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Anger and Hostility in Cardiovascular and Behavioral Disorders

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The Health Consequences of Hostility

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The purpose of this volume is to review recent research on the assessment, correlates and treatment of anger. In this chapter we shall review the rapidly growing body of evidence indicating that level of hostility is associated with a wide variety of health outcomes. We shall also consider briefly the possible biologic mechanisms whereby hostility and anger could lead to pathophysiologic alterations in bodily functions.

Before proceeding with this review, however, it is in order to consider how the construct of "hostility" relates to that of "anger." Based on our previous research and a review of the relevant literature, we offer the following definitions to guide the reader. *Hostility* is considered to be an attitudinal set—perhaps even a personality trait—which stems from an absence of trust in the basic goodness of others and centers around the belief that others are generally mean, selfish and undependable. We feel it likely that this attitude is, to a large extent, learned from caregivers early in life. From the developmental perspective, it may reflect an incomplete development of "basic trust," to use Erikson's (1963) term. *Anger,* on the other hand, is an emotional state made up of feelings ranging in intensity from minor irritation to fury and rage. While different from hostility, it seems clear that anger bears some relation to the latter concept; persons with a strong attitudinal set of hostility will be likely to experience the emotion of anger more frequently and intensively than persons low in hostility.

Finally, *aggression* is overt antagonistic behavior motivated by the acts of others, as well as by one's own hostility and anger. In this volume and elsewhere, Spielberger (Spielberger, Chap. 1; Spielberger, Jacobs, Russell and Crane, 1983) has considered issues involved in defining hostility, anger and aggression, and the reader is referred to these writings for a more comprehensive discussion.

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With regard to assessment, it is fair to say that no single instrument for the measurement of hostility, anger or aggression presently enj universal acceptance. Guided by Rosenman and Friedman's initial descriptions (Rosenman et al., 1964) of those characteristics comprising Type A behavior pattern, in which hostility and anger were emphasized along with chronic speed and impatience, we determined early on to assess these characteristics using the best available instruments in our studies of the psychosocial correlates of coronary atherosclerosis. As we shall review in this chapter, this has been a productive approach, and one that has led to new insights not only regarding the relation of hostility to coronary heart disease but to other debilitating and life-threatening diseases as well.

HEALTH CORRELATES OF HOSTILITY

Our own research into the health consequences of hostility and anger began with initial efforts to determine whether Type A patients undergoing diagnostic coronary angiography have more severe coronary atherosclerosis (CAD) than Type B patients. In the first study, we found that over 90% of patients with very severe CAD were judged to be Type A using the structured interview (SI) (Blumenthal, Williams, Kong, Schanberg and Thompson, 1978). Based on this finding, over eight years ago we began to systematically collect data pertaining to a broad range of psychosocial characteristics (see Williams et al., 1980, for a description of data collection procedures) on all patients referred to Duke University Medical Center for diagnostic coronary angiography.

In our next study (Williams et al., 1980), we replicated the earlier finding of more severe CAD among those patients characterized as Type A using the SI (Rosenman, 1978) in a sample of 424 patients. Since we had also collected MMPI data on these patients, we were in a position to investigate the various hostility scales that had been developed from the MMPI item set over the years (see Spielberger, Jacobs, Russell and Crane, 1983, for a review of MMPI hostility scales). Purely by chance, the first such scale we evaluated in relation to CAD levels was the 50-item Ho scale developed by Cook and Medley (1954) on the basis of manifest content and differentiation between teachers with good versus poor rapport with pupils. As shown in Figure 1, scores on the Ho scale were significantly related to Type A behavior as assessed by the SI; the mean Ho scores were 16, 18, 20, and 21 for Types B, X, A2 and A1, respectively.

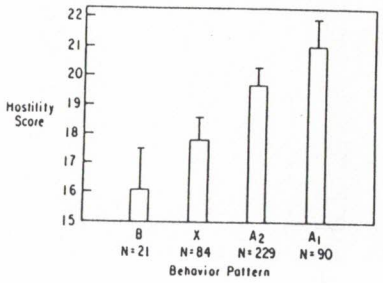

Figure 1 Relationship between scores on the Cook and Medley (1954) Hostility Scale and Type A behavior as assessed by the Structured Interview in patients referred for diagnostic coronary angiography. (Based on data from Williams et al., 1980).

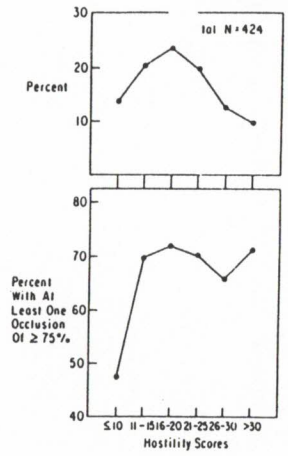

Figure 2 Relationship between Hostility scores and presence of significant (occlusion of 75% or greater) coronary atherosclerosis. (From Williams et al., 1980).

This association between Ho score and Type A behavior provides some support for the construct validity of the Ho scale. Additional support comes from the correlation of 0.59 ($p < 0.0001$) between Ho scores and scores on Spielberger's (Spielberger, Jacobs, Russell and Crane, 1983) Trait Anger Scale. More direct support is provided by a correlation of 0.37 ($p < 0.001$) between Ho scores and behaviorally assessed potential for hostility during the SI among 131 patients in the Duke angiographic sample (Dembroski, MacDougall, Williams, and Haney, Note 2).

In addition to being related to Type A behavior, trait anger and potential for hostility, Ho scores also appear related to the severity of CAD. As illustrated in Figure 2, the relationship between Ho score and prevalence of clinically significant CAD was not linear, but appeared to exhibit a threshold phenomenon; 48% of patients with Ho scores of 10 or less had clinically significant stenosis of at least one coronary artery, whereas, among patients with Ho scores greater than 10, 70% had clinically significant CAD. Thus, in this group of middle-aged patients the prevalence of clinically significant CAD was approximately 1.5 times greater in those with Ho scores higher than 10 as compared to patients with lower scores. Further analysis showed that Type A behavior (SI-assessed), Ho scores and gender were all independently and significantly related to severity of CAD [Figure 3].

It is worth noting, however, that while the significance level of the relation of Ho scores to CAD *increased* from a univariate p-value of 0.02 to a p-value of 0.008 when both gender and Type A were covaried, the significance level of the relation of Type A behavior to CAD decreased from a univariate p-value of 0.01 to a p-value of 0.05 when both gender and Ho score were covaried. A similar decrease in the significance level of the relationship between Type A behavior (SI-assessed) and CAD levels was also observed with statistical adjustment for behaviorally assessed potential for hostility levels. (Dembroski et al., Note 2). These findings suggest that at least some of the variance in prevalence of CAD

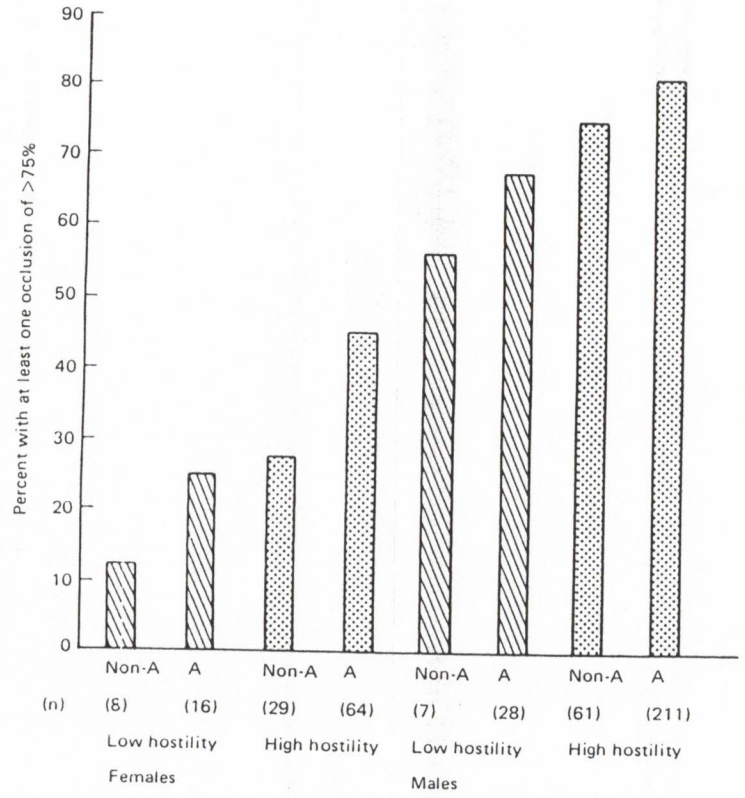

Figure 3 Relationship of Gender, Hostility score and Type A behavior to presence of significant coronary atherosclerosis. (From Williams et al., 1980).

levels associated with Type A behavior is due to the increased Ho levels among Type A patients.

Interpretation of these relationships between hostility and CAD in patients referred for coronary angiography must be qualified by the fact that they are based on concurrent observations in a clinical population with suspected CAD. With respect to the *prospective* relationship between Ho scores and risk of coronary heart disease (CHD), we are fortunate that the Ho scale is based on the MMPI, a psychological test which has been used in previous studies of initially of healthy men whose health status has been followed over periods as long as 25 years after completion of the MMPI.

One such investigation was based on 1877 men in the Western Electric Study. These men, aged 40 to 55 years at time of intake, were employees at the Hawthorne Works of the Western Electric Company in Chicago. They initially completed the MMPI in 1957-58 and again in 1961-62 as part of a larger examination that included blood pressure, cigarette smoking and serum cholesterol. Men continuing in the study were reexamined annually until 1969,

primarily to determine the occurrence of new CHD events. The most recent follow up for mortality was carried out in 1978. Following the earlier report of an association between CAD and Ho scores (Williams et al., 1980), Shekelle and colleagues (Shekelle, Gale, Ostfeld and Paul, 1983) used the Western Electric Study to investigate the relationship among Ho scores obtained at the initial examination, subsequent 10-year incidence of CHD, and 20-year mortality;

One important finding was a correlation of 0.84 between Ho scores obtained at the initial examination and again four years later for 1653 men who took the MMPI on both occasions. This suggests that Ho scores may be measuring an unusually stable psychological characteristic, at least in middle-aged men. Another finding (see Figure 4) was that Ho scores were positively associated with increasing age, cigarette smoking and ethanol use. Therefore, these variables, along with systolic blood pressure and serum cholesterol, were included in multivariate analyses to evaluate the independent, prospective relation of Ho scores to risk of CHD and death. Looking first at the 10-year incidence of major coronary events events (myocardial infarction and CHD deaths), higher Ho scores were prospectively associated with increased CHD morbidity ($p = 0.004$). After adjustment for the variables listed above, the odds of a major CHD event was 1.47 times greater in men with Ho scores greater than 10 compared to men with lower Ho scores. This value is virtually identical to the relative prevalence of clinically significant CAD previously observed by Williams and colleagues (1980). Of equal interest, the shape of the association between level of Ho score and incidence of CHD was nonmonotonic in a manner similar to that noted previously with CAD (see Figure 2). The standardized morbidity ratios for CHD in the Western Electric Study were 0.6, 0.9, 1.5, 1.0, and 0.9, respectively, in the lowest through highest quintiles of the distribution of the Ho score. The cutpoints for these quintiles were 0-8, 9-12, 13-7, 18-23, and 24-44.

The Ho scale was also significantly and positively associated with crude 20-year risk of death from CHD, from malignant neoplasms, and all causes combined (Figure 5). After adjustment for age, cigarette smoking, intake of ethanol, systolic blood pressure, and serum cholesterol level by Cox-type

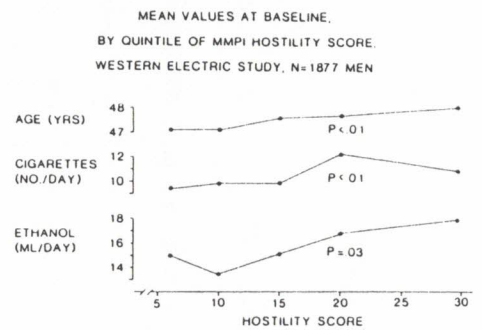

Figure 4 Increasing age, cigarette smoking and ethanol use as a function of Hostility scores in healthy middle-aged men. (Based on data from Shekelle et al., 1983).

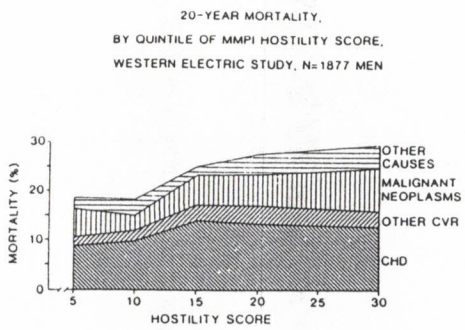

Figure 5 Causes of mortality as a function of Hostility scores in the Western Electric sample. (Based on data from Shekelle et al., 1983).

regression analysis, the Ho scale had a statistically significant ($p = 0.001$), positive association with 20-year total mortality (Figure 6); a difference of 23 points on the Ho scale, which was the difference between the means of the lowest and higher quintiles, was associated with a 42% increase in the risk of death.

Another opportunity to evaluate the prospective relationship between Ho scores and subsequent morbidity and mortality–in this instance among a younger sample than the Western Electric men–arose when Barefoot, Dahlstrom and Williams (1983) carried out a follow up study of 255 male physicians who had completed the MMPI while in medical school 25 years earlier, when their mean age was 25 years. As in the Shekelle et al. (1983) study, test-retest correlation was remarkably high (.85) among a subsample of 42 students who retook the MMPI one year after the first administration, indicating that the psychological characteristic assessed by the Ho scale is as stable at age 25 as at age 47.

With respect to CHD events over the 25-year follow up period, (Figure 7), men with Ho scores that were at or below the median of 13 experienced a CHD

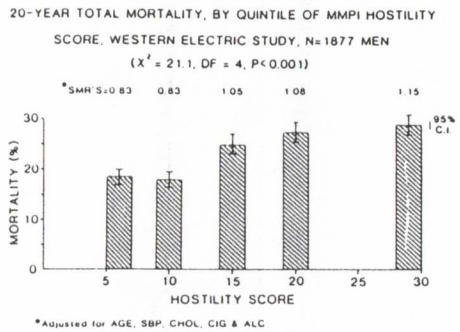

Figure 6 Hostility scores and mortality rates over a 20-year follow up period in healthy middle-aged men. (Based on data from Shekelle et al., 1983).

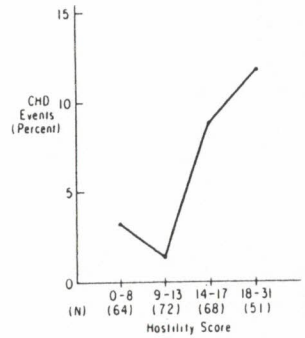

Figure 7 Hostility and coronary heart disease incidence (myocardial infarction or cardiac death) over a 25-year follow up period in 255 physicians who took the MMPI during medical school. (From Barefoot et al., 1983)

incidence (1.5-3%) that was about one-sixth of the incidence (9-12%) observed in men with Ho scores above the median ($p < 0.001$). A similar curve describes the relationship between Ho scores and total mortality over the 25-year follow-up period. As with the relation of Ho scores to CAD in patients at Duke and to 10-year CHD incidence in the Western Electric study, the shape of the curves relating Ho scores to CHD morbidity and total mortality in this sample of physicians appears to have a "threshold"; with Ho scores up to a certain level–13 in this sample of young men–there was a uniformly low risk of CHD, while above that level the incidence increased rapidly. However, the number of persons in this sample was too small to determine whether or not the level of risk become uniform again at higher levels of Ho.

The most convincing impression of the impact of high Ho scores on subsequent total mortality can be gained by contrasting the survival curve over the 25-year follow up period of those men with initial Ho scores at or below the median with that of those with initial Ho scores above the median (Figure 8). Over the entire 25-year follow up period death came to only 2.2% of those in

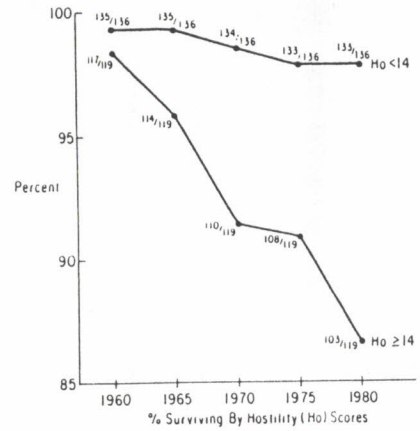

Figure 8 Twenty-five year survival in 136 physicians with Ho scores at or below the median and in 119 physicians with Ho scores above the median on MMPIs completed while they were in medical school. (From Barefoot et al., 1983).

the low Ho group; in marked contrast, 13.4% of those in the high Ho group died. Whereas among middle-aged cardiac patients and Western Electric employees the relative risk of significant CAD or CHD associated with a high Ho score was 1.5, in this sample of healthy young physicians the relative risk of dying in the high versus low Ho group was over 6. Inspection of the survival curve for the high Ho group in Figure 8 suggests one explanation for the lower relative risk associated with a high Ho score among middle-aged persons: by the time middle-age is reached, those who are particularly susceptible to the consequences of high Ho scores will have already died.

What conclusions can we draw from the studies reviewed thus far? First of all, we can have considerable confidence that "something" measured by the Ho scale is in fact associated with a wide range of adverse health consequences. This confidence is based on the observation in three independent studies, one cross-sectional and two prospective, of very reliable associations between high Ho scores and increased prevalence of CAD, increased risk of CHD and increased total mortality over follow up periods of 20-25 years. The similarity of the threshold-type functions relating Ho scores to the various health measures in all three studies further strengthens our conviction that the relationship is real.

Second, with somewhat less confidence, we believe that the "something" being measured by the Ho scale is related to the constructs of hostility and anger and, possibly, aggression, as defined earlier in this chapter. This supposition is based primarily on the evidence cited earlier for the construct validity of the Ho scale, in terms of the strong relationships to Type A, to Spielberger's State Anger scale and to behaviorally assessed potential for hostility in the SI. In addition, it is consistent with some prior findings relating other measures of anger and hostility to adverse health outcomes. Matthews, Glass, Rosenman and Bortner (1977) found that behaviorally rated potential for hostility was the strongest predictor of subsequent CHD events in a subsample of the Western Collaborative Group Study. In the Western Electric Study, results from the Cattell 16PF Questionnaire (Ostfeld et al., 1964) indicated that men who subsequently developed CHD tended to be "more suspicious about the motives of other people." And finally, Harlan, Oberman, Mitchell and Graybiel (1967) found that scores on the Guilford-Zimmerman Temperament Survey that were indicative of an "aggressive personality" were prospectively associated over a 24-year follow up period with increased blood lipid levels among 1,000 naval aviators.

The remarkable stability of Ho scores over periods of one to four years during early adulthood and middle-age suggests that the Ho scale is measuring a rather fundamental psychological characteristic. We have recently completed a principal components factor analysis of the entire MMPI item set in 1500 patients who underwent coronary angiography at Duke (Costa, Zonderman, McCrae and Williams, Note 1). Among the psychometrically valid factors identified was one containing 37 items whose content (e.g., "Most people make friends because friends are likely to be useful to them" and "I have frequently worked under people who seem to have things arranged so that they get credit for good work but are able to pass off mistakes on to those under them") suggested that perhaps a more appropriate label for the psychological construct measured by the Ho scale would be "cynicism."

Also suggesting that cynicism may be the fundamental construct measured by the Ho scale are the results of a replicated split sample principal components

factor analysis of the full MMPI that was carried out in a sample of over 11,000 mental health clinic patients by Johsnon, Butcher, Null and Johnson (1983). The third largest factor, in terms of variance explained, after Neuroticism and Psychoticism, contained 20 items and was described by a panel of experienced psychologists as "cynicism." The two cynicism factors emerging from the Costa et al. and the Johnson et al. analyses shared over 50% of items in common. Although there is considerable item overlap between these cynicism scales and the Ho scale, the correlation between them and Ho (above 0.80) is far in excess of that due to item overlap alone.

The fundamental nature of this cynicism characteristic is suggested by its emergence from two independent factor analyses of the full MMPI item set in two quite diverse populations. It is also supported by the central place accorded to early achievement of a sense of basic trust in theories of personality development (Erikson, 1963). Surely, persons in whom this sense of basic trust in others is incompletely developed would be more likely to endorse the type of attitude suggested by the items making up the cynicism scales emerging from these independent studies. Such a lack of basic trust, could also lead to increased hostility. Since these two constructs–hostility and cynicism–are related, further research will be required to determine which label is more accurate.

Nevertheless, the findings point to an attitudinal set (we might even say a rather stable personality trait) consisting of the belief that people in general are selfish, mean and not to be depended upon to treat one well as the fundamental construct which is being assessed by the Ho scale. By implication, it is this psychological characteristic–whether it be termed hostility, cynicism, or lack of basic trust–which is responsible for the adverse health consequences which are so reliably predicted by the Cook and Medley Ho scale.

It now remains to consider the biological mechanisms whereby this psychological characteristic might be translated into pathophysiological processes. While it is possible to describe plausible pathways for these biobehavioral mechanisms, the reader is cautioned that the discussion which follows must be based on a greater level of speculation than has been necessary with respect to the evidence reviewed thus far in this chapter.

HOSTILITY: PATHOPHYSIOLOGICAL MECHANISMS

Based upon a review of a wide range of evidence, Williams (1984) has proposed two major patterns of motor outflow, or physiologic responses, which occur in association with psychosocial environmental challenges. When cognitive appraisal of a given situation results in either a sense of danger or of the need for continuing mental effort to understand or cope with the situation, the pattern of physiological response generated is that which has been described as the "defense reaction," or "fight/flight" response. This pattern is characterized by increased pumping of blood by the heart and by a shunting of this increased cardiac output away from the skin and abdominal viscera to the skeletal musculature. In contrast, where the cognitive appraisal process leads to a decision that the stimuli in the environment are interesting, or that more information about the stimuli is needed, a different pattern ensues. This pattern, which occurs in association with vigilance, or motivated attention to environmental stimuli, is characterized by no

change, or even a decrease in cardiac output and by an active vasoconstriction in skeletal muscle.

This hypothesis (that qualitatively distinct patterns of physiological response occur in association with situations requiring defensive or mental work behavior versus those requiring attentive observation of environmental stimuli) was evaluated, along with the associated neuroendocrine response patterns, in a recent study (Williams, Lane, Kuhn, Melosh, White and Schanberg, 1982). Young male subjects were required to perform either a mental arithmetic task (mental work) or a reaction time task (vigilance/sensory intake) while cardiovascular functions were monitored and continuous blood samples were obtained to be assayed for a wide variety of hormones. Responses to the tasks were determined by subtracting baseline levels from levels observed during the tasks. Performance of mental arithmetic was accompanied by an active vasodilation in skeletal muscle, increased heart rate and blood pressure and increased secretion of norepinephrine, epinephrine, cortisol, and prolactin, but *not* of testosterone. In contrast, performance of reaction time tasks was associated with tendency (not significant in this study) to muscle vasoconstriction, and significant increases in norepinephrine and testosterone but *not* in prolactin, epinephrine, and cortisol. Compared to Type B subjects, those subjects characterized as Type A using both the SI and the Jenkins Activity Survey exhibited greater muscle vasodilatation and increases in norepinephrine, epinephrine and cortisol during mental arithmetic, and a greater increase in testosterone during reaction time performance.

Thus, it appears that in situations in which the defense/mental effort response pattern is activated a characteristic response pattern is observed, consisting of increased cardiac output with shunting of blood to skeletal muscle and increased secretion of norepinephrine, epinephrine, cortisol, and prolactin. In contrast, in situations in which vigilant observation of the environmental situation is the outcome of the cognitive appraisal process, the response pattern observed consists of muscle vasoconstriction and increased secretion of norepinephrine and testosterone. Type A persons appear to experience greater arousals of these patterns during specific task performance. How might such excessive cardiovascular and neuroendocrine responses account for the increased CHD risk among Type A and, by implication, hostile/cynical persons?

First of all, being unable to depend upon the good behavior of others and, indeed, being on guard against their bad behavior, the hostile Type A person might be expected to spend a good bit of the waking hours in a state of vigilant observation of others. Since our laboratory study (Williams et al., 1982) suggests that increased secretion of testosterone is one concommitant of such vigilant behavior, it would be expected that cynical persons would excrete more testosterone in their urine during the waking hours (when vigilance would be required) but not while asleep. This prediction was confirmed in a recent study by Zumoff, Rosenfeld, Friedman, Byers, Rosenman and Hellmen (1984) in which Type A men were found to excrete more testosterone in the urine than Type B men during the waking hours but not during the overnight period.

Admittedly, Type A men are characterized by other traits (e.g., time urgency) than hostility/cynicism. But, as reviewed above, it is the hostility/cynicism component which appears most strongly related to their increased CHD risk, and, as we have just hypothesized, it is the hostility/cynicism component which we would expect to be most likely to result (via increased vigilance) in increased

testosterone secretion. Supportive of a pathogenic role of testosterone in atherosclerosis the observation that animal models of atherogenesis are potentiated by administration of exogenous testosterone (Uzunova, Ramey and Ramwell, 1978).

Perhaps even more directly suggestive of testosterone's involvement in human atherosclerosis are the recent observations of increased plasma estradiol levels among male heart attack victims compared to men free of coronary disease (Klaiber et al., 1982; Luria et al., 1982; and Phillips, Castelli, Abbott and McNamara, 1983). Since most of the plasma estradiol in men is derived from testosterone via aromatization (a conversion which is stimulated by norepinephrine), and since Type A men appear to secrete more testosterone and norepinephrine in response to daily challenges, (possibly due to their increased hostility/cynicism), the case is strengthened for a pathogenic role of increased testosterone secretion among hostile/cynical Type A men.

Possibly of equal, if not greater, importance in atherogenesis is the increased secretion of epinephrine and cortisol during the experience of anger, which would be expected to occur with greater frequency and intensity among hostile/cynical persons. Cortisol is known to potentiate both the cardiovascular and metabolic effects of catecholamines, which could accelerate processes involved in endothelial "injury," the most widely accepted model of atherogenesis (Ross and Glomset, 1976). In addition, the administration of corticosteroids has been associated with acceleration of atherosclerosis in patients with rheumatoid arthritis (Kalbak, 1972); and patients with more severe angiographically documented CAD have been found to have higher 9 a.m. cortisol levels than patients with minimal disease (Troxler et al., 1977).

With respect to the possible role of increased levels of hostility/cynicism in other diseases, the evidence from both the Barefoot et al. (1983) and Shekelle et al. (1983) studies is intriguing in that it is suggested that hostility/cynicism predisposes not only to increased risk of coronary disease but to other diseases as well. The increased cancer mortality as a function of higher Ho scores in the Western Electric sample, for example, could be related to the finding by Graves and Thomas (1981) in the Johns Hopkins precursors study that future cancer victims display evidence of a lack of closeness to their parents as well as a relative lack of well-balanced patterns of interaction. These characteristics are attributed to "a linkage to disturbed or otherwise unsatisfactory early human ties." (Graves and Thomas, 1981, p. 224). The same sorts of early experience might also be expected to lead to an incomplete sense of basic trust, and perhaps, increased levels of hostility/cynicism. In view of the growing body of evidence that stress can lead to depression of immune function (Ader, 1982), the same chain of events proposed above for the biological pathways whereby hostility/cynicism might contribute to atherogenesis might also be invoked to explain a contribution to carcinogenesis via effects on immune function that could reduce ability to reject tumors in otherwise susceptible individuals.

Since we would expect hostile/cynical persons both to engage in more vigilance-behavior and to experience more anger in daily life as a result of their hostility/cynicism, the evidence just presented regarding the likely biological correlates of vigilance and anger is strongly suggestive of the existence of biological mechanisms whereby the psychological characteristic of hostility/cynicism *could* be translated into disease processes. While perhaps even highly

plausible, the actual participation of these mechanisms in pathogenesis must await further research. Ideally, such research would involve the joint assessment of hostility/cynicism and neuroendocrine responses to both specific laboratory challenges and to the "give and take" of everyday life in several cohorts of young subjects who would then be followed with respect to a variety of disease outcomes. (Although most of the data reviewed has been derived from male samples, undoubtedly at least some of the same mechanisms are relevant to disease processes in women, and studies of female subjects are clearly in order.)

We already know from the studies cited that whatever is being measured by the Ho scale is very reliably predictive of increased rates of developing a wide variety of diseases. It now remains to identify the biological mechanisms responsible for this relationship. Hopefully, the data reviewed and the speculations contained herein will stimulate and guide others toward this end. Ultimately, it is likely that knowledge of the mechanisms responsible for the observed prospective associations will prove most effective in helping to identify the most specific, effective and efficient preventive measures.

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