Psychosocial Influences on the Development and Course of Coronary Heart Disease: Current Status and Implications for Research and Practice

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Psychosocial characteristics predict the development and course of coronary heart disease (CHD). In this review, the authors discussed human and animal research on psychophysiological mechanisms influencing coronary artery disease and its progression to CHD. They then reviewed literature on personality and characteristics of the social environment as risk factors for CHD. Hostility confers increased risk, and a group of risk factors involving depression and anxiety may be especially important following myocardial infarction. Social isolation, interpersonal conflict, and job stress confer increased risk. Psychosocial interventions may have beneficial effects on CHD morbidity and mortality, although inconsistent results and a variety of methodological limitations preclude firm conclusions. Finally, they discussed implications for clinical care and the agenda for future research.

Coronary heart disease (CHD) is the leading cause of death in the United States; each year about 450,000 people die from CHD, and 1,000,000 experience an initial or recurrent coronary event (American Heart Association, 2001). Among healthy 40-year olds, between 40% and 50% of men and between 25% and 35% of women will later develop CHD (Lloyd-Jones, Larson, Beiser, & Levy, 1999). Over $100 billion is spent on CHD each year in the United States in direct medical costs, disability payments, and lost productivity (American Heart Association, 2001). This disease involves the three major topics composing behavioral medicine and health psychology, making it a central focus throughout their 30-year history. In the first (i.e., health behavior and prevention), modifiable behavioral risk factors (e.g., smoking, activity level, diet) are important risk factors for the development of CHD (Stamler et al., 1999; Wannamethee, Shaper, Walker, & Ebrahim, 1998), and behavior change is an essential component of prevention. In the second topic (i.e., stress and disease or psychosomatics), other psychological and social factors have more direct effects on the development and course of CHD through the intervening psychobiological effects of stress and negative emotions. In the third (i.e., psychosocial aspects of medical illness and care), established CHD has extensive emotional and social impacts on patients and their families, behavior is a key element of standard care (e.g., medication adherence, dietary change, exercise), and psychosocial interventions are useful additions to traditional medical and surgical treatment.

Like the article on CHD in the previous special issue on behavioral medicine in this journal (Thorresen & Powell, 1992), we focused primarily on the second major topic—psychosocial influences on the development and course of CHD. We also reviewed one aspect of the third topic—interventions targeting psychosocial risk factors and their underlying psychophysiological mechanisms. Perhaps the most important implication of research on psychosocial risk factors for coronary disease is that interventions targeting these factors could reduce cardiac morbidity and mortality. This is not to say that behavioral approaches to prevention of CHD (e.g., smoking cessation) and management of other psychosocial aspects of established CHD (i.e., adherence to medical regimens) are less important. They are essential in a comprehensive approach (Smith & Ruiz, in press), but simply beyond our present scope.

Research on psychosocial influences on CHD and related interventions has expanded dramatically over the past decade. The landscape is no longer dominated by the Type A behavior pattern, though research evolving from this risk factor continues. Research on the psychobiologic mechanisms linking psychosocial risk factors to the course of CHD has grown in sophistication and is tied more closely to the complex pathophysiology of coronary artery disease (CAD) and CHD. Finally, evidence regarding the efficacy of adjunctive psychosocial interventions has grown substantially, in its technical sophistication, in the number and scale of the trials, and in the array of interventions it addresses. In this update, we review these topics and discuss emerging issues in research and practice. First, however, we review the pathophysiology of CAD and CHD, with a specific emphasis on the potential role of stress and related emotions. This research provides a firm scientific foundation for the role of psychological and social influences on the development and course of CHD and for related intervention strategies.

Mechanisms Linking Psychosocial Characteristics and Coronary Disease

CHD is composed of several manifestations of one underlying condition—CAD. Initially, lipids and related cells (e.g., macrophages, foam cells) accumulate in microscopic amounts in artery walls. These deposits grow into visible fatty streaks as early as
middle childhood and increase in prevalence with age (Strong et al., 1999; Tuzcu et al., 2001). Components of the inflammatory and reparative response to injury (e.g., monocytes, smooth muscle cell proliferation) foster the deposit of lipoproteins into cellular structures within artery walls (Ross, 1999). Later, extracellular accumulation of lipid deposits causes a thickening of the wall, extending outward. Eventually, these lesions include fibrous tissues and calcification and encroach into the artery opening (i.e., lumen) in a progressive manner (Stary et al., 1995). Advanced lesions can occur in late adolescence and early adulthood and become increasingly common and extensive with age (McGill et al., 2000). As lesions intrude into the lumen, blood flow is impeded and oxygen supply reduced in the area of myocardium supplied by the vessel.

Clinical manifestations of CHD appear decades after the initial stages and asymptomatic progression of CAD. Myocardial ischemia occurs when oxygen demand exceeds supply. Many episodes of ischemia are without symptoms or “silent,” but ischemia during physical exertion or, in some instances, emotional stress can produce chest pain (i.e., angina pectoris). Structural narrowing of the lumen at lesion sites can be exacerbated temporarily by contraction of smooth muscle within the artery wall. In advanced lesions, the calcified and fibrous cap may rupture or fragment. Exposed tissues promote clotting (i.e., thrombus), further impeding blood flow. Portions of thrombi may be dislodged (i.e., emboli), often blocking narrower artery segments (Muller, Abela, Nesto, & Tofler, 1994). Thrombi and emboli can cause near or complete blockage of blood flow resulting in severe ischemia. This causes rapidly worsening chest pain (i.e., unstable angina) or death of heart muscle (myocardial infarction, MI) (Stary et al., 1995). Ischemia also renders the myocardium electrically unstable, promoting disturbances in heart rhythm (i.e., arrhythmia). In the most severe (i.e., ventricular fibrillation), myocardial contractions become chaotic, and cessation of circulation may cause sudden cardiac death (SCD).

Statistical associations between psychosocial risk factors and CHD endpoints (e.g., MI, SCD) could reflect an effect on initial stages of CAD, pace of progression, precipitation of manifestations of CHD (i.e., triggers) among individuals with advanced or unstable CAD lesions, or some combination (Cohen, Kaplan, & Manuck, 1994). As we discuss later, the disease stage affected by psychosocial risk factors has implications for research and practice. As for specific mechanisms through which psychosocial factors affect the development of CAD and manifestations of CHD, a growing body of research suggests that stress and negative emotions—the primary psychological pathway hypothesized in current models—alter several physiological processes relevant to this complex pathophysiology (see Kop, 1999; Rozanski, Blumenthal, & Kaplan, 1999, for reviews). Of course, psychosocial risk factors (e.g., hostility, depression, social isolation) might also contribute to CAD and CHD through behavioral pathways (Smith & Gallo, 2001), such as health habits (e.g., smoking, inactivity) and behavioral components of standard care (e.g., adherence to medication regimens, diet restrictions).

**Effects of Psychophysiological Reactivity on CAD**

Cardiovascular reactivity (CVR) has been extensively studied as a mechanism linking psychosocial risk factors and CAD (Manuck, 1994). Briefly, more frequent, pronounced, and prolonged increases in blood pressure and heart rate, as well as related cardiovascular changes (e.g., increased sympathetic stimulation of the myocardium, reduced parasympathetic dampening, increased cardiac output and peripheral resistance), are hypothesized to initiate and hasten the development of CAD. There are two distinct hypotheses regarding CVR (Smith & Gerin, 1998). First, it is seen as an individual difference variable that marks or itself confers risk. Second, CVR is seen as a mediating mechanism through which psychosocial risk factors (e.g., social isolation, trait hostility) affect CAD and CHD.

Findings from several types of studies suggest that CVR promotes development of CAD. The magnitude of CVR to psychosocial stressors is associated with severity and progression of carotid artery atherosclerosis, assessed with ultrasound (Barnett, Spence, Manuck, & Jennings, 1997; Kamarck et al., 1997; Matthews, Owens, Kuller, Sutton-Tyrrell, Lassila, & Wolfson, 1998). Further, individual differences in CVR potentiate the effects of other psychosocial risk factors (e.g., low socioeconomic status; SES) on carotid atherosclerosis (Lynch, Everson, Kaplan, Salonen, & Salonen, 1998). Carotid atherosclerosis contributes to stroke but is also associated with the presence and severity of CAD. Prevailing models suggest that stress-induced increases in heart rate and blood pressure promote damage to the endothelium, making it more susceptible to inflammation and lipid deposition (Fuster, Badimon, Badimon, & Chesebro, 1992; Manuck, 1994). In a recent study of healthy adults, Sherwood, Johnson, Blumenthal, and Hinderliter (1999) found that an underlying determinant of CVR (i.e., increased peripheral resistance) was associated with endothelial dysfunction in healthy young adults, an early indication of atherosclerosis. Hence, CVR may contribute to earlier stages of initiation and progression of CAD. Alternatively, this association could reflect the fact that CVR and early, subclinical CAD reflect a common etiology (e.g., autonomic or neuroendocrine responsiveness) that marks or confers vulnerability to CAD and CHD.

Animal research provides converging evidence regarding CVR and CAD, as well as other psychophysiological mechanisms. In nonhuman primates, the magnitude of stress-induced increases in heart rate is associated with the severity of coronary atherosclerosis (Manuck, Kaplan, Adams, & Clarkson, 1989). In this model, pharmacological blockade of sympathetically mediated CVR eliminates the effects of chronic stress on initial endothelial injury and advanced lesions (J. R. Kaplan, Manuck, Adams, Weingand, & Clarkson, 1987; Skantze et al., 1998). These findings constitute strong evidence that physiological stress responses mediate the effect of psychosocial stress on CAD. Stress-induced changes in circulating concentrations of cortisol, other neuroendocrine factors, and lipids are also associated with atherosclerosis in human and animal models (for a review, see Kop, 1999).

**Psychophysiological Triggers of CHD**

Cardiologic assessments can be used to test the effects of stress on later manifestations of CHD (Rozanski, 1998). In both laboratory- and ambulatory paradigms, these techniques provide evidence that stress can evoke myocardial ischemia and that such changes predict important clinical outcomes (Kop, Gottdiener, & Krantz, 2001; Rozanski et al., 1999). Parallel research in humans and animals has elucidated mechanisms underlying these acute effects.
In an early study using positron emission tomography, Deanfield et al. (1984) found that a stressful mental arithmetic task decreased myocardial perfusion in 75% of CHD patients. Rozanski et al. (1988) used radionuclide ventriculography to demonstrate that a stressful speech task produced transient defects in ventricular wall motion, an indicator of ischemia, and this result was recently replicated by Stone et al. (1999). Related diagnostic techniques and stressors have been used to demonstrate that mental stress evokes ischemia (Burg, Jain, Soufer, Kems, & Zaret, 1993; Goldberg et al., 1996; Gott diener et al., 1994; Legault, Langer, Armstrong, & Freeman, 1995), including anger-arousing events (Irons on et al., 1992). Several studies using ambulatory electrocardiogram recording (i.e., Holter monitoring) demonstrated that stress and negative emotions during daily activities are associated with ischemia (Barry et al., 1988; Gabbay et al., 1996; Gullette et al., 1997; Krantz et al., 1996), including anger (Gabbay et al., 1996), tension, and sadness (Gullette et al., 1997). It is important to note that many of the studies on mental stress and ischemia were based on relatively small and select samples of patients (e.g., those with exercise-induced ischemia). Hence, although there are many positive findings, the generalizability of this association to a broader range of CHD patients requires additional research.

As discussed above, ischemia results when myocardial oxygen demand outstrips supply. Stress and negative emotions increase heart rate and contractile force in both healthy and CHD populations (Brownley, Hurwitz, & Schneiderman, 2000; Goldberg et al., 1996), thereby increasing oxygen demand. CHD patients with greater CVR to laboratory mental stressors are more likely to display ischemia during exercise testing (Kral et al., 1997), laboratory mental stressors (Goldberg et al., 1996; Krantz et al., 1991), and ambulatory monitoring (Blumenthal, Jiang, et al., 1995). Of interest, CVR to mental stress has also been found to predict recurrent events in post-MI patients (Manuck, Olsson, Hjemdahl, & Renqvist, 1992). However, ischemia occurs in response to mental stressors at lower heart rates than in response to physical stressors (Kop et al., 2001). If heart rate provides an index of oxygen demand, then effects of mental stress on ischemia occur during relatively low demand. This suggests that mental stress may also reduce cardiac oxygen supply.

Both human and animal investigations have demonstrated mechanisms involving reduced supply. In these studies, CAD and psychological stress combine to reduce blood flow, primarily through coronary artery spasm or constriction due to endothelial dysfunction. For example, in patients undergoing coronary angiography, Yeung et al. (1991) found that mental stress decreased the diameter of coronary arteries. This decrease did not occur in nondiseased sections, was significant at sites of mild lesions, and was pronounced at more severe lesions. Other studies have replicated this effect (Bol t wood, Taylor, Burke, Grogin, & Giacomini, 1993; Lacy et al., 1995). Ischemia induced by mental stress in patients with CAD might also be due to failure of coronary vessels to dilate in response to stress (Dakak, Quyyumi, Eisenhofer, Gold stein, & Cannon, 1995). Dilatation in response to mental stress does occur in persons without CAD, reflecting an appropriate reaction to increased myocardial oxygen demand. In a canine model, induction of an angerlike state (i.e., access to food threatened by a second dog) evoked a large decrease in coronary artery blood flow in animals with a partially occluded coronary artery (Verrier, Hagestad, & Lown, 1987) and promoted electrical instability of the myocardium, a condition that increases susceptibility to arrhythmia (Kovach, Nearing, & Verrier, 2001).

Stress also affects a variety of factors related to the readiness with which blood coagulates and clots (Von Kanel, Mills, Fainman, & Dimsdale, 2001), perhaps promoting thrombotic events. Further, acute stress increases the viscosity of blood through decreases in plasma volume (Allen & Patterson, 1995). Increased viscosity, in turn, is associated with greater risk of MI, perhaps through increased coagulation or the oxygen demands of circulating more viscous blood (Lowe, Lee, Rumley, Price, & Fowkes, 1997). Stress can also increase the susceptibility of patients with advanced CAD to the development of arrhythmias (Verrier & Lown, 1984).

Regardless of its origins in oxygen demand and supply, ischemia induced during mental stress is potentially quite important. In recent studies, patients who displayed ischemia during laboratory mental stress testing were at increased risk of recurrent coronary events and death (e.g., MI, SCD, bypass graft surgery, or angio-plasty; Jiang et al., 1996; Krantz et al., 1999; Sheps et al., 2002). However, some of these studies have involved relatively small and select samples. Hence, the prognostic importance of mental-stress-induced ischemia should be examined in additional research. These effects of acute stress on ischemia among persons with advanced CAD may contribute to the noticeable increase in acute coronary events following dramatic stressors (e.g., earthquakes, missile attacks; Dobson, Alexander, Malcolm, Steele, & Miles, 1991; Meisel et al., 1991).

Conclusions Regarding Effects of Stress on CAD and CHD

Pathways linking psychological stress and negative emotions with CHD are summarized in Figure 1. From even this brief review, several conclusions are warranted. First, there are several plausible mechanisms linking stress and negative emotions to the initiation and progression of CAD and to the subsequent emergence and course of CHD. Second, associations between psychosocial risk factors and CAD endpoints (i.e., MI, SCD) examined in epidemiological studies of initially healthy populations could reflect an effect at one or more places during its decades-long development. That is, such associations could indicate that these characteristics initiate or hasten the progression of CAD or precipitate manifestations of CHD after the development of severe CAD. Of course, risk factors could have both types of effects. Finally, in studies of the incidence and course of CHD, effects of risk factors could reflect one or more specific psychophysiological mechanisms. Hence, the current literature on mechanisms represents a maturing scientific base, but it also poses important questions for future research.

Two of these issues are likely to receive increasing attention over the next decade. First, traditional models of these psychosomatic effects emphasize the sympathetic branch of the autonomic nervous system. However, more recent research has implicated parasympathetic mechanisms as well. Higher levels of parasympathetically mediated heart rate variability (vagal tone, respiratory sinus arrhythmia, etc.) confer reduced risk of CHD morbidity and mortality (Bigger et al., 1992). As we discuss later in the article, these parasympathetic mechanisms have been linked to several psychosocial risk factors. Second, an intriguing body of research
has indicated that infectious and inflammatory mechanisms contribute to CAD and the course of CHD (Anderson et al., 1998; Mueller et al., 2002; Muhlestein et al., 1999; Zhu et al., 2001; for reviews, see Becker, de Boer, & van der Wal, 2001; Libby, Ridker, & Maseri, 2002). This suggests a point of integration of research on psychosocial mechanisms in CHD with studies of psychosocial influences on the immune system (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002; Kop & Cohen, 2001). That is, effects of stress and negative emotion on immune responses and inflammation may also contribute to the associations of psychological and social characteristics with CAD and CHD.

Recent Research on Psychosocial Risk Factors

In prior decades, cross-sectional comparisons between CHD groups and controls on personality traits, emotional disorders, and aspects of the social environment were common, as were studies in which psychosocial characteristics were correlated with the severity of CAD among patients referred for angiography. However, differences between CHD and control groups in cross-sectional studies may reflect psychosocial consequences of CHD rather than causes (Cohen & Rodriguez, 1995). Further, selection into angiography samples and the inherent restriction in range of predictors and outcomes may produce invalid estimates of associations between psychosocial characteristics and CAD (T. Q. Miller, Turner, Tindale, Posavac, & Dugoni, 1991). Studies of psychosocial risk factors increasingly rely on more definitive methods. Well-controlled, prospective studies of initially healthy populations or groups with carefully documented CHD are now much more common. Further, well-validated assessments of psychosocial predictors and reliable classification of coronary outcomes are more routine, as are appropriate statistical controls for possible confounds. Hence, this literature has grown in quality as well as size.
Hostility as the Toxic Component of the Type A Pattern

Historically, the Type A coronary-prone behavior pattern has been the best known psychosocial risk factor. Despite quantitative reviews indicating that the Type A pattern (as defined by behavioral assessment) is a significant risk factor for CHD in initially healthy populations (Matthews, 1988; T. Q. Miller et al., 1991), inconsistencies in research findings led investigators to examine individual components of the multifaceted pattern. This research has identified individual differences in hostility as an important predictor of CHD, as well as all cause mortality (T. Q. Miller, Smith, Turner, Guijarro, & Hallet, 1996). As typically used in this research, the term hostility itself refers to a multidimensional construct (Smith, 1994). The emotional component involves anger but also includes contempt and scorn. The behavioral component refers to verbal and physical aggression, which share an intent to inflict harm. Finally, the term hostility most accurately describes cognitive factors, such as cynicism, mistrust, and the tendency to interpret others’ actions as reflecting aggressive intent.

A quantitative review of studies published before 1995 found that hostility predicted CHD, though the association was stronger for behavioral ratings of hostility as opposed to self-reports (T. Q. Miller et al., 1996). Subsequent studies have indicated that self-reports of trait hostility and anger predict new coronary events among previously healthy people (Chang, Ford, Meoni, Wang, & Klag, 2002; Everson et al., 1997; Kawachi, Sparrow, Spiro, Vokonas, & Weiss, 1996; J. E. Williams et al., 2000). Further, self-reports of hostility have been associated with the severity and progression of atherosclerosis (Iribarren et al., 2000; Julkunen, Salonen, Kaplan, Chesney, & Salonen, 1994; Matthews, Owens, Kuller, Sutton-Tyrrell, & Jansen-McWilliams, 1998; Matthews, Dreary, & Fowkes, 2000), although there have been negative findings (O’Malley, Jones, Feuerstein, & Taylor, 2000). One study found that the tendency to express anger outwardly predicted the progression of coronary atherosclerosis as measured by repeated angiography, but cynical hostility did not (Angerer et al., 2000).

Finally, hostility also predicts more rapid restenosis of coronary arteries following angioplasty (Goodman, Quigley, Moran, Meilman, & Sherman, 1996; Mendes De Leon, Kop, de Swart, Bar, & Appels, 1996). These studies confirmed that hostility is a CHD risk factor and suggest that it may contribute to the development and course of CAD. However, it is important to note that in prospective studies of patients with established CHD, individual differences in anger and hostility do not appear to be robust predictors of recurrent cardiac events or survival (Hemingway & Marmot, 1999).

However, studies of ischemia and other outcomes provide evidence that anger and hostility can contribute to coronary events in persons with CAD. For example, in samples with documented CHD, hostile persons are more susceptible to ischemia (Burg et al., 1993; Helmers et al., 1993), and preliminary evidence suggests that they may be more susceptible to constriction of the coronary arteries during mental stress (Boltwood et al., 1993). As described above, in the context of significant CAD the arousal of anger can evoke ischemia (Gabbay et al., 1996; Ironson et al., 1992). Finally, in two retrospective but well-controlled studies, episodes of anger conferred a twofold increase in the likelihood of acute MI during the following 1–2 hr (Mittleman et al., 1995; Möller et al., 1999). This risk was greater among persons who did not routinely take aspirin or beta-blocking medication, suggesting that thrombolytic or sympathetically mediated mechanisms may be involved in the effects of anger arousal on acute MI. Hence, although the prospective evidence suggests that trait anger and hostility are more consistent predictors of initial CHD than of its course, clinical studies do suggest that they could contribute to acute events. The more consistent association of hostility with CHD incidence and mortality than with the course of established disease could reflect a selection process; hostile persons who survive initial events to be included in studies of CHD course may be at lower risk or more resilient for other reasons and may therefore be less likely to suffer recurrent or fatal disease (R. B. Williams, 2000).

A substantial body of research supports the prevailing view that psychophysiological correlates of stress and negative emotion compose the mechanism linking hostility and CHD (R. B. Williams, Barefoot, & Shekelle, 1985). Hostility is associated with heightened cardiovascular and neuroendocrine reactivity to stressful social situations in the laboratory involving strangers (Christensen & Smith, 1993; S. B. Miller et al., 1998; Powch & Houston, 1996; Suarez, Kuhn, Schanberg, Williams, & Zimmermann, 1998) and family members (Smith & Brown, 1991; Smith & Gallo, 1999), as well as during daily activities, as assessed by ambulatory assessments of blood pressure and cortisol excretion (Benotsch, Christensen, & McKelvey, 1997; Jammer, Shapiro, Goldstein, & Hug, 1991; Linden, Chambers, Maurice, & Lenz, 1993; Polk, Kamarck, & Shiffman, 2002; Pope & Smith, 1991). When recalling previous anger-arousing events, hostile persons display larger and more prolonged increases in blood pressure (Fredrickson et al., 2000). Also, unlike their more agreeable counterparts, hostile persons do not respond to social support with reduced CVR to stressors (Lepore, 1995; Smith, Uno, Uchino, & Ruiz, 2000). In addition to greater psychophysiological response to stressors, hostility is also associated with lower levels of social support and greater exposure to stress at home and work (T. Q. Miller, Mikesides, Chiriboga, & Ray, 1995; Newton & Kiecolt-Glaser, 1993; Smith, Pope, Sanders, Allred, & O’Keeffe, 1988). This greater psychosocial vulnerability (Smith, 1994), in turn, may reflect a transactional process in which hostile persons undermine sources of support and foster conflicts through their mistrusting thoughts and antagonistic actions (Smith, 1995). Unhealthy lifestyles could also contribute to the CHD risk associated with hostility. However, in most studies, but not all (Everson et al., 1997), statistical controls for health behaviors (e.g., smoking, inactivity) do not eliminate the association between hostility and subsequent CHD.

Dominance as a Potential Coronary-Prone Trait

In their prior review in this journal, Thoresen and Powell (1992) questioned the emerging view that hostility was the only pathogenic component of the Type A pattern. Subsequent studies suggested they may have been correct. Individual differences in social dominance may be a second risk factor within that constellation. In analyses of the original prospective study of Type A (Western Collaborative Group Study; Rosenman et al., 1975), Houston and his colleagues (Houston, Chesney, Black, Cates, & Hecker, 1992; Houston, Babyak, Chesney, Black, & Ragland, 1997) found that behavioral ratings of hostility and social dominance were independent predictors of CHD and mortality. Social dominance was the label given to a set of controlling behaviors, including the tendency to cut off and talk over the interviewer. A cross-sectional study of
patients referred for thalium exercise stress testing found that behavioral ratings of hostility and dominance were independently related to CHD (Siegmam, Townsend, Civelek, & Blumenthal, 2000). In prospective studies, self-report measures of social dominance predicted the development of CHD (Siegmam, Kubzansky, et al., 2000; Whiteman, Deary, Lee, & Fowkes, 1997).

The nonhuman-primate model described above provides an intriguing parallel to this research (J. R. Kaplan & Manuck, 1998). The chronic stress of repeated social reorganization (i.e., housing in unstable vs. stable social groups) produced more severe CAD among male macaques, but only among those in the top half of behaviorally assessed dominance hierarchies. Administration of beta-adrenergic blockade of sympathetic input to the heart eliminates the susceptibility of dominant animals to the atherogenic effects of stress. Hence, physiological effects of recurring efforts to assert social dominance may promote the initiation and progression of CAD (J. R. Kaplan et al., 1987; Skantze et al., 1998). In humans, efforts to assert social influence or interpersonal control evoke heightened CVR (Smith, Nealey, Kircher, & Limon, 1997; Smith, Ruiz, & Uchino, 2000), and persons scoring high on personality measures of dominance display greater CVR during social interaction (Newton, Bane, Flores, & Greenfield, 1999). Although this literature is small, the available epidemiological, animal, and psychophysiological studies suggest that dominance may confer risk for CHD.

Depression, Anxiety, and Negative Affectivity

Negative emotions other than anger have been widely studied over the past decade, and the findings resolve prior debates (Booth-Kewley & Friedman, 1987; Matthews, 1988; Stone & Costa, 1990). In a meta-analysis, Booth-Kewley and Friedman (1987) concluded that symptoms of depression and anxiety predict CHD. This conclusion was criticized (Matthews, 1988; Stone & Costa, 1990) as based in part on “soft” or less definitive CHD endpoints (e.g., chest pain). Individual differences in the tendency to experience negative emotions (i.e., neuroticism or negative affectivity) are associated with somatic complaints in the absence of actual disease, including chest pain in persons with normal coronary arteries (Costa & McCrae, 1987; Watson & Pennebaker, 1989). Hence, the findings of Booth-Kewley and Friedman (1987) could have been biased by an association between individual differences in negative affect and symptom reporting similar to—but not actually reflecting—CHD.

However, over the past decade, a number of methodologically sound studies indicated that symptoms of depression and anxiety, related emotional disorders, individual differences in the tendency to experience negative affect, and related personality traits indeed confer increased risk of MI, SCD, and other “hard” indicators of CHD. Studies of initially healthy populations have shown that symptoms of depression and anxiety and reports of hopelessness predict future coronary events (i.e., MI, coronary death), even with statistical controls for health behavior (e.g., smoking) and other potential confounding factors (Anda et al., 1993; Ariyo et al., 2000; Aromaa et al., 1994; Barefoot & Schroll, 1996; Eaker, Pinsky, & Castelli, 1992; Everson et al., 1996; Everson, Roberts, Goldberg, & Kaplan, 1998; Ford et al., 1998; Jonas & Mussolino, 2000; Kawachi, Colditz, Ascherio, Rimm, & Giovannucci, 1994; Kubzansky et al., 1997; Penninx et al., 2001; Pratt et al., 1996). Although there have also been negative findings (Wassertheil-Smoller et al., 1996). Among patients with established CHD, depression, anxiety, pessimism, and related characteristics have even stronger associations with recurrent coronary events (e.g., MI, cardiac procedures) and reduced survival (Ahern et al., 1990; Allison et al., 1995; Barefoot et al., 1996, 2000; Carney, Rich, Freedland, & Sanai, 1988; Denollet & Brutsaert, 1998; Follick et al., 1988; Frasure-Smith, Lespérance, Juneau, Talajic, & Bourassa, 1999; Frasure-Smith, Lespérance, & Talajic, 1995; Irvine et al., 1999; Lespérance et al., 2002; Penninx et al., 2001; Scheier et al., 1999), although here too there are negative findings (Lane, Carroll, Ring, Bevers, & Lip, 2001; Mayou et al., 2000). A characteristic labeled vital exhaustion—consisting of low energy, irritability, and demoralization—has also been linked to poor prognosis in CHD patients (Kop, Appels, Mendes de Leon, De Swart, & Bar, 1994; Mendes de Leon et al., 1996). Further, the effects of depression and other indicators of distress are significant even when controlling for the possible confounding effects of initial illness severity.

Clinical psychologists would be understandably concerned by pooling measures of depressive symptoms, anxiety symptoms, related personality characteristics, and diagnosable anxiety and affective disorders, because diagnosis and treatment are facilitated in their differentiation. However, questions about a graded—continuous versus qualitative—discontinuous distinction between depressive symptoms and depressive disorders has been the source of considerable controversy (e.g., Coyne, 1994; Fleit, Vredenburg, & Krames, 1997), with recent empirical support for both views (Ruscio & Ruscio, 2000; Santor & Coyne, 2001). Further, diagnosable disorders, subclinical symptoms, and personality traits involving depression and anxiety are closely related (Clark, Watson, & Mineka, 1994; Watson, Clark, & Harkness, 1994), and individual differences in negative affectivity or neuroticism predict future emotional disorders (Zonderman, Herbst, Schmidt, Costa, & McCrae, 1993). Future research may identify important differences among these predictors in the levels of CHD risk they confer (e.g., Herrmann, Brand-Driehorst, Buss, & Ruger, 2000) or their underlying mechanisms, but presently these closely correlated emotional characteristics seem to have similar and perhaps overlapping effects.

Autonomic processes have been identified as possible psychophysiological mechanisms linking this group of risk factors and CHD. For example, both anxiety and depression are associated with reduced heart rate variability—which can reflect either heightened sympathetic activity or decreased parasympathetic activity (or both)—and more specific indicators of vagal tone or parasympathetic responsiveness (Carney et al., 1995, 2001; Hughes & Stoney, 2000; Krittayaphong et al., 1997; Sheffield et al., 1998; Stein et al., 2000; Watkins, Grossman, Krishnan, & Sherwood, 1998). Other studies have found that depressive symptoms are

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1 It is important to note that among females in this model, subordinate rather than dominant social status confers risk. Subordinate females engage in less sexual intercourse. This results in lower levels of estrogen activity in this species, which may account for the association between social status and CAD (J. R. Kaplan et al., 1996).

2 Wassertheil-Smoller et al. (1996) did find that increasing levels of distress over time predicted CHD, although initial levels did not.
associated with sympathetically mediated cardiovascular and neuroendocrine reactivity (Light, Kothandapani, & Allen, 1998).

Depression and individual differences in negative affect are also associated with increased exposure to stressful social circumstances (Bolger & Schilling, 1991; Bolger & Zuckerman, 1995; Coyne, Thompson, & Palmer, 2002; Daley & Hammen, 2002; Daley et al., 1997; Davila, Bradbury, Cohan, & Tochuk, 1997; Fincham, Beach, Harold, & Osborne, 1997; Harkness & Luther, 2001; S. L. Johnson & Jacob, 1997). Through a variety of cognitive and interpersonal processes, emotionally distressed individuals may experience more environmental stress, as well as respond to it with greater psychophysiological reactivity and/or reduced parasympathetic dampening of stress responses. However, the extent to which these mechanisms account for the effects of this group of risk factors on CHD requires further investigation.

Also, depression and other chronic negative affects are associated with suppressed immune function (Herbert & Cohen, 1993; Irwin, 2001), and in one recent study of patients with CAD, depressive symptoms were associated with immunologic markers of chronic infection and inflammation (Appels, Bar, Bruggeman, & De Baets, 2000). Hence, effects of depression in particular—and psychosocial risk factors generally—on immunologic mechanisms warrant further research (Kop & Cohen, 2001). Finally, other psychophysiological (e.g., coagulation) or behavioral (e.g., medical adherence, lifestyle) mechanisms may also contribute to the association of negative affect with CHD (DiMatteo, Lepper, & Croghan, 2000; Von Kanel et al., 2001).

Social Isolation and Conflict

Decades of research has indicated that social isolation and low levels of perceived social support confer increased risk of CHD (for reviews, see Berkman, 1995; Hazuda, 1994; Orth-Gomer, 1994). Recent studies of CHD morbidity and mortality have confirmed this association in initially healthy populations (e.g., G. A. Kaplan et al., 1994; Orth-Gomer, Rosengren, & Wilhelmsen, 1993; Pennix et al., 1997; Seeman et al., 1993; Vogt, Mullooly, Ernst, Pope, & Hollis, 1992). Social isolation is particularly unhealthy in patients with preexisting CHD (Angerer et al., 2000; Berkman, Leo-Summers, & Horwitz, 1992; Case, Moss, Case, McDermott, & Eberly, 1992; Gorkin et al., 1993; Horsten et al., 2000; Krumholz et al., 1998; Welin, Lappas, & Wilhelmsen, 2000; R. B. Williams et al., 1992; Woloshin et al., 1997), although different indicators of support and isolation sometimes produce inconsistent effects (Irvine et al., 1999). In one recent study, in which low social support did not predict post-MI prognosis, high support reduced the negative effects of depression on survival (Frasure-Smith, Lespérance, Gravel, Masson, Juneau, Talajic, & Bourassa., 2000). In nonhuman-primate models, social isolation (i.e., solitary vs. stable group housing) promotes CAD (Shively, Clarkson, & Kaplan, 1989).

Many indicators of social support and isolation have been used in epidemiological studies, ranging from quantitative measures of network characteristics and activities (e.g., membership in organizations, marital status) to more subjective measures of network quality (e.g., perceived adequacy or satisfaction with support). For both types of measures, it is generally assumed that they reflect actual network characteristics and social experiences. However, recent theory and research has challenged this assumption, suggesting that such measures reflect the individual’s general sense of acceptance, the accessibility of internal representations of social ties, and other personality processes to an equal or even greater extent than actual interpersonal events (Lakey & Drew, 1997; G. R. Pierce, Lakey, Sarason, Sarason, & Joseph, 1997). For example, individuals with low levels of social support tend to appraise potentially supportive behavior as less supportive than do individuals with high support (T. Pierce, Baldwin, & Lydon, 1997). Hence, although epidemiological studies have clearly indicated that something tapped by measures of social isolation and support predicts the development and course of CHD, recent research has raised questions about the precise nature of this predictive factor. This ambiguity could complicate the design of risk-reducing interventions, despite the clear evidence of a predictive association.

Studies of stress and adaptation increasingly have recognized that social strain and isolation are distinct concepts with potentially independent effects (Coyne & Bolger, 1990; Rook, 1990; Uchino, Holt-Lunstad, Uno, & Flinders, 2001). Recent studies of patients with cardiovascular disease have suggested that conflict in personal relationships predicts poor outcomes. Orth-Gomer et al. (2000) found that women with CHD who reported high levels of marital conflict were nearly three times as likely to experience a recurrent coronary event as married but nondistressed women. Coyne et al. (2001) reported a similar association between marital conflict and death in a sample of patients with congestive heart failure, most of whom had experienced a prior MI. In a large sample of initially healthy but high-risk men, Matthews and Gump (2002) found that increasing levels of marital stress were associated with increased risk of death from CHD. Nonhuman-primate models suggest that chronic social stress involving conflict can promote atherosclerosis (J. R. Kaplan et al., 1983; J. K. Williams et al., 1993), and this effect has recently been replicated in a rabbit model of atherosclerosis (McCabe et al., 2002). However, compared with the literature on isolation, there has been limited research on this potentially important risk factor.

Psychophysiological studies have indicated that social support and conflict are associated with plausible mechanisms. Individual differences in perceived support and the experimental manipulation of support are generally associated with reduced cardiovascular and neuroendocrine reactivity to stressors (Kamarck, Peterman, & Raynor, 1998; Lepore, 1998; Thorsteinsson & James, 2000; Uchino, Cacioppo, & Kiecolt-Glaser, 1996). For example, the presence of a friend attenuates CVR in response to stressful laboratory tasks (Christenfeld et al., 1997). Consistent with the view that beneficial effects of social support do not require actual supportive transactions, mental activation of supportive network ties also attenuates CVR to stressors (Smith, Ruiz, & Uchino, 2001). Further, positive social ties may lower risk of CAD and CHD not only through direct dampening of CVR and other components of the stress response but also through separate physiological mechanisms (e.g., release of oxytocin) involved in attachment and affiliation (Knox & Uvnas-Moberg, 1998; Uvnas-Moberg, 1997). Finally, conflictual interactions produce heightened cardiovascular and neuroendocrine responses in laboratory (for a review, see Kiecolt-Glaser & Newton, 2001) and ambulatory studies (e.g., Holt-Lunstad, Uchino, & Smith, 2000).
Job Stress

Two models of job stress have been examined as CHD risk factors. The job strain model posits that jobs high in demand (mental and physical effort, etc.) but low in control increase risk (Karasek, 1979; Theorell & Karasek, 1996). The second model suggests that an asymmetry of effort relative to rewards confers risk (Siegrist, 1996). Prospective studies have found that job strain is associated with increased risk of CHD morbidity and mortality (Bosma, Peter, Siegrist, & Marmot, 1998; Hall, Johnson, & Tsou, 1993; Theorell et al., 1998), although low job control (e.g., decisional latitude) may have more impact than job demands or the combination of these characteristics (Bosma et al., 1998; Hammar, Alfredsson, & Johnson, 1998; J. V. Johnson, Stewart, Hall, Fredlund, & Theorell, 1996; Marmot, Bosma, Hemingway, Brunner, & Stansfeld, 1997; Yamal, Mittelman, Horsten, Scheneck-Gustafsson, & Orth-Gomér, 2000). Further, some negative results have been reported (Hlatky et al., 1995). The effort–reward model has been the focus of less research, although this imbalance has been found to predict the progression of atherosclerosis and new coronary events (Lynch, Krause, Kaplan, Salonen, & Salonen, 1997; Peter, 1995; Siegrist, Peter, Junge, Cremer, & Seidel, 1990). Effort–reward imbalance is also associated with increased risk of CHD even when variance associated with job strain is controlled (Bosma et al., 1998). A recent review concluded that both types of job stress confer increased risk of future CHD, independent of any associations between job stress and negative health behaviors (Peter & Siegrist, 2000). Further, Matthews and Gump (2002) recently found that the number of self-reported work stressors was associated with increased risk of death from CHD.

Studies of mechanisms potentially underlying these effects generally indicated that job stress is associated with CVR and other stress responses. For example, persons with high levels of job strain display higher levels of day-to-day blood pressure, as assessed through ambulatory monitoring (Schnall et al., 1990; Schnall, Schwartz, Landsbergs, Warren, & Pickering, 1998). However, other studies have not replicated this effect (Matthews et al., 2000) or found inconsistent effects for men and women (Blumenthal, Thyrum, & Siegel, 1995; Light, Turner, & Hinderliter, 1992). Hence, the mechanisms underlying the effects of job stress on CHD are not yet clearly established.

Conclusions Regarding Risk Factors

Over the past 10 years, evidence has expanded indicating that psychosocial characteristics predict the development and course of CHD. Support for the effects of anger and hostility continues to mount, as does evidence of the association of these personality characteristics with mechanisms that potentially influence CAD and CHD. However, prospective studies of initially healthy persons have produced some negative findings. Further, there is little evidence that individual differences in anger and hostility are consistent risk factors among patients with established disease, even though some studies of persons with CAD find that episodes of anger can trigger ischemia and coronary events. The evolution of research on the Type A pattern has produced preliminary evidence of another possible coronary-prone characteristic—social dominance. Here too, human and animal studies have identified associations between this stable social behavior and plausible pathophysiological mechanisms.

Although there are some inconsistencies, individual differences in negative affect and related disorders and traits confer increased risk of initial development of CHD in initially healthy populations and increased risk of recurrent events and reduced survival among patients with preexisting CHD. The effect of depression on prognosis following MI currently appears to be a particularly important risk factor, underscoring the importance of routine assessments of its potentially unique presentation in cardiac populations (Lespérance & Frasure-Smith, 2000). The mechanisms underlying these effects may involve parasympathetic components of autonomic functioning, sympathetic reactivity, altered homeostasis, and heightened exposure to stressors. Social isolation and low perceived support are clearly associated with increased risk of CHD and reduced survival, and considerable evidence suggests that their impact on stress reactivity is a plausible mechanism. However, recent models of the nature of social support and isolation and the meaning of related measures raise important questions about the specific psychosocial characteristic that confers risk. Social conflict may prove to be an independent interpersonal influence on CHD. Finally, job stress predicts CHD, although the specific work characteristics and underlying mechanisms responsible for these effects remain to be clarified.

With some notable exceptions (e.g., Iribarren et al., 2000; Lynch et al., 1997; Matthews, Owens, Kuller, Sutton-Tyrrell, & Jansen-McWilliams, 1998), most studies have examined indications of CHD that reflect late stages of the disease (e.g., MI, CHD, death). Although these outcomes are obviously important, this approach obscures the point(s) in the natural history of the disease where risk factors exert their effects. Noninvasive measures of the severity and progression of atherosclerosis (e.g., carotid artery ultrasound; computed tomography scans of coronary artery calcium deposits) in representative samples of initially asymptomatic adults can clarify the impact of psychosocial risk factors on earlier stages of disease, as can the use of still earlier indications of arterial changes (e.g., endothelial dysfunction) in adolescents and young adults. Cardiac imaging and other diagnostic procedures can determine the role of psychosocial risk factors in later stages of disease (Rozanski, 1998). Findings from these types of research would not only answer basic questions about the timing of psychosocial effects but also help to refine psychosocial interventions. Further, assessments of subclinical indications of atherosclerosis and ischemia provide alternatives to the less frequent occurrence of clinical events. This permits studies of clinically relevant outcomes without the sample sizes and long follow-up periods necessitated by a focus on clinical events.

Most psychosocial risk factors are clearly related to plausible psychophysiological mechanisms. However, these associations are best seen as consistent with—but not providing direct evidence of—their hypothesized mediational role in the psychosomatic process. Animal models provide important evidence in this regard, but future human studies must incorporate measures of risk factors, psychophysiological mechanisms, and CAD or CHD outcomes for more definitive tests of mediational hypotheses. This is an ambitious research strategy that may be difficult to implement in large epidemiological studies, but analyses of this type are needed to evaluate the mediational models currently guiding the field.

A major challenge in the coming decade will be to develop useful approaches for studying conceptually distinct but often highly correlated risk factors. These risk factors are typically
studied separately, despite their intercorrelation. When multiple psychosocial characteristics are studied, usually their independent statistical effects are tested in multivariate analyses or, in rare occasions, interactive effects (i.e., moderation) are tested. Future research should determine if the overlapping aspect of correlated risk factors (e.g., social conflict, anger, and depression) is the most robust predictor of initial and/or recurrent events to examine possible core dimensions of psychosocial risk. Alternatively, correlations among risk factors may indicate distinct processes through which characteristics of individuals and their social contexts jointly influence the development of CAD and CHD. For example, hostile persons experience increased exposure to stressful interpersonal events as well as low levels of social support (Smith, 1995), and similar patterns have been found in persons with depression (Joiner & Coyne, 1999). Hence, rather than a core dimension of psychosocial risk, these aggregations of risk factors could reflect transactional processes in which people both influence and are influenced by their social networks in such a way as to increase or reduce cardiovascular risk. The interpersonal and cognitive–social traditions in personality psychology (Kiesler, 1996; Mischel & Shoda, 1999) provide concepts and methods for studying connections between the personality traits and social contexts that predict CHD. Further, they can be adapted to research on both risk factors (Gallo & Smith, 1999) and underlying mechanisms (Smith, Gallo, & Ruiz, in press). Such approaches to correlated risk factors could help construct a more accurate “psychosocial epidemiology of everyday life”\(^3\) and a social psychophysiology of the underlying mechanisms.

**Psychosocial Interventions for CHD**

At the time of the review by Thoresen and Powell (1992), the Recurrent Coronary Prevention Project (Friedman et al., 1986) represented the most compelling evidence that psychosocial risk factors for CHD could be modified through psychological interventions, with beneficial effects on medical outcomes. Patients randomized to a control condition received counseling about appropriate lifestyle changes following MI, whereas patients randomized to the active intervention received group therapy consisting of relaxation training, self-monitoring of stress and Type A behavior, cognitive restructuring, and other cognitive–behavioral techniques. The intervention reduced nonfatal recurrent cardiac events by 44\% (Friedman et al., 1986). Among patients with less severe initial disease, the intervention also significantly reduced cardiac deaths (Powell & Thoresen, 1988). Internal analyses suggested that larger reductions in Type A behavior were related to reduced risk of recurrent events. In a second influential study from that period, Frasure-Smith and Prince (1985) found that an intervention in which nurses monitored stress levels of post-MI patients and provided supportive counseling when needed (i.e., the Ischemic Heart Disease Life Stress Monitoring Program, IHDLSM) produced a significant reduction in cardiac deaths, relative to randomized controls. At the time of the previous special issue, these studies and a number of smaller controlled trials suggested that such interventions were useful additions to CHD care (Thoresen & Powell, 1992).

**Recent Studies**

Intervention trials designed to modify psychosocial risk factors among CHD patients have produced mixed results over the past decade. It is important to distinguish between interventions where stress reduction, modification of coronary-prone behavior, or related risk factors are the primary focus and those focusing on modification of traditional behavioral risks (e.g., smoking, exercise, diet; Blumenthal & Emery, 1988). As we discuss later in the article, the latter type of intervention has been found to have beneficial effects, some of which include reductions in stress and related psychological risk factors. However, specific comparisons of stress management and similar interventions with appropriate control conditions permit clear evaluations of the effects of psychosocial risk interventions.

In a large and well-controlled replication of the IHDLSM intervention, Frasure-Smith et al. (1997) did not find significant intervention effects. A second large and well-controlled trial of stress management for post-MI patients also found no effects on cardiac recurrences (Jones & West, 1996). However, Blumenthal et al. (1997) did find that a stress management intervention reduced clinical cardiac events. The intervention also reduced the amount of ischemia evident during ambulatory (i.e., Holter) monitoring, particularly among patients with high initial levels of daily ischemia. It is important to note, however, that although controls were well matched to intervention participants on important medical and demographic risk factors, the study relied on a nonrandomized no-treatment comparison group.

Of the behavioral interventions in CHD, a multicomponent program developed by Ornish et al. (1990) has received the most attention. Stress management through meditation and other techniques is combined with aerobic exercise, a very-low-fat diet, and group support. In recent tests, the approach produced clear reductions in recurrent events, CAD severity, and evidence of improved coronary circulation compared with standard care (Gould et al., 1995; Ornish et al., 1998). However, it is not clear which feature of the multicomponent intervention is most responsible for its effects, and the extent of behavior change required has raised concerns about its usefulness in general patient populations (Billings, 2000). In a small study, Gidron, Davidson, and Bata (1999) found that a cognitive–behavioral intervention specifically targeted at modifying hostility was effective in reducing hostility and blood pressure in CHD patients. Preliminary results also indicate that treated patients in this trial experienced fewer and briefer rehospitalizations, with significantly lower associated medical costs (Davidson, 2000). In a study of high-risk persons before the onset of CHD, Castillo-Richmond et al. (2000) randomized hypertensive African American participants to receive a stress management intervention or usual care. Relative to control participants, those receiving the intervention were found to have a reduction in carotid atherosclerosis.

**Findings From Quantitative Reviews**

This diverse literature has been evaluated in several quantitative reviews (e.g., Linden, Stossel, & Maurice, 1996). The most recent

\(^3\) We are indebted to George A. Kaplan for this descriptive phrase.
and complete of these (Dusseldorp, van Elderen, Maes, Meulman, & Kraaij, 1999) found evidence of beneficial effects and provided a potential explanation for inconsistent findings. Health education (e.g., targeted toward behavioral risk reduction) and stress management had equivalent significant effects on cardiac recurrences, producing on average a 34% reduction in cardiac mortality and a 29% reduction in recurrent MI. However, small sample sizes in many of the treatment studies, limitations in randomization and the documentation of clinical events, and other methodological issues may have resulted in inflated estimates of treatment effects.

Of importance, Dusseldorp et al. (1999) found that intervention effects were moderated by effects on intermediate targets, such as change in behavioral risk factors, reductions in blood pressure, and reductions in emotional distress. Overall treatment effects on cardiac outcomes were significantly greater in studies where positive results were found for proximal intervention targets—especially proximal psychological outcomes. Also of interest, the large recent studies that failed to replicate beneficial effects of psychosocial interventions (i.e., Frasure-Smith et al., 1997; Jones & West, 1996)—included in the analyses of Dusseldorp and colleagues (1999)—did not find significant treatment effects on emotional distress. In contrast, the positive findings for cardiac events and ambulatory ischemia reported by Blumenthal et al. (1997)—not included in this meta-analysis—were accompanied by significant reductions in reported stress and hostility. Also consistent with the potential importance of intervention effects on emotional outcomes, in a nonrandomized trial Denollet and Brutsaert (2001) found that participation in a multicomponent cardiac rehabilitation program (i.e., exercise, stress management, individual counseling) as opposed to standard medical care was associated with less negative affect over the 3-month intervention period and improved survival over the subsequent 9 years.

Conclusions Regarding Intervention Research

The results of the quantitative review discussed previously suggest that interventions intended to prevent recurrent cardiac events through the reduction of stress and modification of related psychosocial risk factors are clearly promising, and there is considerable evidence in support of their efficacy (Kendall, Flannery-Schroeder, & Ford, 1999). Were it not for the heterogenous treatments evaluated, the intervention literature would seem to satisfy recently proposed criteria for empirically supported psychological therapies (i.e., internally valid evidence of treatment effects; Chambless & Hollon, 1998). This research has included variations in treating personnel, modes of delivery, and settings, though perhaps not in a sufficiently systematic or extensive manner as to support firm conclusions about effectiveness (i.e., external validity or generalizability to typical clinical settings; Kendall et al., 1999). The clinical significance (Kendall, 1999) of these intervention effects (e.g., reductions in cardiac mortality of 30%) seems obvious, but comparisons with other standard interventions provide further evidence. For example, widely utilized medical treatments (e.g., beta-adrenergic blocking medications, anticoagulants) reduce mortality on average by 20% (Lau et al., 1992). In a quantitative comparison across types of studies, Ketterer (1993) concluded that psychosocial interventions produced reductions in mortality at least as large as those observed for medical and surgical interventions. It is important to note that evidence of the efficacy of medical therapies has generally come from larger and better controlled trials and that this comparison is somewhat dated. The specific medical therapies and protocols continue to be refined. Nonetheless, this literature indicates that interventions intended to reduce psychosocial risk in established CHD may improve medical outcomes.

However, a careful examination of the relevant studies suggests that these conclusions are quite tentative, and many questions remain for future research. Of most importance, many of the available studies were small and/or contained methodological limitations (i.e., nonrandomized designs). Hence, large, well-controlled replications are needed. Many of the psychosocial intervention studies included in recent reviews are 10 and even 20 years old. The medical management of CHD has changed significantly during this period, raising two important concerns. First, it is not clear that results of older psychosocial treatment studies generalize to the context of current cardiology care that involves treatments (e.g., greater use of beta-blockers, aspirin and anticoagulants, lipid lowering agents) that impact several of the pathways through which psychosocial risk factors may affect the pathophysiology of CHD. Second, the changes in standard care have resulted in improved prognosis for CHD, and the reduced variance in morbidity and mortality may make it more difficult to detect the incremental beneficial effects of psychosocial treatments.

At a minimum, the improved prognosis for CHD resulting from refinements in routine care increases the sample size requirements for trials intended to evaluate the effects of psychosocial interventions on cardiac recurrences and mortality. Blumenthal et al. (1997) recently illustrated the intermediate strategy of using ambulatory ischemia as an outcome variable. Ambulatory ischemia is a robust predictor of subsequent cardiac events (Kop et al., 2001). Further, ambulatory ischemia is much more common than recurrent events and therefore can provide a sensitive, clinically relevant index of intervention outcomes. Smaller studies that demonstrate positive results on this measure could then be replicated in larger trials with adequate power and longer follow-ups required to detect effects on morbidity and mortality.

The focus on cardiac recurrences and mortality may actually underestimate intervention effects. Psychosocial interventions also improve emotional adjustment and functional status or activity levels (e.g., Johnston, Foulkes, Johnston, Pollard, & Gudmundsdottir, 1999; Trzciniecka-Green & Stepoe, 1996). These are important consequences of CHD (Swenson & Clinch, 2000) and integral components of comprehensive evaluations of health care interventions (R. M. Kaplan, 1994). The use of standardized outcome units, such as quality of life adjusted years (QALYs; R. M. Kaplan, 1994), in future studies of psychosocial risk reduction would not only capture these additional benefits but also facilitate comparisons with a variety of other treatments including standard medical therapies (Kaplan & Groesl, 2002). It may be that stress management and related interventions produce improvements in QALYs that match or exceed some medical or surgical approaches and do so at less cost. Further, emotional distress is associated with significant health care expenditures in CHD patients, primarily because of greater rates of rehospitalization and related procedures (Allison et al., 1995; Frasure-Smith, Lespérance, Gravel, Masson, Juneau, & Talajic, 2000). Hence, effective treatments could reduce these costs (e.g., Davidson, 2000). Cost-utility and cost-
effectiveness analyses in future intervention studies have obvious importance in the current climate of health care financing and related policy debates.

In studies with null results for cardiac outcomes (Frasure-Smith et al., 1997; Jones & West, 1996), it is not clear whether the failure to find significant reductions in psychosocial risk factors reflects ineffective interventions provided to appropriate patients or use of otherwise-effective treatments with patients who did not need them (Linden, 2000). For example, in Jones and West’s (1996) study, stress management was provided to an unselected sample of consecutive patients, who reported generally low levels of psychological distress. Future research should examine the efficacy of these interventions in patients selected for higher levels of psychosocial risk and, perhaps, examine interventions targeted to patients’ predominant problem (i.e., general stress, anger, depression).

Despite mounting evidence of their status as risk factors, only recently have social isolation and depression been specific targets in controlled intervention trials. They were addressed in a recently completed, multicenter trial—Enhancing Recovery in Coronary Heart Disease (ENRICHD; ENRICHD Investigators, 2000). Approximately 3,000 acute-MI patients who met criteria for depression or social isolation (or both) were randomized to either standard care or a psychosocial intervention on the basis of cognitive therapy techniques. Depressed patients received cognitive therapy for depression, and isolated patients received treatment to increase support using similar techniques. Preliminary evidence suggested that the psychosocial intervention reduced depression and improved social functioning, but it had no overall effect on cardiac events (recurrent MI or death; National Heart, Lung, and Blood Institute, 2001).4 However, the potential importance of effective treatments for depression in CHD is evident in its multiple effects. Depression is itself a major threat to quality of life, predicts poor medical outcome, and can undermine adherence to other components of care (DiMatteo et al., 2000; Ziegelstein et al., 2000).

In addition to evaluating the usefulness of adjunctive treatments, intervention studies also provide opportunities to test the relatively well-developed mediational models of psychosocial risk. Intervening psychophysiological or transactional—stress exposure mechanisms could be assessed in intervention studies and used in formal mediational analyses. Such studies are valuable in theory testing and could also suggest directions for refining interventions.

General Conclusions, Implications, and Future Directions

Over the past decade, evidence regarding the role of psychosocial risk factors in the development of CHD has grown considerably. Pathways through which stress and negative emotions influence the development of CAD and CHD have been identified in an extensive body of human and animal research. Epidemiological studies have demonstrated generally consistent and substantial prospective effects of hostility, depression, related individual differences in negative affect, and social isolation on CHD. Smaller but potentially important literatures suggest similar roles for job stress, social dominance, and social conflict. In each case, these risk factors are associated with psychophysiological mechanisms through which stress and emotions could influence CAD and CHD. Finally, a small and methodologically varied literature suggests that psychosocial interventions may improve CHD prognosis. In each topic, as we have outlined previously, there are also important limitations of this research and many equally important issues for future investigations.

Implications for Patient Care

Although acceptance of the potential role psychosocial factors in the development and management of CHD is growing among medical professionals (Rozanski et al., 1999), it has not become a standard component of care for most patients. Additional evidence of the reliability and predictive utility of psychosocial and psychophysiological assessments in clinical cardiologic settings would likely prompt further progress in this regard. Of even more importance, additional supportive evidence of effective interventions from large and well-controlled randomized trials is needed to guide current care, as are criteria for the identification of patients likely to benefit from specific psychosocial interventions.

Given the incidence and typical course of CHD and the supportive evidence regarding psychosocial factors available to date, many health care professionals understandably believe they cannot wait for these remaining issues to be resolved definitively before implementing these variables in risk stratification and intervention strategies. Although more detailed discussions are available elsewhere (Allan & Scheidt, 1996; Bellg, 1998; Smith & Ruiz, in press), we can draw some implications from the research over the past decade for current clinical practice. Psychosocial risk factors certainly should be included in the evaluation of CHD patients, and following such assessments, adjunctive psychosocial interventions should be considered. The efficacy findings generally support their use. However, an excessive set of behavior change requirements would likely discourage or overwhelm patients. Hence, interventions should be prioritized and approaches with multiple benefits given particular consideration.

For example, smoking cessation among CHD patients is associated with a 40% or larger reduction in mortality (Wilson, Gibson, Willan, & Cook, 2000), and its cost effectiveness compares favorably with standard medical treatments (e.g., thrombolytic therapy, cholesterol lowering medication) and behavioral approaches to rehabilitation (e.g., exercise; Ades, Pashkow, & Nestor, 1997). Hence, these interventions should be a priority among smokers with CHD. Exercise interventions reduce cardiac recurrences and death, and they also compare favorably to medical approaches in cost-effectiveness analyses (Ades et al., 1997). Further, exercise interventions can reduce hypertension (Blumenthal et al., 2000; 2002) and depressive symptoms (Babyak et al., 2000; Blumenthal et al., 1999) and have been found to increase heart rate variability among CHD patients (Stahle, Nordlander, & Bergfeldt, 1999). Hence, unless medically contraindicated, the broad psychological and physiological benefits of exercise (Dubbert, 2002; Salmon,

4 It is important to note that this pattern of outcomes is inconsistent with the meta-analytic finding of Dusseldorp et al. (1999) in which interventions that improved psychosocial functioning were more likely to have beneficial effects of morbidity and mortality. However, additional—albeit preliminary—analyses from the ENRICHD trial indicate that the psychosocial intervention significantly reduced recurrent CHD events among White men (Schniederman, 2002). Hence, it may be that the treatment was effective for subgroups of patients.
Implications for Prevention

Decades of research on behavioral risk factors has shaped agendas for CHD prevention. Smoking cessation, reductions in dietary fat and excess weight, and increases in physical activity among the sedentary are important public health goals and the focus of evolving behavior change technologies. Further, the prevention of smoking, high-fat diets and obesity, and inactivity before these risks are established relatively early in life are potentially even more useful strategies. Preventing costly disease through behavior change in childhood and adolescence has an obvious appeal, especially given that early indications of CAD appear in these age groups.

In light of these increasingly accepted preventive approaches to the public health challenges posed by CHD, the literature on psychosocial risks and related interventions suggests additional avenues for research and application. There is limited evidence regarding the developmental origins of specific psychosocial risk factors as measured in studies of adults. However, there is a vast literature on related concepts in emotional and social development (Casp, 1998; Coie & Dodge, 1998; Rubin, Bukowski, & Parker, 1998). This field has guided the development of effective interventions for other prevention goals (e.g., reducing emotional distress and aggressiveness, increasing social and emotional competence) in children and adolescents (e.g., Blechman, 1996; Greenberg, Kusche, Cook, & Quamma, 1995; Tolan, Guerra, & Kendall, 1995), and they could be adapted to examine their effects on early indications of psychosocial risk for CHD and early indications of cardiovascular disease (e.g., blood pressure, endothelial dysfunction) among vulnerable children and adolescents. Certainly, the traditional psychosocial research agenda in CHD is rather full. Yet, the benefits of past and future studies might not be limited to treatments for established CHD or risk reduction programs for physically healthy but hostile, depressed, or socially isolated adults approaching the age of onset for CHD. Rather, partnerships with developmental and prevention scientists could identify new directions and applications for psychosocial research on CHD to younger populations (R. B. Williams, 1998).

Emerging Issues

Future studies of psychosocial influences on CHD should attend to the generalizability of results across sociodemographic characteristics, particularly gender, ethnicity, and SES. These characteristics are themselves related to CHD risk, perhaps in part through mechanisms involving the psychosocial risk factors reviewed here. Further, these sociodemographic variables may moderate effects of risk factors on mechanisms or CHD outcomes, as well as the effectiveness of interventions. For example, whether defined as a characteristic of individuals (e.g., income, occupational status; Gonzalez, Rodriguez, & Calero, 1998) or the neighborhoods where they live (Yen & Kaplan, 1999), low SES confers increased risk of CHD morbidity and mortality. Further, at least some of this risk is attributable to psychosocial risk factors (Lynch, Kaplan, Cohen, Tuomilehto, & Salonen, 1996). Some ethnic minorities are at increased risk, and again, this effect may be attributable at least in part to psychosocial factors such as discrimination and stressful living circumstances (Anderson & Armstead, 1995; D. R. Williams & Collins, 1995). In both human and animal models, there are gender differences in the association between psychosocial risk factors and CHD, as well as in the likely underlying mechanisms (J. R. Kaplan et al., 1996; Kiecolt-Glaser & Newton, 2001). Ultimately, interventions should be evaluated in specific underrepresented sociodemographic groups (cf. Castillo-Richmond et al., 2001) to determine their generalizability.

Developments in medical science will also shape the psychosocial research agenda in CHD. Advances in noninvasive assessment methods have permitted more informative tests of the influence of psychosocial factors on asymptomatic atherosclerosis. Other noninvasive procedures have provided clear evidence that psychological stress and related variables can evoke myocardial ischemia (Rozanski, 1998). These same procedures have been used to evaluate the outcomes of psychosocial interventions (Blumenthal et al., 1997; Castillo-Richmond et al., 2000; Gould et al., 1995). Continuing refinements of cardiologic assessments and related procedures will encourage even more compelling tests of psychosomatic hypotheses and more sensitive and persuasive evidence of intervention effects. As in all areas of biomedical science, developments in the genetics of CAD and CHD will pose new questions for psychosocial research. Genes implicated in atherosclerotic processes (e.g., Anderson et al., 2000) or in psychophysiological individual differences (R. B. Williams et al., 2001) could identify higher and lower risk groups, and this genetic status could moderate the effects of psychosocial risk factors or identify groups most likely to benefit from psychosocial intervention.

Finally, future research will addresses new versions of classic psychological questions. The interplay of early experience and biology in social and emotional development will inform CHD prevention research and, perhaps, suggest additional psychosomatic mechanisms (Caldji, Diorio, & Meaney, 2000; Repetti, Taylor, & Seeman, 2002). Matching subgroups of CHD patients or...
persons at risk to different psychosocial interventions could improve their efficacy. Last, the study of psychosocial aspects of this costly and prevalent disease will continue to reflect the cutting edge of research on connections between mind and body.

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