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Relationship of Anger Trait and Anger Expression to C-Reactive Protein in Post-Menopausal Women

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by

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Dedicated to
E’desanya’m Irenk’a

I would not exist except by your grace and the grace of God. For my dear Mother, who always told me I could do anything I set my mind to, become whatever I wished, and always cheered me on, in good times and bad.

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ABSTRACT

Coronary heart disease is the leading cause of death in American women, accounting for one in six deaths in 2004. One third of women over the age of forty will develop coronary heart disease in their lifetime. The role of chronic and excessive inflammation and risk factors, such as smoking and high cholesterol, are now well-established factors contributing to coronary heart disease pathology. A knowledge gap exists in that little is known about the mechanisms by which psychosocial factors, such as anger, may be associated with pro-inflammatory processes that contribute to cardiovascular morbidity and mortality in women. The purpose of this study was to determine if there were differences in serum levels of the proinflammatory biomarker, C-reactive protein, in post-menopausal women who scored high on anger characteristics compared to those with low anger characteristics. Mean levels of C-reactive protein were not found to be different in a sample of 42 women with high trait anger or high anger expression compared to those with low trait anger or low anger expression. Significant relationships were found in C-reactive protein

and some anger control characteristics (anger control-in) and might imply that certain anger expression styles may play a role in pro-inflammatory responses in post-menopausal women.

Chapter One: Introduction to the Study

Statement of the Problem

Cardiovascular disease is the leading cause of mortality in American women with coronary heart disease (CHD) responsible for 50% of deaths in 2004. One third of women over the age of 40 will develop coronary heart disease in their lifetime (Rosamond et al., 2007). Two-thirds of women who experience sudden death from CHD had no previous symptoms of their illness (Wenger, 2004). Chronic and excessive inflammation and risk factors such as smoking and hypercholesterolemia, are now well-established factors contributing to CHD pathology. However, little is known about the mechanisms by which psychosocial factors, such as anger, may be associated with proinflammatory processes that play a role in cardiovascular morbidity and mortality in women.

Background and Significance

Anger is a universal powerful and generally negative emotion that is expressed throughout the lifespan and is associated with enhanced vascular tone, elevated heart rate, and elevated blood pressure responses, similar to those elicited by the fear response (Bongard, Pfeiffer, Al-Absi, Hodapp, & Linnenekember, 1997). Anger has been associated with angina, myocardial infarction, and sudden cardiac death (Kop, 1999; Stuart-Shor, Buselli, & Carroll, 2003) as a result of direct acute and indirect chronic biological processes. These

include cardiovascular reactivity (CVR), which is an increased heart rate and blood pressure in response to stress, stress-induced hypertension (Abel, Larkin, & Edins, 1995), carotid atherosclerosis (Matthews, Owens, Kuller, Sutton-Tyrrell, & Jansen-McWilliams, 1998; Troxel, Matthews, Bromberger, & Sutton-Tyrell, 2003), existing CHD, (Linfante, Allan, Smith, & Mosca, 2003), incident heart disease (Gallacher, Yarnell, Sweetnam, Elwood, & Stansfeld, 1999), and metabolic syndrome (Raikkonen, Matthews, & Kuller, 2001).

Current theories regarding mechanisms for the potential relationship of CHD to dysphoric emotional states and traits, such as anger, date back to the early 20th century and are based on the association of a recurrent pattern of an exaggerated sympathetic nervous system response. Alexander (1939) first proposed that anger contributed to the development of sustained elevated blood pressure because of chronic activation of the autonomic and cardiovascular systems. Alexander's theory led to the identification by Dunbar (1943) of the "coronary prone personality" that subsequently formed the now famous designation of the Type A behavior pattern and especially the harmful anger-hostility personality component (Spielberger et al., 1985). Research investigating anger, specifically trait anger (anger proneness), emerged in the 70s and 80s, when researchers began to explore physiological reactivity relationships and personality characteristics (Schum, Jorgensen, Verhaeghen, Sauro, & Thibodeau, 2003).

Many large prospective designs have examined the significant role that anger and hostility have on CVR and CHD. The majority of these studies suggest

that anger directly or indirectly predisposes individuals to heightened CVR, which may lead to increased risk of development of hypertension and heart disease (Eng, Fitzmaurice, Kubzansky, Rimm, & Kawachi, 2003; Everson, Goldberg, Kaplan, Julkunen, & Salonen, 1998; Everson-Rose & Lewis, 2005; Fichera & Andreassi, 1998; Julkunen & Ahlstrom, 2006; Lovallo & Gerin, 2003; Swartz, Gerin, Davidson, Pickering, Phil, Brosschot, et al., 2003; Thomas, 1997).

As research continued to reveal the complex interrelationships of the mind-body connection and cardiovascular disease Kawachi, Sparrow, Spiro, Vokonas, and Weiss (1996) proposed a biopsychosocial model of anger interactions that promote CHD as a result of the direct biological effects of elevated catecholamines, increased myocardial oxygen demand, vasospasm, and increased platelet aggregability. Pro-inflammatory cytokines, specifically interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNFα) have been identified and found to be increased in systemic inflammation and recognized as risk factors for poor health outcomes associated with cardiac disease, diabetes mellitus, and osteoporosis (Segerstrom & Miller, 2004). TNFα has been found to alter endothelial cell function and promote the expression of adhesion molecules that contribute to accumulation of cellular debris and also promote the production of C-reactive protein (CRP) (Suarez, Lewis, & Kuhn, 2002). CRP, a well-established marker for CHD risk, is an acute phase reactive protein that is triggered by the release of pro-inflammatory cytokines, particularly IL-6, and also appears to play a role in the development of

atherogenesis and subsequent CHD (Hapuarachchi, Chalmers, Winefield, & Blake-Mortimer, 2003).

Finally, new evidence shows that chronic activation of the stress response with subsequent persistent release of glucocorticoid hormones and catecholamines, may also dysregulate immune function (Padgett & Glaser, 2003) including primary and secondary antibody responses (Vedhara, Fox, & Wang, 2005). Because the effects of stressors differ over time and between individuals, the nature of the stressor, its contextual meaning, and host differences likely determine the degree to which stress reactions produce immune changes (Segerstrom, Kemeny, & Laudenslager, 2001). Current researchers studying psychoneuroimmunology (PNI) hypothesize that chronic stress and stressful emotions, like anger and anxiety, elicit both innate and specific immune responses by enhancing patterns of pro-inflammatory cytokine secretion which, in turn, activate the hypothalamic-hypophyseal-adrenocortical (HPA) axis and stimulate the acute phase response (Black, 2006; Black & Garbutt, 2002; Bryndon, Magid, & Steptoe, 2005; Lovallo & Gerin, 2003; Padgett & Glasser, 2003; Segerstrom, Kemeny, & Laudenslager, 2001) and produce a variety of sickness behaviors, such as depression and anxiety.

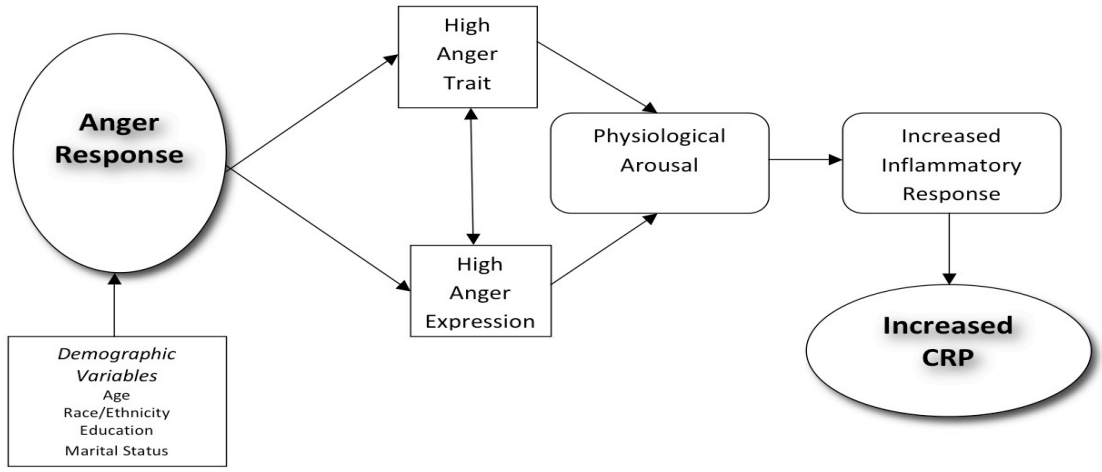
The emotion of anger is also very complex and involves cognitive, affective, and behavioral aspects that are biologically and culturally based (Cox, Stabb, & Bruckner, 1999). For women in particular, especially as a result of Western socialization of the female gender as less powerful, the interpersonal interactions of anger are intricately woven within the relationships of women's

everyday lives (Thomas, Smucker, & Droppleman, 1998). The effects of acculturation and socialization of anger etiquette, which fosters overt displays of anger and aggression by men generally result in women internalizing angry feelings (Gilligan, 1982). As girls and boys grow up to be men and women, different biobehavioral patterns are developed, especially related to internalization and externalization of feelings. Subsequently, many women experience dichotomous experiences of anger, whether to suppress or express their thoughts and feelings (Cox et al.).

Trait anger, a key feature of anger, describes a relatively stable personality trait consisting of one's proneness to perceive situations as anger provoking and to respond with feelings of annoyance, irritation, or fury (Spielberger, Jacobs, Russell, Crane & Worden, 1985). High trait anger women frequently experience angry feelings, feel others treat them unfairly, and experience a great deal of frustration (Spielberger, 1999). Anger expression includes angry feelings held in or suppressed (anger-in), and angry feelings that are expressed (anger-out) (Spielberger et al.). High anger-in women frequently experience angry emotions but control the outward expression of angry feelings, while high anger-out women frequently express their anger by verbal or physical aggression towards others (Spielberger).

Utilizing the theoretical framework proposed by Kawachi, Sparrow, Spiro, Vokonas, and Weiss (1996) of the mind-body anger connection to cardiovascular disease a conceptual model of the study is presented in Figure 1.

Figure 1. Concept model of the relationship of anger and CRP.



Purpose of the Study

The purpose of this study was to examine differences in biobehavioral variables in healthy post-menopausal women who were classified as high and low in trait anger and anger expression. The specific aims of the study were to compare differences in serum levels of CRP in high and low anger groups. The associated research questions for this study asked:

1) Are there significant differences in mean levels of CRP in women who are classified as high trait anger compared to those classified as low trait anger? *Directional hypothesis: High trait anger women will have higher mean levels of CRP compared to low trait anger women.*

2) Are there significant differences in mean levels of CRP in women who are classified as high in anger expression compared to those classified as low in anger expression?

Directional hypothesis: Women who score high on anger expression will have higher mean levels of CRP than those who are score low on anger expression.

Chapter Two: Review of Literature

The study of the relationship of psychosocial factors and reactions to emotional stressors such as anger, and immune dysregulation and inflammatory responses has emerged within the new body of research devoted to stress-neuroendocrine-immune interactions, known as PNI (Vedhara, Fox, & Wang, 1999). The impact of these interactions on health involves a multifaceted set of signals that work in bi-directional communication among the nervous, endocrine, and immune systems, primarily through the HPA axis and sympathetic-adrenal-medullary axis (Padgett & Glasser, 2003). Definitions of key anger terms used for the review of literature are presented in Table 1, followed by a review of research on cardiovascular responses to anger and a review of research on inflammatory and immunological responses to anger.

Table 1.

Definitions of Anger Constructs (Spielberger et al., 1985

Anger	An emotional state consisting of subjective feelings that vary in intensity from mild annoyance or irritation to intense fury and rage accompanied by muscular tension and arousal of the autonomic nervous system.
State Anger	A psychobiological emotional state consisting of subjective feelings that vary in intensity from mild annoyance or irritation to intense fury and range accompanied by muscular tension and arousal of the autonomic nervous system.
Trait Anger	Individual differences in anger proneness, i.e., the tendency to perceive a wide range of situations as annoying or frustrating, and the disposition to respond to such situations with elevations in state anger.
Anger-In	Individual differences in the frequency that angry feelings are held in or suppressed.
Anger-Out	Individual differences in the frequency that state anger is expressed in aggressive behavior towards other people or objects in the environment
Anger-Control	Individual differences in the frequency that individuals attempt to control the outward expression of angry feelings.

Overview of Cardiovascular Responses to Anger

Briefly, psychological or emotional stress, such as anger, causes impulses released from the cerebral cortex to transmit via the limbic system to nuclei in the hypothalamus where corticotropin-releasing factor (CRF) and arginine vasopressin are synthesized. CRF travels to the anterior pituitary gland that responds by producing adrenocorticotropic hormone (ACTH) that then stimulates the adrenal cortex to produce glucocorticosteroids. Glucocorticosteroids are permissive to the catecholamines. Arginine vasopressin also activates secretion of ACTH and is released by the posterior pituitary gland. Together with norepinephrine and epinephrine produced by the sympathetic nervous system, these chemicals constitute the major stress hormones which systemically

upregulate the cardiovascular system. Sympathetic nervous stimulation, sensed by the juxtaglomerular apparatus of the kidneys, affects the renin-angiotensin response by stimulating powerful enzymatic reactions with subsequent systemic vasoconstriction and increased CVR (Black & Garbutt, 2002).

Enhanced sympathetic tone and increased CVR, often seen in acute anger, has been associated with an increased risk of development of CHD and has been correlated with increased morbidity and mortality (Abel et al., 1995; Shapiro, Bagiella, Myers, & Gorman, 1999). However, the latest evidence reveals that enhanced CVR may also directly contribute to the inflammatory etiology of atherogenesis, the precursor to CHD (Lovallo & Gerin, 2003).

Overview of Inflammatory Responses to Anger

Atherogenesis begins with the development of atherosclerotic lipid-filled macrophages, known as foam cells, which contribute to plaque formation within the endothelial lining of the arterial blood vessels. Plaque formation initially occurs in areas where there is increased turbulence from shear forces such as bifurcations in carotid and coronary arteries. Macrophages, along with circulating monocytes, add to the ongoing thickening of these plaques and the development of new plaques through the innate immune response (Lovallo & Gerin, 2003). The innate immune response mounts a localized inflammatory response, which results in the release of communication molecules known as cytokines.

Cytokines are glycopeptide-signaling molecules that regulate both innate cell-mediated immunity and humoral immunity including the acute phase response, which provoke key steps involved in immune responses that include T-

and B- lymphocytes, monocytes, and macrophages (Maes et al., 1998). The pro-inflammatory cytokines, specifically interleukins IL-1, IL-6, and TNFα, have been identified and found to be increased in systemic inflammation and are beginning to be recognized as biochemical markers of poor health outcomes associated with cardiac disease, diabetes mellitus, and osteoporosis (Segerstrom & Miller, 2004). TNFα has been found to alter endothelial cell function and promote the expression of adhesion molecules which contribute to accumulation of cellular debris and promote the production of CRP (Suarez, Lewis, & Kuhn, 2002).

C-reactive protein is an acute phase reactive protein released by the liver that is activated by the release of pro-inflammatory cytokines, particularly IL-6, and appears to play a role in the development of atherogenesis and subsequent CHD (Hapuarachchi, Chalmers, Winefield, & Blake-Mortimer, 2003). In response to elevated levels of IL-6 following inflammation, infection, tissue injury or stress, CRP is thought to directly activate endothelial cells to express cellular adhesion molecules which further contribute to vascular inflammation (Gotto, 2006). Based on large prospective studies, CRP has been shown to be a reliable biomarker of underlying systemic inflammation and a strong predictor of future myocardial infarction and stroke (Willerson & Ridker, 2004). Contemporary research in PNI suggests that psychological stress-induced changes also contribute to the increased production of pro-inflammatory cytokines and lymphocytic alterations (Black, 2006; Black & Garbutt, 2002; Bryndon et al., 2005; Lovallo & Gerin, 2003; Padgett & Glasser, 2003; Segerstrom et al., 2001).

Research on Cardiovascular Reactivity Responses to Anger

The particular mechanism linking anger to CHD and hypertension remains elusive. One leading hypothesis implicates activities of the sympathetic adrenomedullary system and the hypothalamic-pituitary-adrenocortical axis. In reaction to psychological stress, such as an angry emotional response, excess stress hormones including catecholamines and corticosteroids may negatively impact CVR by increasing platelet aggregation which leads to endothelial injury and plaque formation triggering the surge of proinflammatory actions involved in atherogenesis described above (Williams, Couper, Din-Dzietham, Nieto, & Folsom, 2007).

Anger and CVR have been extensively studied and measured with various instruments relative to risk of CHD, hypertension, and stroke; both positive and negative associations have been found. Fontana and McLauglin (1998) used Lazarus' stress and coping framework to measure whether stressful situations might predict heart rate and blood pressure and hypothesized that the more stressful the perception of daily stressors, the higher CVR would be. Differences in problem-focused or emotion-focused coping processes and appraisal of daily stressors were thought to predict physiological response to stress. A small sample of 33 college women were measured pre- and post-menstrual cycle while performing mental arithmetic and interpersonal conflict tasks within an anger-provoking paradigm. Results demonstrated that tension reduction techniques and positive appraisal were related to lower CVR while anger suppression increased CVR. The researchers concluded the transactional model of stress could assist

in generating further ideas about which psychological factors might predict CVR (Fontana & McLauglin).

Webb and Beckstead (2002) looked at the relationship between blood pressure, anger, coping resources, and strain. In the 90 African-American women who were studied, women with elevated blood pressure, and women treated for hypertension had higher anger suppression scores than normotensive women. These findings approached statistical significance (p=.06) after covariates (age, waist/hip ratio, and pack-year smoking history) were entered. The clinical significance of this study may imply that anger and stress management interventions for women with elevated blood pressure and hypertension might be helpful in the prevention and progression of cardiovascular disease.

The use of mental arithmetic tasks described above (Fontana & McLauglin, 1998), challenge tasks, videogames and hostile, challenging confederates in staged discussions have been used in a number of studies to induce anger states while different measures of CVR were collected. Abel et al. (1995) studied 67 female college students' anger expression styles during video gaming and mental arithmetic tasks while measuring heart rate and blood pressure changes. Anger expression as measured by Spielberger's highly reliable Anger Expression Scale revealed that women who had moderate anger-out styles had lower blood pressure responses to the arithmetic stressor than low (p=<0.05) or high (p=0.01) anger-out women. The latter group had the highest

reactivity to the arithmetic task compared to the moderate anger-out group (*p*=0.05*).*

Bongard et al. (1997) used a 4-way experimental design to look at CVR response to a mental arithmetic task. Active coping style, number reading (nonactive coping), and anger provocation versus no provocation were compared to reports of angry feelings. Large effect sizes (*p*= <0.001) were seen in provoked participants' heart rates, diastolic blood pressures, and angry affect. Although the experimental design of the study was well thought out, the lack of information including reliability and validity of the scale to measure affect limits the applicability of findings.

Lawler et al. (1998) also used a mental arithmetic challenge and an anger recall interview in an exploratory study to determine whether college students with a family history of hypertension would have greater physiological responses to anger than those without. For men, large effect sizes (*p*=<0.001) were found for cardiac output and in women, for total peripheral resistance (*p*=<0.004). All measures at baseline were higher in those with positive family history (*p*=<0.001). Less significant correlations were found between low anger expression, low anger experience, and high anger control with the math challenge on all measures of CVR in those with positive family history (*p*=<0.10).

In another study of college women, Powch and Houston (1996) also used confederate discussion and challenge to measure psychological variables while subjects were provoked during blood pressure and heart rate recordings. Relationships between cynicism, mistrust, disagreeableness, and anger-in were

studied with the Cook-Medley Hostility Scale, State-Trait Anger Scale, and two other less reliable instruments. High hostility was related to greater systolic blood pressure reactivity during high interpersonal stress (*p*=<.001*),* however no significant relationship was found to anger-in among this all white sample.

In a similar study reported by Davis, Matthews, and McGrath (2000) college students with high hostility had significantly (*p*=<0.05) larger increases in diastolic blood pressure and total peripheral resistance than low hostile individuals when engaged in a controversial topic discussion with a confederate who was argumentative and aggressive. Although no effect was seen on affect response of the students as to difficulty of task, the perception of interpersonal control varied by level of hostility. This raised the question whether low and high hostile individuals perceive their interactions during their everyday lives in terms of their perception of control.

Lavoie, Miller, Conway, and Fleet (2001) used a subject friendship quality scale with physiological recordings to see if greater elevations in women's blood pressure, heart rate, cardiac output, stroke volume, and total peripheral resistance would be seen in an anger-provoking situation in defense of self or defense of their friend. Equal significant effects (*p*=<0.01*)* of anger, irritation, and annoyance resulted whether they or their friend were harassed but only women in the self-harass group had very significant elevations (*p*=<0.001*)* in peripheral resistance.

Even though these six studies were conducted with college students in a laboratory, all anger responses resulted in increased CVR and theoretically

increased the risk for development of CHD. However, one of the questions often raised in an analysis of studies on anger is whether simulated anger situations cause the same physiological and psychological reactions to anger as those experienced within every day lives of women. As noted by Brondolo et al. (2003) individuals in a laboratory setting may use different strategies for expressing anger than in unobserved “real life” interactions (p. 1003).

Although Thomas (1997) found no main effect for anger frequency or intensity in blood pressure changes in a community sample of 210 women age 18 to 71, suppressed anger, especially in the home setting with spouse or best friend, was positively related to elevated blood pressure. Thomas hypothesized that anger suppression in women and elevations in blood pressure as a result of interpersonal conflicts and daily stressors may be of greater significance than blood pressure elevations related to an angry event with a stranger.

Horsten et al. (1999) asked about the association of social isolation, depressive symptoms, anger, and heart rate variability (HRV). Using the concept of allostasis, which proposes that physiological systems within the body fluctuate to meet demands from external forces, they hypothesized that psychosocial strain, as a stressor, may be related to decreased HRV in a healthy population and an important measure of disturbed autonomic nervous system. Using a large (*n*=300) random sample of healthy women, scores from the Stress Process Questionnaire (Cronbach’s alpha=.85) and the previously validated Framingham Anger Scale were correlated with 24-hour EKG recordings, social support systems, and lifestyle factors. Although no effect was seen on three of the four

anger scales, not discussing anger was associated with decreased HRV; being married and larger household size showed a similar association. This study demonstrated the effect of daily psychosocial strain as a possible antecedent to CHD, especially in women who lived alone, reported lack of social support, and did not relieve anger by talking to others.

Harris, Matthews, Sutton-Tyrell, and Lewis (2003), questioned whether psychosocial traits are related to endothelial function. They hypothesized that negative psychosocial characteristics may be risk factors for CHD and that circulating estrogens and hormone replacement therapy (HRT) may be protective in delaying declines in endothelial function. The use of the highly valid and reliable Bortner Type A Rating Scale, Framingham Tension Scale, Beck Depression Inventory, and Spielberger Trait Anger and Anxiety Scales revealed that Type A behavior, anger, anxiety, and depression were significantly (p <.05*)* related to impairments in endothelial function among 193 healthy postmenopausal women. However, some of these relationships may be masked by HRT.

Type A behavior pattern and CVR were explored by Anderson and Lawler (1995) in a mixed methods study of 58 female students between 18 and 42 years old. A semi-structured interview recalling an anger incident was analyzed against blood pressure, heart rate, and classification of Type A and Type B personalities. There was a main effect of behavior on diastolic blood pressure in Type A women (p=<0.02) in response to frustration over autonomy needs. Type B women had higher CVR in response to frustration over affiliation needs. Further,

all women who suppressed anger had higher CVR than those who expressed anger. Given the known relationship of Type A personality and CHD, chronic anger suppression may be an additional risk factor for CHD.

Utilizing a similar framework that chronic anger suppression may exacerbate potential or existing CHD and contribute to early mortality, Fichera and Andreassi (1998) hypothesized that women who demonstrate high CVR to some stressor are more likely to develop CHD. Looking at reaction time to an oral IQ quiz, Type A women showed significant (p=<0.05) increased CVR on both reaction time and oral quiz compared to Type B, women but the Type A high hostile women were more reactive (p=<0.05) than Type B low hostile women.

As measured in the social milieu of the everyday lives of women, anger suppression alone and in combination with a Type A personality may further increase a women's risk for CHD. Analysis of several prospective studies does provide evidence of possible links between these variables especially in relation to anger suppression and hostility, although many of the studies had small numbers of women or were completed on men.

Everson, Goldberg, Kaplan, and Salonen (1998) described the relationship between anger expression and hypertension in a four-year prospective study of 537 men and found a large effect of anger-out (p=<0.002) and anger-in (p=<0.01) and hypertension, increasing risk of hypertension by 12% for every 1 point increase in either scale of anger expression. Findings from this study could not be implied for women.

Harburg, Julius, Naciroti, Gleiberman, and Schork (2003) utilizing the conceptual framework that chronic suppressed anger exacerbates potential or existing pathology and leads to mortality, prospectively .considered the landmark Tecumseh Community Health Study to assess anger-coping styles in men and women. Responses to hypothetical anger-provoking scenarios were examined in relation to anger styles, blood pressure, and all cause mortality. Women showed a significant (p=<.01*)* relationship between suppressed anger and risk of early mortality for all-cause CHD, and cancer endpoints.

Similar findings were reported by Raikkonen, Matthews, and Kuller (2002). In a large prospective study (n=425) women who had high levels of depression, tension, and anger at baseline had elevated risk for developing metabolic syndrome 7.4 years later (p=<.04*)*. Further, a reciprocal relationship between development of metabolic syndrome and increasing anger were found over time (p=<.001*).* Although CVR was not measured, hypertension is one of the criteria for metabolic syndrome.

In another large prospective study of 688 women, Rutledge et al. (2001) also looked at cardiac related variables to determine associations between atherosclerosis risk factors and psychological characteristics linked to CHD. Anger expression was significantly related to dyslipidemia and larger body mass index (BMI). A four-fold increased risk was found between high anger-out, high levels of low-density lipoprotein (LDL), and low levels of high-density lipoprotein (HDL). Although not measuring CVR directly, high LDL and low HDL contribute to

the development of atherosclerosis and CHD. Therefore, the implication that anger-out is related to the development of CHD may be made.

Troxel, Matthews, Bromberger, and Sutton-Tyrell (2003) took a random sample (n=334) from the longitudinal Study of Women's Health across the Nation (SWAN) study and found significant differences in carotid artery intima thickness in African-Americans. Looking at biobehavioral risk factors related to chronic stress, they found combined stressors, economic hardship, and unfair treatment (an antecedent to anger) were associated with increased subclinical carotid artery disease over time.

Hostility, which is generally described as a more pervasive and enduring antagonistic mental attitude (Thomas, 1993), has been extensively studied and measured in several prospective studies of men and women (Brondolo et al., 2003; Matthews et al., 1998; Williams et al., 2000; Williams et al., 2001). All of these studies showed large significant effects of high trait anger, strong angry temperament, and high trait hostility with increased CVR. In the Atherosclerosis Risk in Community (ARIC) Study, Williams et al. (2000, 2001, 2007) showed a twofold increased risk in CHD and threefold increase risk for CHD events and subclinical atherosclerosis in over 13,000 men and women who were studied over 5 years that scored high in trait anger and angry temperament. Hostility was found to be an independent risk factor for recurrent CHD events in women from the Heart and Estrogen Replacement (HERS) study that were followed for four years (Chaput et al., 2002).

Brondolo et al. (2003) wrote that the transactional model suggests that hostility influences health partly through its effects on social relationships and that increased CVR associated with interpersonal and other stressors may contribute to development of CHD. However, they cautioned that the cognitive, affective, and behavioral measurements of hostility as measured by the Cook-Medley Ho scale are associated in different ways to CHD and the subcomponents of hostility that measure negative interpersonal reactions and CVR correlates have not been adequately studied.

In summary, the majority of the studies of anger and CVR were descriptive and correlational with small effect sizes. Two thirds of the studies used well-known and reliable instruments, however interpretation of results was limited by inadequate definitions and distinctions between the constructs of anger and hostility. Most of the studies used convenience samples of college students and were further limited by inadequate samples of women and minorities. However, ten large prospective studies used community samples with some reporting significant correlations between anger and other psychosocial factors, hypertension, CHD and carotid atherosclerosis. These results provide good evidence for the anger-CVR connection.

Research on Inflammatory and Immunological Responses to Anger

Research examining immunological relationships and anger are meager and have been mostly examined within the context of the role of inflammation as a precursor to CHD. However, the findings from these studies tend to indicate that an angry emotional state has an effect on changes in natural killer (NK) cells,

natural killer cell activity (NKCA), and CRP. The negative impact on inflammatory and immune responses provide further support for the role of atherogenesis in the development of CHD.

Mills, Dimsdale, Nelesen, and Dillon (1996) seeking possible relationships between CVR and immune reactivity, looked at the connection between anxiety, anger expression, hostility, and enumerative immune responses to a 6-minute laboratory speech stressor in 104 healthy community volunteers. Citing prior research that had found stress, depression, and interpersonal conflict to be associated with long-term immune dysfunction, and daily hassles associated with short-term immunological changes, Mills et al. measured acute immune reactions by videotaping subjects' oral defense against a false accusation of shoplifting. Pre- and post-speaking biochemical and psychological measurements were obtained to determine the effects of the speaking stressor on the various cell populations. Multiple linear regressions were analyzed to determine factors associated with cellular responses and psychological characteristics, accounting for age and smoking status. Leukocyte populations were analyzed via flow cytometry and quantified by total white blood cell count, lymphocyte subsets, and NK cells. NK cells are a class of lymphocytes that attack and kill malignant cells, foreign cells, and virally infected cells.

Moderate but statistically significant ($p<.03$) associations between NK cell responses and anger expression suggested that persons who expressed angry emotions had lower increases in immune response compared to individuals identified as hostile with higher numbers of NK cells ($p=.02$).

Suppressor/cytotoxic cell increases were related to pre- and post-anxiety scores with those reporting the greatest amount of chronic stress showing the smallest acute increases in WBC (p=.006). Overall, these findings suggested that certain emotional responses or personality characteristics, like anger and hostility, may be associated with short-term immune function changes, similar to CVR responses, reinforcing the PNI connection (Mills et al., 1996).

Larson, Ader, and Moynihan (2001) also employed an acute laboratory stressor to identify correlates of neuroendocrine, immune, and CVR responses by examining stress-related changes in NKCA, cortisol, and cytokines that elicit macrophage and antibody activity, interferon gamma (IFN-g), and interleukin-10 (IL-10) in 56 healthy subjects. Heart rate, blood pressure, and blood samples were obtained 30 minutes before, during, and immediately after a stress-inducing speech task in which subjects were asked to describe their best and worst characteristics. Additionally, they were under the assumption that they were being evaluated by psychologists to determine how persuasive each subject's speech was compared to each other. As expected, increased CVR was seen all subjects and 91% showed significant increases in NKCA (p<.001); 69% showed significant IFN-γ increases (p<.009). NKCA was found to be significantly and positively correlated with CVR (p<.004). Anger suppression was also found to be significantly and positively correlated with CVR (p<.02), cortisol (p<.007) and IL-10 (p<.02). Of note, the use of almost 40 regression equations at a significance level of p<.05 likely led to some spurious findings. However, the hypothesis that

increased anger suppression as a psychological risk factor for increased CVR and lowered altered immune response was supported.

An early PNI study examined how emotion contributes to immunologic changes in response to psychological stress during marital conflict. Miller, Dop, Myers, Stevens, and Fahey (1999) explored the idea that emotions induced by naturalistic stressors would also elicit stress-induced changes in immune parameters. They hypothesized that spouses would respond with negative emotions to an episode of marital conflict and these responses could be measured by increases in blood pressure, heart rate, circulating catecholamines, and increases in NK cells, NKCA, and CD8 T-lymphocytes. Further, they sought to determine if the relationship between anger and physiological changes was moderated by hostility. Married couples (*n*=113) were extensively screened to reduce confounders that might be produced by pre-existing medical, social, and lifestyle conditions. From this pool, 41 couples completed a marital problem inventory and several psychological scales prior to having blood samples and biological measurements taken. Based on their responses to the marital problem inventory, the researchers suggested a topic (such as household management or communication) that had been identified by both spouses as a source of conflict.

During a 15-minute videotaped problem-solving discussion, several blood samples, heart rate, and blood pressure measures were taken, concluding with a final sample taken after a 25-minute rest period at the end of each couple's session. Emotional affect scores were also developed by trained observers who assigned one of nine emotion codes to each subject for every 5-second interval

of discussion. Scores were used to compute a series of correlations between affect scores and reactivity and recovery scores for each of the physical parameters.

Controlling for baseline physiological values, partial correlations revealed that high levels of husbands' affective anger covaried with greater systolic blood pressure increases ($p<.01$) but wives' anger did not. Affective anger scores for both genders were unrelated to neuroendocrine and immune parameters during and after conflict discussion. Husbands who scored high on hostility showed significantly greater increases in NKCA during discussion and less recovery response ($p<.01$). Also, higher levels of anger covaried with greater increases in NK cell numbers during discussion ($p<.05$) but were unrelated to recovery. No significant findings were found in any parameters for wives. In general, men high in cynical hostility displayed more anger during conflict and had greater increases in heart rate, blood pressure, cortisol, NK cells, and NKCA.

The lack of similar findings in women in this observational design was thought to be possibly related to the differences in the more pronounced testosterone secretion elicited in men during anger expression. Perhaps, as pointed out by Abel et al. (1995), the overall differences in anger expression among men and women affected how emotion coding was recorded in that what may have been an angry response by a wife was coded as dissatisfaction or sadness, rather than anger. Further, the large number of statistical comparisons likely produced some correlations that were actually due to chance.

A naturalistic stress design was used to study lymphocyte proliferation in spousal caregivers of persons with Alzheimer's disease (Scanlan, Vitaliano, Zhang, Savage, & Ochs, 2001). Dyads of 82 spouse caregivers of patients with Alzheimer's and 83 age- and gender-matched spouses of normal controls were included in the final analysis of carefully screened volunteers. Extensive inclusion and exclusion criteria, as well as psychiatric and medical confirmations of a diagnosis of Alzheimer's disease in the absence of all other neurological, cardiovascular, and immune related diseases, medications, psychological disorders, etc., supported this repeated-measures design to eliminate as many confounding variables as possible.

Participants completed several psychological instruments which were correlated to lymphocyte proliferation responses to mitogens. Mitogens are agents that induce *in vitro* mitosis and are considered a reliable measure of immune system function in depressed subjects (Vedhara & Irwin, 2005). For anger-related measurements, in all cases and both times, no statistically significant main effect of anger expression was found. However, anger expression did significantly interact with caregiving status at Time 2 (but not at Time 1) for all changes in lymphocyte production resulting in lower immune responses ($p<.05$) and was negatively correlated in caregivers. Caregivers with the highest levels of outward anger expression showed significantly lower mitogen responses than those with controlled anger expression styles ($p<.05$).

The authors concluded that these results appeared to be consistent with other findings (Mills et al., 1996) that suggest high degrees of anger expression

and/or hostility may be the anger components most likely associated with negative health outcomes as a result of decreased immune response. However, since stress-related hormones (cortisol and catecholamines) may also mediate relationships of depression and anger with lymphocytic proliferation, lengthier longitudinal studies are needed to determine if altered immune responses result from anger or depression alone or the synergistic effect of both emotions.

Suarez (2003) examined the relationship of IL-6 to anger, hostility, and depression as a function of multivitamin (MVI) supplement use in 96 healthy, non-smoking men. Based on studies that reported daily use of antioxidants and/or MVIs had been linked to reduced morbidity and mortality from cardiovascular disease, Suarez hypothesized that anger, hostility, and severity of depressive symptoms independently and as a composite psychological risk factor score, would be positively associated with IL-6 among non-MVI users compared to those taking MVIs. Following collection of blood samples, subjects completed depression, hostility, and personality inventories which were then used to generate a composite psychological risk score. Serial multiple regression analysis was used to test the combined psychological risk factor score with MVI use on IL-6 levels. IL-6 levels were significantly and independently positively correlated with all psychological measures including the composite score ($p<.05$) with the exception of the personality inventory ($p<.10$) in the non-MVI users; significant correlations were not found for these same associations in the MVI users. The individual instruments were significantly and positively intercorrelated

(p<.01), providing support for their use of a composite psychological risk factor score.

These findings suggest that significant associations between IL-6 and psychological risk factors were moderated by the use of MVI supplements among healthy men, especially those who might have a propensity to exhibit anger and/or hostility. Limitations included the lack of testing for differences in health behaviors in the high and low psychosocial risk factor groups as well as the comparison of traditional risk factors for CHD (body mass index, resting blood pressure, cholesterol, etc.), serum vitamin levels, and testing of only male subjects.

Based on studies looking at recognized psychosocial risk factors for CHD, such as poverty and depression that are known to increase TNFα, Suarez, Lewis, and Kahn (2002) proposed that anxiety, hostility, and anger would be associated with increased TNFα secretion in lipopolysaccharide stimulated cultures and would also be identified as additional psychosocial risk factors for CHD. Lipopolysaccharide (LPS) is a natural endotoxin released by Gram negative bacteria which powerfully and non-specifically stimulates immune responses *in vitro*. Subjects were 62 healthy, non-smoking males who completed a psychological inventory that included a 5-item anger subscale prior to analysis of LPS-stimulated blood samples for TNFα expression. Parallel multiple regression models supported their hypothesis and showed significant positive correlations between total anxiety, hostility, and anger scores and TNFα expression (p=.007). Limitations included the constricted focus of anger in

the psychological inventory that was used and that depression, which has also been associated with increased TNFα expression, was not measured in this study. Therefore, since the unique and combined relationships of psychological risk factors of CHD such as depression, anger, hostility, and aggression also affect inflammatory responses (Everson-Rose & Lewis, 2005), these results should be interpreted with caution.

Suarez, Lewis, Krishnan, and Young (2004) conducted a study of hostility and depressive symptoms in 44 women to determine if LPS-stimulation of monocytes was correlated in a similar fashion as in men. Healthy, non-smoking, premenopausal women were recruited and screened for medical and psychological conditions that could alter monocyte marker expression (e.g. oral contraceptives). Separate and combined effects of hostility and depression were examined on the capacity of blood monocyte expression of IL-1, interleukin-8 (IL-8), TNFα, and monocyte chemotactic protein, which stimulates up-regulation of cellular adhesion molecules on endothelial cells, leukocytes, and platelets. Separate depression inventory and hostility scales were used to assess psychological symptoms and scores were compared individually and as a composite psychological risk factor score. Multiple regression formulas were used to look at BMI, total cholesterol, race, alcohol, 17b estradiol, and progesterone levels as covariates. In contrast to their earlier study (see above), anger expression was not measured, yet results for this study were reported as similar. Hostility and depression scores, but not psychological risk factor scores, were associated with greater general expression of proinflammatory cytokines

(p<.05). Significant results were also noted when all scores were used to predict LPS-stimulated expressions (p<.05). However, there were enough variances by level of hostility and severity of depressive symptoms in that some cytokines were up-regulated and others were not. Hostility enhanced expression of IL-1 and IL-8, while depression was associated with increased expression of TNFα and IL-8 but not IL-1. Therefore, conclusions based on the general directions of the associations using a psychological risk factor score and causality could not be made.

Hapuarachchi, Chalmers, Winefield, and Blake-Whitemore, (2003) measured homocysteine, CRP, salivary immunoglobulin-A (IgA), and lymphocytic 5'ectonucleotidase (NT) using a theoretical model that psychological stress is associated with a pro-inflammatory state as a result of increased lymphocyte mobilization and subsequent higher cellular oxidative stress. Lymphocytic NT is a lymphocytic maturation marker and has been found to have a lower activity level in decreased immunity states and is a measure of oxidative stress. Oxidative processes produce free radicals which damage cells and initiate inflammatory reactions.

Forty three participants volunteered blood and saliva samples and completed various psychometric questionnaires, including an anger expression scale. Correlation analysis was used to examine the strength of the relationships between psychological and biochemical parameters. CRP was significantly and positively correlated with outward expression of anger and anger experience (p<.05*)* and significantly negatively correlated with anger control (p<.05*)*. These

findings may indicate that a pro-inflammatory state is associated with unmanaged anger expression while a cognitive anger coping style was not. Limitations included the use of a cross-sectional design that mostly relied on correlational analysis and therefore causality cannot be implied. Additionally, the authors acknowledge the subjects' individual cognitive perceptions of overall stress and the stress-illness process are multifactorial and complex. Also, other variables could be confounding the results.

The relationship of psychological factors that influence the immune system and accelerate the progress of CHD was explored by Ishihara, Makita, Imai, Hashimoto, and Nohara (2003) who focused on anger expression. Known CHD subjects were matched with healthy controls and measurements of NKCA were analyzed against anger expression scores. In the CHD group, NKCA was found to be significantly elevated ($p<.05$) by the suppression of anger and negative emotions. Since this study was not prospective, the researchers were uncertain whether the development of CHD or the power of psychological factors influenced the immune response and promoted CHD. Additionally, the lack of concomitant measurements of T-lymphocytes and cytokines limited any implications of causation. Ishihara et al. speculated, based on this study and earlier studies referenced in their findings, that emotional states such as anger experienced in day-to-day living are the function of an acute psychological stress response that up-regulates NKCA, and that suppression of anger is an important factor that increases NK cell numbers through enhanced sympathetic and endocrine system responses.

Gouin, Kiecolt-Glaser, Malarkey, and Glaser (2008) recently published their findings related to patterns of anger expression on wound healing. They proposed that outward and inward expression of anger and lack of anger control would be associated with delayed healing of standardized blister wounds. The Anger Expression Scale of the STAXI-2 was administered (along with five other psychological questionnaires) to 98 (40 men and 58 women) community-dwelling subjects who were part of a larger study of the effects of relaxation on wound healing. Salivary cortisol and IL-1a IL-1b IL-6, IL-8, and TNFα were examined in both the relaxation intervention group and the control group over an eight-day period.

The rate of healing did not differ between groups and no significant differences were found in anger expression, however, results showed that higher levels of anger control were associated with a higher level of wound healing at day four (r=.45, p=<.01) even after differences in hostility, negative affect, sleep, exercise, etc., were controlled. Anger out and anger in separately were not related to speed of healing. Overall, individuals displaying less anger control secreted more cortisol (but not cytokines, which were measured at the wound site). This was the first study showing that anger dysregulation may delay healing.

Summary of Review of Literature

To summarize, research studies examining immunological relationships and anger are meager and have been mostly examined within the context of the role of inflammation as a precursor to CHD. As noted earlier, anger and

cardiovascular reactivity have been extensively studied and measured with various instruments relative to risk of CHD, hypertension, and stroke revealing both positive and negative associations. The cited PNI studies tend to indicate that an angry emotional state may affect changes in NK, NKCA, CRP, and some cytokines, contributing to the negative impact of inflammatory and immune responses which further contribute to atherogenesis and the development of CHD.

The majority of these studies were done on young, healthy, primarily male populations with the use of multiple psychometric or psychological scales that were subjected to extensive correlational analyses. Other studies used principal components analysis to generate a composite personality factor score that may not truly represent anger trait as a personality characteristic. The primary use of correlational analysis in cross-sectional designs, especially with numerous instruments, contributes to loss of statistical power and increases the likelihood of spurious findings. Limited reports of repeated measures and prospective designs greatly limit interpretation of data from this review.

Further, the blurring of the constructs of anger, hostility, and aggression, and use of anger subscales from larger hostility, anxiety, depression, and other psychosocial and personality instruments, as well as the lack of clarity in describing anger expression, anger control/suppression, and other characteristics of anger style, have made interpretation and generalizability of research findings difficult. As Spielberger et al. (1985) pointed out over 20 years ago, definitions for anger used in research instruments are often inconsistent and

ambiguous. Most studies made use of self-report anger subscales of hostility, anxiety, aggression, and depression inventories; few used only unique anger expression scales, and only two studies measured anger trait as a separate personality variable.

Chapter Three: Methodology

Study Design, Setting, and Sample

A quantitative, cross-sectional between-groups design was used to examine differences in CRP between high and low anger groups. The researcher completed administration of all research instruments and questionnaires exclusively. Participants who met the inclusionary/exclusionary criteria as determined by the researcher were tested individually in a reserved private room in the student health center at Florida Gulf Coast University in Ft. Myers, Florida. All procedures were reviewed and approved by the Florida Gulf Coast University and the University of South Florida (USF) Institutional Review Board (IRB# 106379D) and conducted according to protocols outlined by the USF Human Research Protections Program.

The study was conducted on a convenience sample of healthy community-dwelling women recruited from an urban college campus in southwest Florida. Participants were recruited through announcements (Appendix A) and networking to faculty, staff, and women's groups, via electronic mail, and recruitment posters placed in common areas, such as the SHC, cafeteria, student union, and library. Men were excluded because

women have been understudied in research examining anger and cardiovascular disease risk (Abel et al., 1995; Kielcolt-Glaser, McGuire, Robles, & Glaser, 2002).

Eligible women were between the ages of 45 and 65 and either post-menopausal or post-hysterectomy. Women under the age of 45 were excluded because CHD normally develops during middle age. Women who were still experiencing menses were excluded to control for the effect of endogenous hormone levels. To insure a healthy sample, participants were non-smokers, not on any hormone contraceptives or hormone replacement therapy, had no history of any cardiovascular diseases (CHD, congestive heart failure, transient ischemic attacks, stroke, etc.), diabetes mellitus, autoimmune diseases, severe mental illness, or recent (90 days) history of acute infection, trauma, major surgery, or other inflammatory conditions such as chronic bronchitis, gastric inflammation, chronic renal disease, or recent (10 day) history of minor surgery. Participants who were taking medications that are known to confound PNI studies (cholesterol-lowering agents, prescribed non-steroidal anti-inflammatory drugs, cortisone, prednisone, and other steroid preparations, large doses [more than 650 mg] of aspirin, etc.) were also excluded (Zeller, McCain, McCann, Swanson, & Colletti, 1996). Participants who smoked cigarettes and/or used recreational drugs, or drank more than two alcoholic beverages daily were excluded as these substances are also known to increase CRP independently (Zeller).

Procedures

Women who either called or emailed in response to recruitment announcements were told that the total time to complete the initial study instruments (which would determine whether they qualified for the rest of the study) would take less than 10 minutes and if they were suited for the study, an additional 15 to 20 minutes would be needed to complete the second part of the questionnaire, and an additional 5 minutes to obtain their waist measurement and a sample of their blood. Women who agreed to volunteer for the study were given an appointment to meet with the researcher at which time further information was provided regarding the risks and benefits of participating in the second part of the study, particularly in relation to the need for providing a blood sample. Women were told they might feel slight discomfort from having a needle poked into their vein and that there might be a small chance of a bruise at the place where the sample was taken.

Women were informed they would need to provide personal information about their age, race/ethnicity, marital status, and years of education. Women were assured that their personal information would be kept confidential by the researcher and numerically coded to prevent any association between their biographical information and their scores on the various research instruments, waist measurements, and blood samples. Participants were reminded that their inclusion in the study was voluntary and they could withdraw from the study at any time, for any reason without any adverse effects to their status as a member of the community.

Following completion of the verbal explanation of the study, the investigator reviewed the written informed consent form (Appendix B) with each woman. After answering any questions posed by the subject, women were asked to read and sign the informed consent form. Subjects then completed a researcher-designed questionnaire (Appendix C) to verify study inclusion criteria were met and were assigned a unique identification number. Next, qualifying participants were asked to complete the biographical data section of the State-Trait Anger Expression Inventory-2 (STAXI-2) and provide information about their age, race/ethnicity, marital status, and years of education (Appendix D). Next, subjects were asked to complete the Trait Anger subscale of the STAXI-2. Upon completion of the subscale, the researcher immediately tallied each subjects' responses and those women who scored in the uppermost quartile (high anger) and lowest quartile (low anger) of the trait anger subscale (as determined by the age-matched normative groups provided in the STAXI-2 Professional Manual [Psychological Assessment Resources, 1999]) were then asked to complete the Anger Expression subscale of the STAXI-2. Women who failed to score in either quartile were thanked for their time and excused.

Because there is a strong relationship ($r \geq .35$) between waist circumference and CRP (Festa et al., 2001), immediately following completion of the STAXI-2, the researcher measured and recorded the subject's waist circumference using a cloth measuring tape placed at the top of the iliac crests and around the umbilicus.

Finally, using universal precautions, a licensed practical nurse obtained a 5 millimeter blood sample from each subject via antecubital venipuncture into serum separator tubes and immediately refrigerated at 5º C. Subjects were offered a $10.00 cash payment and thanked for their participation.

Within 24 hours of collection, the researcher spun the tubes in a cold centrifuge at 3800 rpm for 25 minutes. Serum was immediately aliquoted and frozen at -80º C until retrieved for analysis. Under the direct supervision of the researcher's chairperson in the University of South Florida College of Nursing Biobehavioral Laboratory, serum was defrosted at room temperature and prepared for measurement by the researcher using a high-sensitivity enzyme-linked immunosorbent assay (ELISA). Serum was diluted 1:100 for the assay.

The assay uses unique polystyrene-coated monoclonal antibodies to CRP which in the presence of CRP agglutinate causing an increase in the intensity of scattered light which can be measured spectrophotometrically. The increase in scattered light is directly proportional to the amount of CRP in the sample.

Subject serum samples, reference standards, and control serum samples were prepared in duplicate exactly according to assay procedure protocol (DRG International, 2005) and measured using a plate reader at 450 nm. A standard curve was produced plotting the mean absorbance obtained for each reference standard against its CRP concentration in mg/l with absorbance on the vertical axis and concentration on the horizontal access. Data reduction was accomplished by GraphPad Prism and obtained values of subject samples were multiplied by 100 to obtain CRP results in mg/l.

The assay range was 0.63 mg/l to 119.3 mg/l. Expected values for adult serum range between 0.068 to 8.2 mg/l. Intra-assay coefficient variations ranged from 2.3 to 7.5% and inter-assay coefficient variations ranged from 2.5 to 4.1%.

Assessment of Trait Anger and Anger Expression

Trait anger and anger expression were measured using the STAXI-2. The STAXI-2 is a 57-item, two-part self-report questionnaire that assesses the experience, expression, and control of anger on six major scales and five subscales. The STAXI-2 measures State Anger, Trait Anger, Anger-In, Anger-Out, and Anger Control. A composite Anger Expression Index is calculated from the combined Anger-In, Anger-Out, and Anger Control subscales and is computed to determine the overall level of anger expression with higher scores indicating greater levels of overall anger expression (Spielberger, 1999). Table 2 describes the subscales used for this study.

Table 2.

STAXI-2 Subscale Descriptions

STAXI-2 Subscale	No. of items & Score Range	Measurement	Example
Trait Anger	10 10 - 40	Differences in anger proneness as a personality trait or general tendency of a person to get angry	"I am a hot-headed person." "When I do a good job and get a poor evaluation, I feel furious."
Anger Expression-Out	8 8 - 32	Frequency of angry feelings expressed in verbally or physically aggressive behavior	"When angry or furious, I slam doors…argue with others…say nasty things."
Anger Expression-In	8 8 - 32	Frequency of angry feelings that are experience that are held in or suppressed	"When angry or furious, I boil inside but don't show it."
Anger Control-Out	8 8 - 32	Frequency of controlling outward expression of angry feelings	"I strike out at whatever infuriates me."
Anger Control-In	8 8 - 32	Frequency of controlling angry feelings by calming down or cooling off	"I control my urge to express my angry feelings."

The internal consistency of the STAXI-2 scales and subscales for normal adults (*n*=1,572) are high as measured by alpha coefficients and range from .76 to .93 for females and .72 to .94 for males. The STAXI-2 takes approximately 15-20 minutes to complete and requires a sixth grade reading level or below (Spielberger).

Statistical Analysis

Data was analyzed using SPSS Version 16.0. Preliminary analysis was conducted to examine the accuracy of data entry, missing values, outliers, and normality. Next, descriptive statistics for all variables for both high and low anger groups were determined. Variables were reported as means $\pm$ standard deviation.

Next, differences in mean levels of CRP in women who were classified as high trait anger were compared to those classified as low trait anger and those classified as high expression anger compared to women who were in the low expression anger group. To determine the effect of group membership on CRP, an independent *t*-statistic compared the computed value to the critical value of *t* based on 40 degrees of freedom (*df* = *nHIGH* + *nLow* – *2)*.

Finally, Pearson associations of bivariate correlation coefficients between the anger variables and CRP and other continuous variables were examined. All statistical testing was conducted with a $p < 0.05$ level of significance.

Chapter Four: Results

Descriptive Statistics

An initial cohort of 79 women met inclusion and exclusion criteria and led to the final 42-woman sample of 45 to 65 year-old post-menopausal women. Based on the STAXI-2 Trait Anger Subscale reference quartiles provided by Spielberger (1999) for females 30 and older, women were qualified for the low trait anger group (*n*=25) if their STAXI-2 trait subscale score was 14 or less or the high trait anger group (*n*=17) if their score was 21 or greater. Descriptive statistics for the cohort, sample, and trait groups are summarized in Table 3 and described below.

Table 3.

Descriptive Statistics of Cohort, Sample, and Trait Groups

Variable		Cohort n=79	Sample n=42	High Trait n=17	Low Trait n=25
Age, mean years		55.87	55.81	54.35	56.80
Race/Ethnicity	Caucasian	69 (87%)	36 (86%)	16 (94%)	20 (80%)
	African-American	9 (11%)	6 (14%)	1(6%)	5 (20%)
	Hispanic	1 (1%)	0	0	0
Marital Status	Married	58 (73%)	29 (69%)	13 (76%)	16 (64%)
	Unmarried	21 (27%)	13 (31%)	4 (24%)	9 (36%)
Education, mean years		16.40	16.12	15.80	16.40
Anger Trait Score, mean		17.00	17.00	23.71	12.44
Anger Expression Index, Score, mean			30.10	41.59	22.28
Waist Circumference, mean inches			33.27	33.00	33.50
CRP, mean mg/L			2.74	2.69	2.77

The average age for the cohort, sample, and trait anger groups were similar with mean values of 55.87 (± 5.01) years for the cohort, 55.81 (± 4.68 SD) years for the sample, 54.35 (±5.16) years for the high trait group, and 56.80

(±4.14) years for the low trait group. Caucasian women made up 87% (*n*=69) of the cohort. Of the remaining ten women, 11% were African-American (*n*=9), and 1% (*n*=1) Hispanic. The study sample was 86% Caucasian (*n*=36) and 14% (*n*=6) African American. Of the high trait group, 94% (*n*=16) were Caucasian, with the remaining six percent (*n*=1) African-American. In the low trait group, 80% (*n*=20) were Caucasian and 20% (*n*=5) were African-Americans.

Of the cohort, 73% (*n*=58) were married and 27% (*n*=21) were unmarried (single, widowed, divorced, or separated). Of the study sample, 69% (*n*= 29) were married and 31% (*n*=13) were unmarried. In the high trait group, 76% (*n*=13) were married and 24% (*n*=4) were unmarried. In the low trait group, 64% (*n*=16) of the women were married with the remaining 46% (*n*=9) unmarried.

The average years of education for the cohort was 16.40 (± 5.01) years with a range of 6 to >20 years. The average years of education for the study sample was 16.12 (±3.43). The high trait group mean for years of education was 15.80 (± 3.65) and the low trait group mean was 16.40 (± 3.33). The average waist circumference for the sample was 33.27 (± 4.99) inches with a high trait waist circumference average of 33.00 (± 5.57) and a low trait mean waist circumference of 33.50 inches (± 4.66).

CRP results were positively skewed with the majority of the values at the low end of the range (.07 – 8.93). The study sample mean was 2.74 (±2.19) for the sample. The high trait group levels ranged from 0.33 to 7.71 with an average of 2.69 (±2.15) and the low trait mean was 2.77 (±2.29) with a range of .07 to 8.93. Prior to data analysis, CRP values were transformed to their square roots

and generated non-skewed transformed CRP values that were not statistically different from those in a sample drawn from a theoretical normal distribution according to the Shapiro-Wilks test for normality.

The average anger trait score for the cohort was 17.00 (±4.00) and ranged from 10 to 30 which also represents the 50th percentile score for females 30 years and older (Spielberger, 1999). The trait score means of the high and low trait anger groups were significantly different ($t_{(40)}$=16.54, p <.001) between groups. Cohen's d was 2.62, which is considered a large effect size (Cohen, 1999). In this study, the groups' means were > 2.5 SD from each other indicating they were substantially different from each other in anger trait.

The average anger expression index was 30.10 (±14.66) with a range from 7 to 62. The anger expression score means were also statistically significant ($t_{(40)}$=5.47, p=<.001) between the high and low trait groups. The groups' mean anger expression scores differed by <1 SD with a large effect size (d= .87) which also supports the assumption that the two trait groups are substantially different from each other in anger expression.

Mean CRP Differences between High and Low Trait Anger Women

The first research question asked whether there were statistically significant differences in mean levels of CRP in women who were classified as high trait anger compared to those classified as low trait anger. A directional hypothesis was proposed that high trait anger women would have higher mean levels of CRP compared to low trait anger women. An independent samples

t-test statistic was calculated using the square root transformed CRP values and failed to reject the null hypothesis ($t_{(40)}$=0.13, *p*=.90, *d*= 0.02).

Mean CRP Differences between High and Low Anger Expression Women

The second research question asked whether there were statistically different CRP values in women who had a high anger expression index score compared to those who scored low in anger expression index. A directional hypothesis was proposed that women who scored higher on anger expression would have higher mean levels of CRP compared to low anger expression women. An independent samples *t*-test statistic was calculated using the 50th percentile anger index cut-off score of 29 (Spielberger, 1999) and the square root transformed CRP values which failed to reject the null hypothesis ($t_{(40)}$=.50, *p*=.62).

Other Findings

Pearson product-moment correlation (PPMC) coefficients (*r*) were assessed to determine if any variables were linearly related. As noted in Table 2, results of the correlational analysis showed no statistically significant associations between CRP and anger trait or anger expression scores. Waist circumference was strongly and positively correlated with CRP (*r* = .48, *p*=.002). CRP was found to be moderately and negatively associated with anger control-in (*r*= -.34*, p*=.029). Although the relationship of CRP and anger control-out was not significant (*r*= *-.28, p*= .07), a smaller negative association was also noted.

Table 4.

Correlations among C-reactive protein, Waist Circumference, Anger Trait, Anger Control, and Anger Expression

	Waist Circumference	Anger Trait	Anger Control-Out	Anger Control-In	Expression Index
C-Reactive Protein	.473**	-.047	-.283	-.338*	.197
	.002	.767	.070	.029	.212

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Figure 2 depicts the scatterplot between CRP and waist measurement and indicates a linear relationship that as waist circumference increases, CRP levels also increased. Scatterplots depicted in Figures 3 and 4 show that as scores on the anger control in and anger control out increased, CRP levels decreased.

Figure 2. Scatterplot of CRP and Waist Circumference.

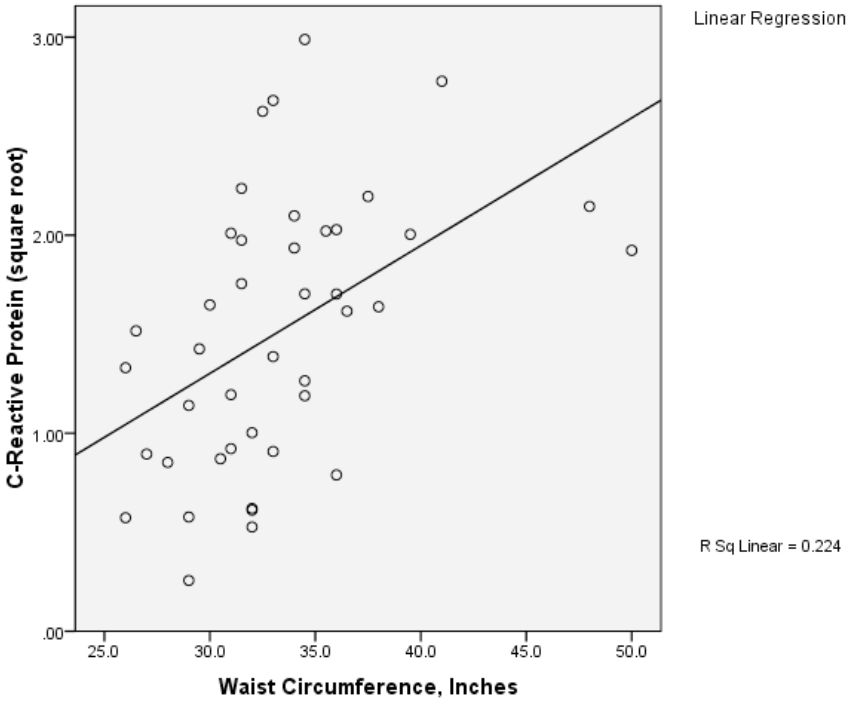


Figure 3. Scatterplot of CRP and Anger Control Out.

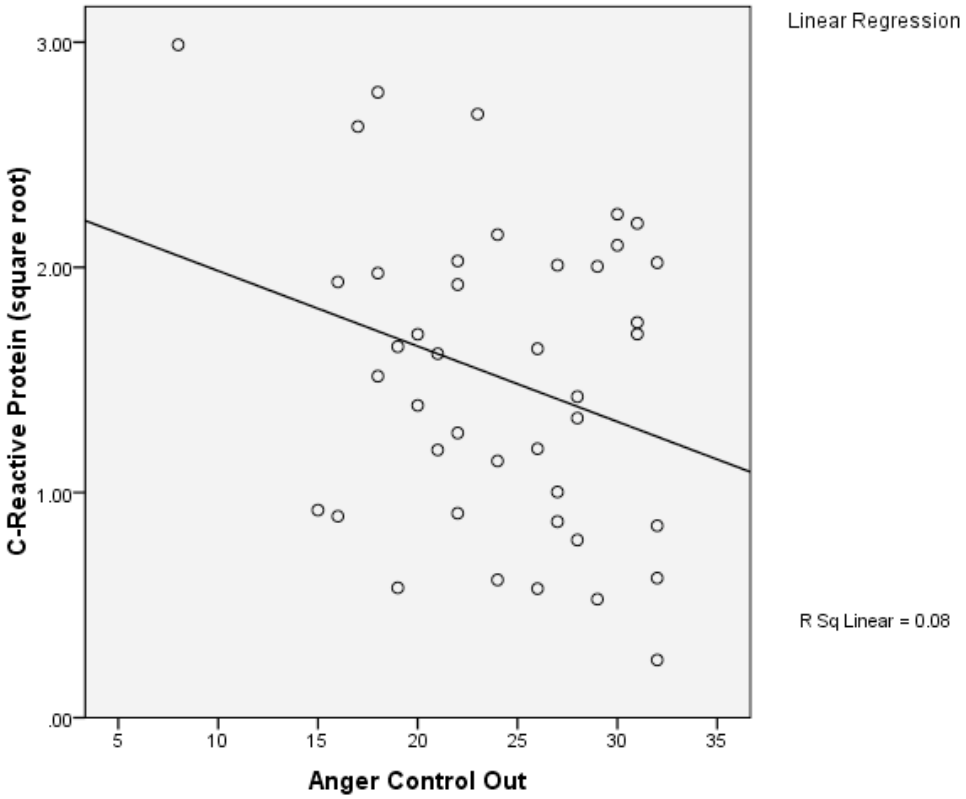
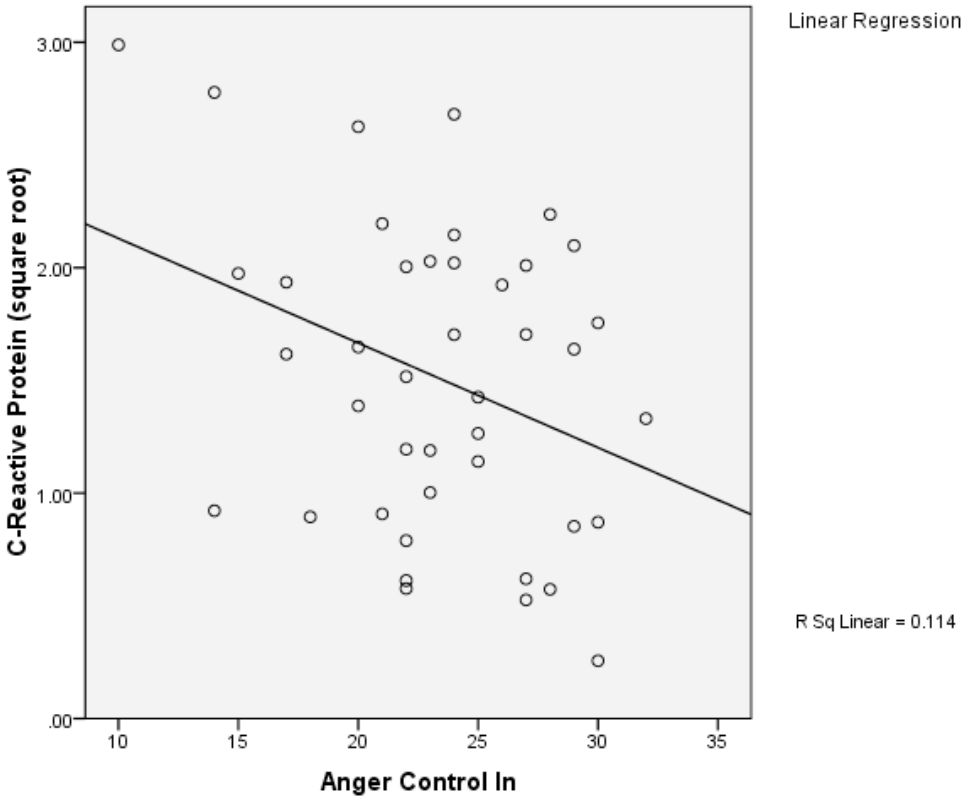


Figure 4. Scatterplot of CRP and Anger Control In



Chapter Five: Discussion

One third of women currently over the age of forty will develop CHD in their lifetime. The roles of chronic and excessive inflammation are well-known factors that contribute to atherogenesis and CHD. Less is known about how stressful emotions, such as anger, are associated with proinflammatory processes and how unhealthy anger expression styles might contribute to CHD morbidity and mortality.

Anger is a strong and generally negative emotion that includes both the felt emotion of anger and how anger is expressed or suppressed. Anger is also a common stress response based on the association of a recurrent pattern of an exaggerated sympathetic nervous system response. Research has shown how the direct and indirect effects of both acute and chronic angry emotions contribute to atherogenesis and subsequent CHD through increases in blood pressure and heart rate (CVR), and inflammatory responses.

The review of literature for this study reports significant correlations between anger, hypertension, CHD, premature death from CHD, and carotid atherosclerosis and provide solid evidence for the anger-CVR-CHD connection. Research examining immunological relationships and anger are meager and were mostly examined within the context of the role of inflammation as a precursor to CHD. Cited PNI studies seemed to indicate that anger may affect

changes in NK, NKCA, CRP, and some cytokines with an overall negative impact on inflammatory and immune responses.

In general, research to date has been limited by the use of convenience samples of primarily male populations and the use of instruments that capture more of the constructs of hostility, aggression, or anxiety rather than anger. Very few studies related anger control to measureable cytokine levels, with most being related to measures of CVR.

Discussion of Findings

The specific aims of this study were to compare differences in serum levels of CRP in 45-65 year-old post-menopausal women who were classified as either high or low anger trait. Mean CRP levels were not significantly related total trait anger scores or total anger expression scores. There were strong and positive correlations with waist circumference in that levels of CRP increased as waist circumference increased. This linear association has been repeated in multiple studies over many years and was not unexpected. The CRP-waist circumference relationship replicated in this study is based on the well-known role of excessive adipose tissue, particularly visceral fat in the abdominal area, as key regulators of inflammation and a major source of pro-inflammatory cytokines (Tracy, 2001; Yudkin, Humphries, & Mohamaed-Ali, 2000).

CRP levels were significantly inversely related to anger control-in scores; as anger control-in scores increased, CRP levels decreased. This same inverse relationship was also noted, although not statistically significant, between CRP and anger-out scores.

Exactly which components of anger trait and anger expression contribute to positive health outcomes have been studied with mixed results (Hogan & Linden, 2004; Thomas, 2007). The comparison of this study to previous research is limited because only a handful of studies used the STAXI, STAXI-2, and/or STAXI-2 subscales applying Spielberger's (1999) definition of anger control-in and anger control-out (see Table 2). As noted earlier, many studies used questionnaires that actually measured hostility, anxiety, and negative mood, but reported the results as anger trait and anger expression characteristics.

This study found that higher anger control, especially anger control-in was associated with lower levels of CRP, a marker of inflammation. Anger control-in is anger controlled through suppression, and the induction of calm and relaxation at the moment an angry feeling arises. Persons with high anger control-in scores tend to focus on calming down and reducing their anger as soon as possible. High anger control-out scores indicate that a person spends a great deal of time and energy in monitoring their outward expression and experience of anger. This finding was consistent with two other studies that measured CRP with the STAXI-2 reported in this paper (Gouin, et al, 2008; Hapuarachchi, et al., 2003).

Gouin et al. (2008) used the STAXI-2 and found no significant differences in wound healing among high and low anger expressers, but did show that higher levels of anger control were associated with a higher likelihood of faster healing. Anger control predicted healing over and above differences in negative affect, social support, and health behaviors. Perhaps anger control creates a beneficial

physiological state that ameliorates the effects of stress on the inflammatory process.

Hapuarachchi et al. (2003) found CRP levels to be significantly lower as anger control scores increased although he did not differentiate between anger control-in and anger control-out levels. He surmised that the use of productive anger coping skills may provide physiological benefit. These findings are similar to the results of this study, supporting the idea of health benefits through anger control.

Although not measuring CRP, Ishihara et al. (2003) observed high values of anger control significantly increased NK cell activity in CHD patients, but not in normal controls. NK cytotoxic function is affected by positive emotions, in general, and is an index of the ability of the immune system to kill viruses, cancer cells, and foreign cells (Vedhara & Irwin, 2005). He speculated that this was likely an over response related to anger experiences of daily life and was a function of the acute neuroendocrine response rather than anger expression style. He proposed that frequent exposure to anger provoking events could contribute to chronic stress and downregulate the immune response.

Lawler et al. (1998) found high anger control correlated with lower levels of systolic blood pressure in subjects with a family history of hypertension, and to a lesser extent in those without a family history during an anger recall interview. These results were attributed to increased awareness of CVR risk related to family history and the conscious response to control anger expression styles (calming down).

Williams' et al. (2000) large prospective study revealed that over time, healthy high anger trait individuals were three times as likely to be at risk for cardiovascular events compared to their low anger trait counterparts. These anger-prone persons, by their propensity to experience frequent high anger arousal over long periods of time, are particularly likely to suffer pathophysiological consequences related to chronic anger mismanagement.

As noted, research in this area is sparse, particularly related to measuring immune variables in relation to anger control and anger expression styles and health outcomes, particularly in women. Even less research has been done on measuring these biomarkers after cognitive behavioral interventions have been completed. Research on depression has shown a direct relationship between depressive emotional states and stress induced immune activation, similar to an acute phase response, where downregulation of the NK cell and T-cell-mediated response might adversely affect health (Zorilla et al., 2001.)

Strengths and Limitations

A significant limitation to the study was the small sample size (*N*=42) and unequal group sizes. The sample size was lower than the *a priori* calculation requiring 26 women in each group for a total sample size of 52 which would have been large enough to allow calculation of a large effect size with a power of *d*=.80. The CRP levels of the sample study were generally low across groups. For example, the overall sample mean was 2.74 mg/l. Normal levels are considered to be below 3 mg/l with ranges of 0.3 to 6.6 mg/l (Ridker, 2004).

This study consisted of post-menopausal, 45 to 65 year-old women who had an average of 16 years of education, were mostly Caucasian and married. The results of this study may not be generalizable to men, women of other age groups, ethnicity, marital status, or educational level.

Because a convenience sample was used and women were offered a cash payment to participate, selection bias is possible and may have influenced the subjects. The subject questionnaire and the STAXI-2 were both self-report measures. Since women knew the purpose of the study they may have responded in a manner that would be more likely to include them in the study.

Although subjects were excluded if they reported a personal history of CHD, diabetes, or other chronic diseases, a detailed health history was not obtained and CRP levels may have been affected by the presence or absence of unknown conditions that might trigger an inflammatory response.

Implications for Future Research and Practice

Psychosocial factors indirectly and directly affect the risk for and the development of CHD. The extent to which anger and other negative emotions contribute to sustained CRP production and dysregulation of the immune system provides opportunity for early intervention. As women age and the prevalence and incidence of women with CHD increases, research that identifies modifiable psychosocial risk factors becomes increasingly important and can be examined on both biological and psychosocial scales.

The theoretical framework of this study was based on the biopsychosocial model of mind-body interactions (see Figure 1) and proposed high trait anger and high anger expression responses may promote CHD. However, as pointed out by

Thomas (2007) not all anger coping styles are unhealthy. Anger-discuss describes talking about angry feelings with the provocateur or with a supportive close friend. This type of anger control-out, whether a result of personal anger coping strategies or anger management intervention strategies has been associated with lower blood pressure (Abel et al., 1995; Hogan & Linden, 2004; Thomas, 1997) and better glycemic control in diabetic subjects (Yi, Yi, Vitaliano, & Weinger, 2008).

Given the accumulating evidence from large prospective studies that anger influences the development of CHD (Williams et al., 2000), angry temperament and exposure to chronic and repeated stressors sustain CVR, and affect immune responses (Lovallo & Gerin, 2003), opportunity is created to further research these intricate relationships. However, which components of anger expression are more likely contribute to adverse health outcomes needs further study since not all anger forms of anger expression are necessary unhealthy.

For example, management of unhealthy anger expression styles might contribute to downregulation of pro-inflammatory responses in women with chronic diseases could also be evaluated for anger expression styles that may negatively influence disease distress. Active anger coping activities (relaxation, deep breathing) and cognitive anger management strategies could be taught to provide women with positive ways to cope with the daily stressors inherent with chronic diseases and minimize the deleterious effects of inflammatory responses of acute and chronic stress responses to angry emotions.

In conclusion, measuring PNI responses is a relative new science to nursing. The measurement of proinflammatory biomarkers provides objective and relatively accurate and precise measurements. Combined with *in vivo* (CVR) and *in vitro* (cytokines) measurements, subjective dimensions of anger characteristics provide opportunity to validate the health risks associated with stressful emotions like acute and chronic anger. For example, a prospective study which included the contributions of age, genetics, medical history, history of stressors, immune activation, socioeconomic status, depression, perceived stress, and daily lifestyle habits could examine the effect of stress reduction and positive anger coping education on proinflammatory cytokines, including CRP, against anger trait and expression scales and subscales over time to partial out the independent and deleterious effects of unhealthy anger coping strategies. Repeating these measurements following angry behavior modification could provide evidence of the positive effects of anger control on heart health.

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Appendix A: Recruitment Poster

Appendix A

Women Needed for a Research Study on Anger

- Women between the ages of 45-65 who are post-menopausal or post-hysterectomy are needed to be part of a confidential study about the emotion of anger and a blood protein called CRP.
- You will be asked to fill out a survey about how you experience anger. Based on your survey score, you may be asked to complete the second part of the study, have you waist measured, and provide a small sample of blood obtained from your arm.
- The entire study will take about 30-40 minutes and you will be offered $10 for your time if you are eligible to complete both parts of the study.
- The study will be completed confidentially in a private room.

You would not be eligible to participate in this study if you:

- cannot speak or read English.
- weigh less than 110 pounds.
- smoke cigarettes, use drugs, or drink more than 2 alcoholic beverages/day.
- have a history of heart disease, stroke, diabetes, or autoimmune diseases.
- taking cholesterol medications, hormones, or steroids.
- have had major surgery, trauma, infection, or inflammation in the past 90 days.

If you would like to take part in this study, please contact Rosalyn Gross 239-590-7521 (office) or 239-564-2903 (cell) or rgross@fgcu.edu

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Permission to conduct this study has been granted by the University of South Florida Institutional Review Board and Florida Gulf Coast University

Appendix B: Informed Consent Form

Appendix: B

UNIVERSITY OF SOUTH FLORIDA

Rosalyn Gross: Dissertation

Informed Consent Minimal

Informed Consent to Participate in Research
Information to Consider Before Taking Part in this Research Study

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Researchers at the University of South Florida (USF) and Florida Gulf Coast University (FGCU) study many topics. To do this, we need the help of people who agree to take part in a research study. This form tells you about this research study.

We are asking you to take part in a research study that is called:

Relationship of Anger Trait and Anger Expression to C-Reactive Protein in Post-Menopausal Women

The person who is in charge of this research study is Rosalyn Gross, MS, MSN, APRN-BC.

The research will be done at FGCU.

Purpose of the study

The purpose of this study is to look at the differences in women's anger and how these differences are associated with a certain normal protein found in blood called C - reactive protein or CRP.

Study Procedures

If you take part in this study, you will be asked to provide confidential personal information about your age, race/ethnicity, whether you are married or unmarried, and how many years of school you have completed. You will also be asked to complete a short 10-item survey. Your score on the survey will be worked out and if your score fits into one of two groups, you will then be asked to complete a second survey of 32 questions, have your waist measured and provide a small

amount (5 ml or about 1 teaspoon) of your blood that a licensed nurse will draw from a vein in your arm through a sterile needle. The most amount of time you will spend for both parts of the study will be no more than 40 minutes. The first part of the study will take about 10 minutes; if you are asked to complete the second part of the study, it will take an additional 20-30 minutes. You will only have to be in the study one time. The study will take place in a private room at the Florida Gulf Coast University Student Health Center. There will be no audiotaping or videotaping of you or any of the study.

Alternatives

You have the alternative to choose not to participate in this research study.

Benefits

We don't know if you will get any benefits by taking part in this study.

Risks or Discomfort

There following risks may occur:

- There may be slight discomfort from having a needle poked through your skin and into your vein while having a blood sample taken. There may be a small chance that you will have some minor discomfort and/or bruising at the place where the blood sample was taken. There may be a rare chance that the skin around the area would get infected if it was not kept clean immediately after your blood sample was drawn.
- If you are a person who finds it hard to look at needles, syringes or their own blood, you may feel dizzy or light-headed and would need to be careful when standing up after the blood sample is drawn.

Compensation

We will pay you for the part of the time you volunteer while being in this study. If you spend more than 10 minutes in the study you will be offered a $10 cash payment.

Conflict of Interest Statement

None.

Confidentiality

We must keep your study records confidential.

Information about your study records will be kept confidential and kept secure by the researcher by labeling your record with a number and matched to your information through an encoded computer database. Nobody other than the researcher will have access to your study records.

However, certain people may need to see your study records. By law, anyone who looks at your records must keep them completely confidential. The only people who will be allowed to see these records are:

- The research team, including the Principal Investigator and the licensed nurse who draws your blood.
- Certain government and university people who need to know more about the study. For example, individuals who provide oversight on this study may need to look at your records. This is done to make sure that we are doing the study in the right way. They also need to make sure that we are protecting your rights and your safety. These include:
    - the University of South Florida Institutional Review Board (IRB) and the staff that work for the IRB. Other individuals who work for USF that provide other kinds of oversight may also need to look at your records.
    - the Florida Department of Health, people from the Food and Drug Administration (FDA), and people from the Department of Health and Human Services (DHHS).

We may publish what we learn from this study. If we do, we will not let anyone know your name. We will not publish anything else that would let people know who you are.

Voluntary Participation / Withdrawal

You should only take part in this study if you want to volunteer. You should not feel that there is any pressure to take part in the study, to please the investigator or the research staff. You are free to participate in this research or withdraw at any time. There will be no penalty or loss of benefits you are entitled to receive if you stop taking part in this study. Decision to participate or not to participate will not affect your student, job, or professional status.

Questions, concerns, or complaints

If you have any questions, concerns or complaints about this study, call Rosalyn Gross at 239-564-2903.

If you have questions about your rights, general questions, complaints, or issues as a person taking part in this study, call the Division of Research Integrity and Compliance of the University of South Florida at (813) 974-9343.

If you experience an adverse event or unanticipated problem, call Rosalyn Gross at 239-564-2903.

Consent to Take Part in this Research Study

It is up to you to decide whether you want to take part in this study. If you want to take part, please sign the form, if the following statements are true.

I freely give my consent to take part in this study. I understand that by signing this form I am agreeing to take part in research. I have received a copy of this form to take with me.

_____ _____

Signature of Person Taking Part in Study Date

_____

Printed Name of Person Taking Part in Study

Statement of Person Obtaining Informed Consent

I have carefully explained to the person taking part in the study what he or she can expect.

I hereby certify that when this person signs this form, to the best of my knowledge, he or she understands:

- What the study is about.
- What procedures/interventions/investigational drugs or devices will be used.
- What the potential benefits might be.
- What the known risks might be.

I also certify that he or she does not have any problems that could make it hard to understand what it means to take part in this research. This person speaks the language that was used to explain this research.

This person reads well enough to understand this form or, if not, this person is able to hear and understand when the form is read to him or her.

This person does not have a medical/psychological problem that would compromise comprehension and therefore makes it hard to understand what is being explained and can, therefore, give informed consent.

This person is not taking drugs that may cloud their judgment or make it hard to understand what is being explained and can, therefore, give informed consent.

_____ _____

Signature of Person Obtaining Informed Consent Date

_____

Printed Name of Person Obtaining Informed Consent

Appendix C: Subject Screening Form

Appendix C: Subject Screening Form

Are you between the ages of 45-65?	Yes	No
Are you postmenopausal or post hysterectomy?	Yes	No
Do you take hormone replacement therapy (pills/patches)?	Yes	No
Do you take medication to lower your cholesterol?	Yes	No
Do you take prescribed anti-inflammatory medication?	Yes	No
Do you take more than two aspirins daily?	Yes	No
Do you smoke?	Yes	No
Do you drink more than two alcoholic beverages daily?	Yes	No
In the past **ten (10) days**, have you had any minor surgery?	Yes	No
In the past **ninety (90) days,** have you had any of the following?		
Hospitalization for major trauma, surgery or illness	Yes	No
Acute infection or inflammation	Yes	No
Do you have or have you had any of the following conditions?		
Coronary heart disease	Yes	No
Congestive heart failure	Yes	No
Cerebral vascular disease or stroke	Yes	No
Diabetes	Yes	No
Autoimmune disease (rheumatoid arthritis, lupus, etc.)	Yes	No
Chronic bronchitis	Yes	No
Chronic renal disease	Yes	No
Severe mental disease	Yes	No

Appendix D: State Trait Anger Expression Inventory-2

SIDE 1

SELF-RATING QUESTIONNAIRE STAXI—2

Printed in the U.S.A. CP98-1520 (C3,F3)

IDENTIFICATION NUMBER	AGE	TODAY'S DATE MO	DAY	YR	SEX	YEARS OF EDUCATION	MARITAL STATUS	DIRECTIONS FOR MARKING ANSWER SHEET
0 0 0 0 0 0 0 0 0 0 0 0	0 0	Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec	0 0 0 1 1 1 2 2 2 3 3 3 4 4 4 5 5 5 6 6 6 7 7 7 8 8 8 9 9 9	0 0 0 1 1 1 2 2 2 3 3 3 4 4 4 5 5 5 6 6 6 7 7 7 8 8 8 9 9 9	○ MALE ○ FEMALE	○ 6th grade or less; 7 8 9 10 11 12 13 14 15 16 17 18 19 20; ○ more than 20	○ SINGLE ○ MARRIED ○ WIDOWED ○ SEPARATED ○ DIVORCED	• Use a No. 2 black lead pencil. Do NOT use ink or ball point pen. • Make each mark heavy and black. Mark should fill circle completely. • Erase clearly any answer you wish to change. Make no stray marks.

ETHNIC CODE: ○ AFRICAN AMERICAN ○ ASIAN ○ HISPANIC ○ CAUCASIAN (WHITE) ○ OTHER

IMPROPER ✓ ✗ ●

PROPER ● ● ●

Part 1 Directions: A number of statements that people use to describe themselves are given below. Read each statement and then blacken the appropriate circle to indicate how you feel *right now*. There are no right or wrong answers. Do not spend too much time on any one statement, but give the answer which seems to *best* describe your *present feelings*.

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. I am furious	1	2	3	4
2. I feel irritated	1	2	3	4
3. I feel angry	1	2	3	4
4. I feel like yelling at somebody	1	2	3	4
5. I feel like breaking things	1	2	3	4
6. I am mad	1	2	3	4
7. I feel like banging on the table	1	2	3	4
8. I feel like hitting someone	1	2	3	4
9. I feel like swearing	1	2	3	4
10. I feel annoyed	1	2	3	4
11. I feel like kicking somebody	1	2	3	4
12. I feel like cursing out loud	1	2	3	4
13. I feel like screaming	1	2	3	4
14. I feel like pounding somebody	1	2	3	4
15. I feel like shouting out loud	1	2	3	4

Part 2 Directions: Read each of the following statements that people have used to describe themselves, and then blacken the appropriate circle to indicate how you *generally* feel or react. There are no right or wrong answers. Do not spend too much time on any one statement. Mark the answer which best describes how you *generally* feel or react.

	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
16. I am quick tempered	1	2	3	4
17. I have a fiery temper	1	2	3	4
18. I am a hotheaded person	1	2	3	4
19. I get angry when I'm slowed down by others' mistakes	1	2	3	4
20. I feel annoyed when I am not given recognition for doing good work	1	2	3	4
21. I fly off the handle	1	2	3	4
22. When I get mad, I say nasty things	1	2	3	4
23. It makes me furious when I am criticized in front of others	1	2	3	4
24. When I get frustrated, I feel like hitting someone	1	2	3	4
25. I feel infuriated when I do a good job and get a poor evaluation	1	2	3	4

Continue on reverse side...

Developed by C.D. Spielberger, PhD, in collaboration with G.A. Jacobs, E.H. Johnson, L. Barker, R.S. Crane, S.S. Krasner, S.E. Oesterle, E. Rehelser, S.F. Russell, E.P. Solomon, L. Westberry, T.J. Worden, C. Wasala, and P.R. Vagg.

SIDE 2

SELF-RATING QUESTIONNAIRE
STAXI—2

Part 3 Directions: Everyone feels angry or furious from time to time, but people differ in the ways that they react when they are angry. A number of statements are listed below which people use to describe their reactions when they feel *angry* or *furious*. Read each statement and then blacken the appropriate circle to indicate how *often* you *generally* react or behave in the manner described when you are feeling angry or furious. There are no right or wrong answers. Do not spend too much time on any one statement.

WHEN ANGRY OR FURIOUS...	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
26. I control my temper	1	2	3	4
27. I express my anger	1	2	3	4
28. I take a deep breath and relax	1	2	3	4
29. I keep things in	1	2	3	4
30. I am patient with others	1	2	3	4
31. If someone annoys me, I'm apt to tell him or her how I feel	1	2	3	4
32. I try to calm myself as soon as possible	1	2	3	4
33. I pout or sulk	1	2	3	4
34. I control my urge to express my angry feelings	1	2	3	4
35. I lose my temper	1	2	3	4
36. I try to simmer down	1	2	3	4
37. I withdraw from people	1	2	3	4
38. I keep my cool	1	2	3	4
39. I make sarcastic remarks to others	1	2	3	4
40. I try to soothe my angry feelings	1	2	3	4
41. I boil inside, but I don't show it	1	2	3	4
42. I control my behavior	1	2	3	4
43. I do things like slam doors	1	2	3	4
44. I endeavor to become calm again	1	2	3	4
45. I tend to harbor grudges that I don't tell anyone about	1	2	3	4
46. I can stop myself from losing my temper	1	2	3	4
47. I argue with others	1	2	3	4
48. I reduce my anger as soon as possible	1	2	3	4
49. I am secretly quite critical of others	1	2	3	4
50. I try to be tolerant and understanding	1	2	3	4
51. I strike out at whatever infuriates me	1	2	3	4
52. I do something relaxing to calm down	1	2	3	4
53. I am angrier than I am willing to admit	1	2	3	4
54. I control my angry feelings	1	2	3	4
55. I say nasty things	1	2	3	4
56. I try to relax	1	2	3	4
57. I'm irritated a great deal more than people are aware of	1	2	3	4

About the Author

Rosalyn Gross is a nursing professor at Florida Gulf Coast University School of Nursing in Ft. Myers, Florida and a board certified Family Nurse Practitioner. She has been a registered nurse since 1975, an advanced practice nurse since 1997, and a nurse educator since 1995. She holds a Master's of Science degree in Community Health from the University of Oregon, Eugene and a Master's of Science in Nursing from the University of South Florida, Tampa. Her research interests include women's health and childhood obesity.