular fibrillation (Baron et al., 1983; Otto, Janxe, & Cobb, 1984) and have been linked to stress arising from the clash between life in a primitive mountain culture and the demands of adapting to a modern urban environment.

The mechanism(s) mediating behavioral influences on VPBs, ventricular tachycardia, ventricular fibrillation, and SCD remain uncertain. These effects could be attributable to such factors as acute stimulation of the myocardium, alterations in coronary artery tone (and thus blood flow), platelet activation (with consequent effects on blood flow), or modification of the electrophysiological properties of the Purkinje fibers (Lown, 1987). Whatever the exact mechanism, it is likely that sympathetic nervous system stimulation plays a role. It has been shown experimentally, for example, that surgical sympathectomy, beta-adrenergic blockade, and relaxation can all reduce the profibrillatory effects of stress (Verrier, 1987) and that beta antagonists reduce the incidence of arrhythmia in CHD patients (Podrid & Lown, 1982). Moreover, the balance between vagal and sympathetic tone also affects the cardiac predisposition to arrhythmia. Hence the deleterious effects of stress on vulnerability to ventricular fibrillation can be reduced by enhancement of vagal tone (as with morphine); conversely, administration of the vagal antagonist atropine can increase vulnerability to ventricular fibrillation in stressed animals (Kuller et al., 1987; Lown, DeSilva, & Lenson, 1978).

We noted the distinction between sudden and nonsudden cardiac death. This distinction is more than heuristic and may relate importantly to behavioral influences in CHD (Friedman et al., 1973; Segal et al., 1985). Relevant here is a prospective study of post-MI patients in which SCD was found to be predicted predominantly by psychosocial factors (e.g., Type A behavior, low socioeconomic status, lack of a college education), whereas nonsudden cardiac death was produced by biological characteristics of the patients (e.g., severity of preexisting disease, location of infarction; Brackett & Powell, 1988). These findings are consistent with our understanding of the biological processes underlying sudden and nonsudden cardiac

death, inasmuch as the former is probably associated with arrhythmia (and therefore subject to neurogenic influences) and the latter more strongly related to acute anatomical alterations (which may be less susceptible to autonomic and neuroendocrine reactions induced by behavioral stimuli).

We have already suggested that only those dimensions of social support that are stable over long periods of time are likely to affect the decades-long processes of atherogenesis. The acute clinical manifestations of coronary disease (e.g., myocardial ischemia and ventricular arrhythmia), though, might be triggered by autonomic nervous system responses associated with transient episodes of emotional arousal. Because perceived social support has been found to operate as a stress buffer, and because its modest temporal stability would probably be sufficient to protect persons from transient stress-triggered events, we expect that perceived support is an important predictor of arrhythmia and SCD. Although social integration's stability is sufficient to operate in this context, there is little empirical reason at this point to believe that SI operates to protect persons from stress-induced coronary events.

Discussion and Summary

We provided evidence that different conceptions of social networks and supports are related to CHD morbidity and mortality, and we discussed the psychological and behavioral underpinning of such relations. The development of CHD, however, subsumes numerous stages, each accompanied by a somewhat different set of pathophysiological processes. Conditions that provoke endothelial injury and early plaque development, for instance, may not be the same as those responsible for plaque rupture and hemorrhage, outcomes associated with tissue necrosis, or the initiation of ischemic events and precipitation of myocardial infarction or SCD. It is plausible (and there is initial experimental evidence) that acute hemodynamic or neuroendocrine responses to stress contribute to coronary artery atherosclerosis and at least some of the functional expressions of CHD, such as cardiac arrhythmia and SCD. In turn, these relationships may mediate psychosocial influences on the development of CHD. Because of the differing temporal parameters that define events at each stage of pathogenesis, though, the types of behavioral factors that may either predispose or protect against coronary disease might also differ at varying points in the natural history of CHD.

The primary characteristic in relating a support concept to a pathophysiological process is the *stability of the support concept over time*. Plausible

models assume either that (a) the support conception under examination is relatively stable over the period of development of a disease stage, or (b) a short-term exposure to a particular level of social support is sufficient to influence the process underlying the disease stage. Social integration is a temporally stable conceptualization of social support; hence it is plausible that it could influence a process (e.g., development of atherosclerotic plaques) that has a very long and slow course of development. Thus there is a reasonable match here between stability of the support measure and the temporal characteristics of a pathogenic process (i.e., exposure to relatively lower levels of social integration lasts over the period of disease stage development).

Conceptualizations of social support with much shorter temporal stabilities, such as support satisfaction or perceived availability, would *not* be plausible predictors of atherosclerosis (see Cohen & Matthews, 1987). It is possible, however, to propose plausible models of CHD pathogenesis that focus on support measures with shorter stabilities. Consider, for example, modeling sudden cardiac death incidence. Assume that persons with undetected coronary artery disease (CAD) are more likely to suffer SCD if they experience stress (e.g., Glass, 1977). A severe stressor might trigger onset of the event. In this case, perceived available support may be important if it is stable over the course of stressor exposure and operates to buffer persons from stress *at the trigger point*.

In sum, the question of whether a particular stage of disease is susceptible to support influence depends on (a) whether the conceptualization of support under consideration affects processes that influence disease pathogenesis, (b) the temporal stability of the support concept, and (c) the nature and time course of the disease stage. The issue of temporal stability is important methodologically as well as conceptually. Consider a prospective study in which perceived support is measured at the onset in healthy individuals who are followed for 10 years. Because perceived support may not be a highly stable concept, the measure taken at onset may provide a poor estimate of the level of support at a later point when an acute stressor triggers an event. Hence, in order to study prospectively the role of an unstable support concept, it is necessary to repeatedly measure the concept over the course of the study at intervals that guarantee stability. A similar problem applies to retrospective studies. Consider, for example, the research on the relation between support and coronary artery occlusion in persons undergoing angiography. Because atherosclerosis emerges gradually over a lifetime, behavioral factors assessed at the time of angiographic evaluation could only have contributed to lesion development if the same factor also characterized that individual over a substantial portion of his or her life. Again, an unstable measure

may provide a poor estimate of the level of support over the course of atherogenesis.

Our general message is to enter this work with clear hypotheses regarding both the psychosocial and biological processes by which specific conceptualizations of support influence specific stages of coronary heart disease. Choices of social support concepts and of disease stages should be driven by theory specifying the psychological and biological pathways by which such outcomes could occur. These choices must consider the temporal parameters of both social and biological variables in forming plausible hypotheses and designing valid tests of these hypotheses

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References

Adams, M. R., Kaplan, J. R., Clarkson, T. B., & Koritnik, D. R. (1985). Ovariectomy, social status, and atherosclerosis in cynomolgus monkeys. *Arteriosclerosis, 53*, 192–200.

Baron, R. C., Thacker, C. O., Gorelkin, L., Vernon, A. A., Taylor, W. R., & Choi, K. (1983). Sudden death among Southeast Asian refugees: An unexplained nocturnal phenomenon. *Journal of the American Medical Association, 250*, 2947.

Berkman, L. F. (1985). The relationship of social networks and social support to morbidity and mortality. In S. Cohen & S. L. Syme (Eds.), *Social support and health*. New York: Academic Press.

Berkman, L. F. (1986). Social networks, support, and health: Taking the next step forward. *American Journal of Epidemiology, 123*, 559–562.

Berkman, L. F., & Syme, S. L. (1979). Social networks, host resistance, and mortality: A nine-year follow-up study of Alameda County residents. *American Journal of Epidemiology, 109*, 186–204.

Billman, G. E., & Randall, D. C. (1981). Mechanisms mediating the coronary vascular response to behavioral stress in the dog. *Circulation Research, 48*, 214.

Blazer, D. G. (1982). Social support and mortality in an elderly community population. *American Journal of Epidemiology, 115*, 684–694.

Blumenthal, J. A., Burg, M. M., Barefoot, J., Williams, R. B., Haney, T., & Zimet, G. (1987). Social support, Type A behavior, and coronary artery disease. *Psychosomatic Medicine, 49*, 331–339.

Bovard, E. (1959). The effects of social stimuli on the response to stress. *Psychology Reviews, 66*, 267–277.

Brackett, C. D., & Powell, L. H. (1988). Psychosocial and physiological predictors of sudden cardiac death after healing of acute myocardial infarction. *American Journal of Cardiology, 61*, 979–983.

Broadhead, W. E., Kaplan, B. H., James, S. A., Wagner, E. H., Schoenbach, V. J., Grimson, R., Heyden, S., Tibblin, G., & Gehlbach, S. H. (1983). The epidemiologic evidence for a relationship between social support and health. *American Journal of Epidemiology, 117*, 521–537.

Cassel, J. C. (1976). The contribution of the social environment to host resistance. *American Journal of Epidemiology, 104*, 107–123.

Cohen, S. (1988). Psychosocial models of the role of social support in the etiology of physical disease. *Health Psychology, 7*(3), 269–297.

Cohen, S., & Matthews, K. A. (1987). Editorial: Social support, Type A behavior and coronary artery disease. *Psychosomatic Medicine, 49*, 325–330.

Cohen, S., & McKay, G. (1984). Social support, stress and the buffering hypothesis: A theoretical analysis. In A. Baum, S. E. Taylor, & J. E. Singer (Eds.), *Handbook of psychology and health*. Hillsdale, NJ: Erlbaum.

Cohen, S., Sherrod, D. R., & Clark, M. S. (1986). Social skills and the stress protective role of social support. *Journal of Personality and Social Psychology, 50*, 963–973.

Cohen, S., & Syme, S. L. (1985). Issues in the study and application of social support. In S. Cohen & S. L. Syme (Eds.), *Social support and health*. New York: Academic Press.

Cohen, S., & Wills, T. A. (1985). Stress, social support, and the buffering hypothesis. *Psychological Bulletin, 98*, 310–357.

Cooper, C. L., Faragher, E. B., Bray, C. L., & Ramsdale, D. R. (1985). The significance of psychosocial factors in predicting coronary disease in patients with valvular heart disease. *Social Science and Medicine, 20*, 315–318.

Corse, C. D., Manuck, S. B., Cantwell, J. D., Giordani, B., & Matthews, K. A. (1982). Coronary-prone behavior pattern and cardiovascular response in persons with and without coronary heart disease. *Psychosomatic Medicine, 44*, 449–459.

Davies, P. F. (1986). Vascular cell interactions with special reference to the pathogenesis of atherosclerosis. *Laboratory Investigation, 55*, 5–24.

Dembroski, T. M., MacDougall, J. M., & Lushene, R. (1979). Interpersonal interaction and cardiovascular response in type A subjects and coronary patients. *Journal of Human Stress, 5*, 28–36.

Dembroski, T. M., MacDougall, J. M., Williams, R. B., Haney, T., & Blumenthal, J. A. (1985). Components of Type A, hostility, and anger-in: Relationship to angiographic findings. *Psychosomatic Medicine, 47*, 219–233.

Frank, K. A., Heller, S. S., Kornfeld, D. S., Sporn, A. A., & Weiss, M. B. (1978). Type A behavior pattern and coronary angiographic findings. *Journal of the American Medical Association, 240*, 761–763.

Friedman, M., Manwaring, J. H., Rosenman, R. H., Donlon, G., Ortega, P., & Grube, S. M. (1973). Instantaneous and sudden deaths, clinical and pathological differentiation in coronary artery disease. *Journal of the American Medical Association, 225*, 1319–1328.

Furchgott, R. F. (1983). Role of endothelium in responses of vascular smooth muscle. *Circulation Research, 58*, 373–376.

Glass, D. C. (1977). *Behavior patterns, stress, and coronary disease*. Hillsdale, NJ: Erlbaum.

Gordon, D., Guyton, J. R., & Karnovsky, M. J. (1981). Intimal alterations in rat aorta induced by stressful stimuli. *Laboratory Investigation, 45*, 14–27.

Hammer, M. (1981). "Core" and "extended" social networks in relation to health and illness. *Social Science and Medicine, 17*, 405–411.

Haynes, S., & Feinleib, M. (1980). Women, work and coronary heart disease: Prospec-

tive findings from the Framingham Heart Study. *American Journal of Public Health, 70*, 133–141.

Herd, J. A. (1983). Physiological basis for behavioral influences in atherosclerosis. In T. M. Dembroski, T. H. Schmidt, & G. Blumchen (Eds.), *Biobehavioral bases of coronary heart disease* (pp. 248–256). Basel, Switzerland: Karger.

Hirsch, E. Z., Maksem, J. A., & Gagen, D. (1984). Effects of stress and propanolol on the aortic intima of rats [Abstract]. *Arteriosclerosis, 4*, 526.

House, J. S., & Kahn, R. L. (1985). Measures and concepts of social support. In S. Cohen & S. L. Syme (Eds.), *Social support and health*. New York: Academic Press.

House, J. S., Landis, K. R., & Umberson, D. (1988). Social relationships and health. *Science, 241*, 540–545.

House, J. S., Robbins, C., & Metzner, H. L. (1982). The association of social relationships and activities with mortality: Prospective evidence from the Tecumseh Community Health Study. *American Journal of Epidemiology, 116*, 123–140.

Houston, B. K. (1986). Psychological variables and cardiovascular and neuroendocrine reactivity. In K. A. Matthews, S. M. Weiss, T. Detre, T. M. Dembroski, B. Falkner, S. B. Manuck, R. B. Williams (Eds.), *Handbook of stress, reactivity, and cardiovascular disease* (pp. 207–230). New York: Wiley.

Johnson, J. V., & Hall, E. M. (1988). Job strain, work place social support, and cardiovascular disease: A cross-sectional study of a random sample of the Swedish working population. *American Journal of Public Health, 76*, 1336–1342.

Joseph, J. (1980). *Social affiliation, risk factor status, and coronary heart disease: A cross-sectional study of Japanese-American men*. Unpublished doctoral dissertation, University of California, Berkeley.

Kaplan, G. A. (1985). Psychosocial aspects of chronic illness: Direct and indirect associations with ischemic heart disease mortality. In R. M. Kaplan & M. H. Criqui (Eds.), *Behavioral epidemiology and disease prevention* (pp. 237–269). New York: Plenum.

Kaplan, G. A., Cohn, B. A., Cohen, R. D., & Guralnik, J. (1988). The decline in ischemic heart disease mortality: Prospective evidence from the Alameda County study. *American Journal of Epidemiology, 127*, 1131–1142.

Kaplan, G. A., & Hahn, M. N. (1989). Is there a role for prevention among the elderly? Epidemiologic evidence from the Alameda County study. In M. G. Ory & K. Bond (Eds.), *Aging and health care: Social science and policy perspectives* (pp. 27–55). London: Tavistock.

Kaplan, G. A., Salonen, I. T., Cohen, R. D., et al. (1988). Social connections and mortality from all causes and cardiovascular disease: Prospective evidence from eastern Finland. *American Journal of Epidemiology, 128*, 370–380.

Kaplan, J. R., Adams, M. R., Clarkson, T. B., & Koritnik, D. R. (1984). Psychosocial influences on female "protection" among cynomolgus macques. *Atherosclerosis, 53*, 283–295.

Kaplan, J. R., Manuck, S. B., Adams, M. R., Weingand, K. W., & Clarkson, T. B. (1987). Propanolol inhibits coronary atherosclerosis in behaviorally predisposed monkeys fed an atherogenic diet. *Circulation, 76*, 1364–1373.

Kaplan, J. R., Manuck, S. B., Clarkson, T. B., Lusso, F. M., & Taub, D. B. (1982). Social status environment, and atherosclerosis in cynomolgus monkeys. *Arteriosclerosis, 2*, 359–368.

Keys, A., Aravnis, C., Blackburn, H., Van Bucham, F. S., Bezina, R., Djordjevic, B. S. Fidanza, F., Karkonen, M., Menotti, A., Puddu, V., & Taylor, H. L. (1972). Probability of middle-aged men developing coronary heart disease in five years. *Circulation, 45*. 815–828.

Keys, A., Taylro, H. L., Blackburn, J., Brozek, J., Anderson, J. T., & Somonson, E. (1971). Mortality and coronary heart disease among men studied for 23 years. *Archives of Internal Medicine, 128*, 201–214.

Kessler, R. C., & McLeod, J. D. (1985). Social support and mental health in community samples. In S. Cohen & S. L. Syme (Eds.), *Social support and health*. New York: Academic Press.

Krantz, D. S., Schaeffer, M. A., Davis, J. E., Dembroski, T. M., MacDougall, J. M., & Shaffer, R. T. (1981). Extent of coronary atherosclerosis, Type A behavior, and cardiovascular response to social interaction. *Psychophysiology, 18*, 654–664.

Kuller, L. H., Talbott, E. O., & Robinson, C. (1987). Environmental and psychosocial determinants of sudden death. *Circulation, 76*(Suppl. I), 48–56.

Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal and coping*. New York: Springer.

Lown, B. (1987). Sudden cardiac death: Biobehavioral perspective. *Circulation, 76*(Suppl. I), 186–196.

Lown, B., DeSilva, R. A., & Lenson, R. (1978). Roles of psychologic stress and autonomic nervous system changes in provocation of ventricular premature complexes. *The American Journal of Cardiology, 41*, 979–985.

MacDougall, J. M., Dembroski, T. M., Dimsdale, J. E., & Hackett, T. P. (1985). Components of Type A, hostility, and anger-in: Further relationships to angiographic findings. *Health Psychology, 4*, 137–152.

Manuck, S. B., Kaplan, J. R., & Clarkson, T. B. (1983). Social instability and coronary artery atherosclerosis in cynomolgus monkeys. *Neuroscience and Behavioral Reviews, 7*, 485–491.

Manuck, S. B., Kaplan, J. R., & Clarkson, T. B. (1985). Stress-induced heart rate reactivity and atherosclerosis in female macaques [Abstract]. *Psychosomatic Medicine, 47*, 90.

Manuck, S. B., Kaplan, J. R., & Matthews, K. A. (1986). Behavioral antecedents of coronary heart disease and atherosclerosis. *Arteriosclerosis, 6*, 2–14.

Manuck, S. B., Muldoon, M. F., Kaplan, J. R., Adams, M. R., & Polefrone, J. M. (1989). Coronary artery atherosclerosis and cardiac response to stress in cynomolgus monkeys. In A. W. Siegman & T. M. Dembroski (Eds.), *In search of coronary prone behavior* (pp. 207–227). Hillsdale, NJ: Erlbaum.

McGill, J. C. (1968). *The geographic pathology of atherosclerosis*. Baltimore: Williams & Wilkins.

McGill, J. C. (1972). Atherosclerosis: Problems in pathogenesis. *Atherosclerosis Reviews, 2*, 27–66.

McKinlay, J. B. (1973). Social networks, lay consultation and help-seeking behavior. *Social Forces, 51*, 275–292.

Medalie, J. H., & Goldbourt, U. (1976). Angina pectoris among 10,000 men: II. Psychosocial and other risk factors as evidenced by a multivariate analysis of a five year incidence study. *American Journal of Medicine, 60*, 910–921.

Neri-Serneri, G. G., Masotti, G., Gensini, G. F., Abbate, R., Poggessi, L., Galanti, G., & Favilla, S. (1981). Prostacyclin thromboxane and ischemic heart disease. *Atherosclerosis Reviews, 8*, 139–157.

Orth-Gomér, K., & Johnson, J. V. (1987). Social network interaction and mortality: A six year follow-up study of a random sample of the Swedish population. *Journal of Chronic Disease, 40*, 949–957.

Orth-Gomér, K., Rosengren, A., & Wilhelmsen, L. (1993). Lack of social support and incidence of coronary heart disease in middle-aged Swedish men. *Psychosomatic Medicine, 55*, 37–43.

Orth-Gomér, K., Undén, A. L., & Edwards, M. E. (1988). Social isolation and mortality in ischemic heart disease. *Acta Medica Scandanavica, 224*, 205–215.

Otto, C. M., Janxe, R. V., & Cobb, L. A. (1984). Ventricular fibrillation causes sudden death among Southeast Asian immigrants. *Annals of Internal Medicine, 100*, 45.

Podrid, P. J., & Lown, B. (1982). Pindolol for ventricular arrhythmias. *American Heart Journal*, 491–496.

Reed, D., McGee, D., & Yano, K. (1984). Psychosocial processes and general susceptibility to chronic disease. *American Journal of Epidemiology, 119*, 356–370.

Reed, D., McGee, D., Yano, K., & Feinleib, M. (1983). Social networks and coronary heart disease among Japanese men in Hawaii. *American Journal of Epidemiology, 117*, 384–396.

Ross, R. (1981). Atherosclerosis: A problem of the biology of arterial cell walls and their interactions with blood components. *Arteriosclerosis, 1*, 293–311.

Rozanski, A., Bairey, C. N., Krantz, D. S., Friedman, J., Resser, K. L., Morell, M., Hilton-Chalfen, S., Hestrin, L., Bietendorf, J., & Berman, D. S. (1988). Mental stress and the induction of silent myocardial ischemia in patients with coronary artery disease. *New England Journal of Medicine, 318*, 1005–1012.

Ruberman, W., Weinblatt, E., Goldberg, J., & Chaudhary, B. S. (1984). Psychosocial influences on mortality after myocardial infarction. *New England Journal of Medicine, 311*, 552–559.

Sanders, G. S. (1982). Social comparison and perceptions of health and illness. In G. S. Sanders & J. Suls (Eds.), *The social psychology of health and illness*. Hillsdale, NJ: Erlbaum.

Sarason, I. G., Sarason, B. R., & Shearin, E. N. (1986). Social support as an individual difference variable: Its stability, origins, and relational aspects. *Journal of Personality and Social Psychology, 50*, 845–855.

Schneiderman, N. (1977). Animal models relating behavioral stress and cardiovascular pathology. In T. M. Dembroski, S. M. Weiss, J. L. Shields, S. G. Haynes, & M. Feinleib (Eds.), *Coronary-prone behavior* (pp. 155–182). New York: Springer-Verlag.

Schoenbach, V. J., Kaplan, B. H., Fredman, L., & Kleinbaum, D. G. (1986). Social ties and mortality in Evans County, Georgia. *American Journal of Epidemiology, 123*, 577–591.

Schwartz, S. M., Campbell, G. R., & Campbell, J. H. (1986). Replication of smooth muscle cells in vascular disease. *Circulation Research, 58*, 427–444.

Seeman, M., Seeman, T. E., & Sayles, M. (1985). Social networks and health status: A longitudinal analysis. *Social Psychology Quarterly, 48*, 237–248.

Seeman, T. E., Kaplan, G. A., Knudsen, L., Cohen, R., & Guralnik, J. (1987). Social network ties and mortality among the elderly in the Alameda County study. *American Journal of Epidemiology, 126*, 714–723.

Seeman, T. E., & Syme, S. L. (1987). Social networks and coronary artery disease: A comparison of the structure and function of social relations as predictors of disease. *Psychosomatic Medicine, 49*, 340–353.

Segal, B. L., Kotler, M. N., & Iskandrian, A. S. (1985). Sudden cardiac death. In J. Morganroth & L. N. Horowitz (Eds.), *Sudden cardiac death* (pp. 1–21). Philadelphia: Grune & Stratton.

Selwyn, A. P., Sheal, M., Deanfield, J. E., Wilson, R., Horlock, P., & O'Brien, H. A. (1986). Character of transient ischemia in angina pectoris. *American Journal of Cardiology, 58*, 21B–25B.

Shiffer, F., Hartley, L. H., Schulman, C. L., & Abelmann, W. H. (1976). The quiz electrocardiogram: A new diagnostic and research technique for evaluating the relation between emotional stress and ischemic heart disease. *Journal of Human Stress, 6*, 39–46.

Shumaker, S. A., & Brownell, A. (1984). Toward a theory of social support: Closing conceptual gaps. *Journal of Social Issues, 40*, 11–36.

Sigler, L. (1967). EKG changes observed on the recall of past emotional disturbances. *British Journal of Medical Psychology, 40*, 55–64.

Sokolow, M., & McIlroy, M. B. (1987). *Clinical cardiology* (4th ed.). Los Altos, CA: Lange Medical Publications.

Sung, B. H., Wilson, M. F., Robinson, C., Thadani, U., & Lovallo, W. R. (1988). Mechanisms of myocardial ischemia induced by epinephrine: Comparison with exercise-induced ischemia. *Psychosomatic Medicine, 50*, 381–393.

Taggart, P., Carruthers, M., & Somnerville, W. (1973). Electrocardiogram, plasma catecholamines and lipids and their modification by oxprenolol when speaking before an audience. *Lancet, 2,* 311.

Taggart, P., Gibbons, D., & Somnerville, W. (1969). Some effects of motor-car driving on the normal and abnormal heart. *British Medical Journal, 4,* 130–134.

Thoits, P. A. (1983). Multiple identities and psychological well-being: A reformulation and test of the social isolation hypothesis. *American Sociological Review, 48,* 174–187.

Thoits, P. A. (1985). Social support processes and psychological well-being: Theoretical possibilities. In I. G. Sarason & B. R. Sarason (Eds.), *Social support: Theory, research and applications.* The Hague, Netherlands: Martinus Nijhoff.

Troxler, R. G., Sprague, E. A., Albanese, R. A., Fuchs, R., & Thompson, A. J. (1977). The association of elevated plasma cortisol and early atherosclerosis as demonstrated by coronary angiography. *Atherosclerosis, 26,* 151–162.

Turner, R. J. (1983). Direct, indirect and moderating effects of social support upon psychological distress and associated conditions. In H. B. Kaplan (Ed.), *Psychosocial stress: Trends in theory and research* (pp. 105–156). New York: Academic Press.

Vatner, S. F., Franklin, D., Higgins, C. B., Detrick, T., White, S., & VanCitters, R. L. (1971). Coronary dynamics in unrestrained conscious baboons. *American Journal of Physiology, 221,* 1369.

Verrier, R. L. (1987). Mechanisms of behaviorally induced arrhythmias. *Circulation, 76*(Suppl I), 48–56.

Vogt, T. M., Mullooly, J. P., Ernst, D., Pope, C. R., & Hollis, J. F. (1992). Social networks as predictors of ischemic heart disease, cancer, stroke, and hypertension: Incidence, survival and mortality. *Journal of Clinical Epidemiology, 45,* 659–666.

Wallston, B. S., Alagna, S. W., DeVellis, B. M., & DeVellis, R. F. (1983). Social support and physical health. *Health Psychology, 4,* 367–391.

Welin, L., Tibbin, G., Svardsudd, K., Tibbin, B., Ander-Peciva, S., Larsson, B., & Wilhelmsen, L. (1985). Prospective study of social influences on mortality. *Lancet, 1,* 915–918.

Wethington, E., & Kessler, R. C. (1986). Perceived support, received support, and adjustment to stressful events. *Journal of Health and Social Behavior, 27,* 78–89.

Wilcox, B. L., & Vernberg, E. (1985). Conceptual and theoretical dilemmas facing social support research. In I. G. Sarason & B. R. Sarason (Eds.), *Social support: Theory, research and application.* The Hague, Netherlands: Martinus Nijhoff.

Williams, R. B., Barefoot, J. C., Haney, T. L., Harrell, F. E., Blumenthal, J. A., Pryor, D. B., & Peterson, B. (1988). Type A behavior and angiographically documented coronary atherosclerosis in a sample of 2,289 patients. *Psychosomatic Medicine, 50,* 139–152.

Williams, R. B., Haney, T. L., Lee, K. L., Kong, Y. H., Blumenthal, J. A., & Whalen, R. E. (1980). Type A behavior, hostility, and coronary atherosclerosis. *Psychosomatic Medicine, 42,* 539–549.

Wills, T. A. (1983). Social comparison in coping and help-seeking. In B. M. DePaulo, A. Nadler, & J. D. Fisher (Eds.), *New directions in help seeking, vol. 2.* New York: Academic Press.

Wills, T. A. (1985). Supportive functions of interpersonal relationships. In S. Cohen & S. L. Syme (Eds.), *Social support and health.* New York: Academic Press.

Wright, R. A., Contrada, R. J., & Glass, D. C. (1985). Psychophysiologic correlates of Type A behavior. In E. D. Katkin & S. B. Manuck (Eds.), *Advances in behavioral medicine* (pp. 39–88). Greenwich, CT: JAI Press