NEGATIVE PSYCHOLOGICAL STATES: PREDICTORS FOR IMMUNOLOGICAL HEALTH

DISSERTATION

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Relationships of negative psychological conditions with general status of cell-mediated and humoral immune systems were investigated. A unique approach was utilized in that indexes representing multiple aspects of each branch of the immune system were employed to better indicate general immunological status. Participants were 35 females and 40 males, drawn mainly from a graduate student population and ranging in age from 25 to 55 years old. Depression conditions included Agitated Depression, Anxious Depression, Low Energy Depression, Guilt and Resentment, and Boredom and Withdrawal. Anger conditions included State Anger, Trait Anger, Angry Temperament, Angry Reaction, Anger In, Anger Out, Anger Control and Anger Expression. The Cell-Mediated Immunological Index represented total lymphocytes, absolute concentrations and percentages of total T-cells and their subtypes (helper- and suppressor-T cells) and the ratio of helper to suppressor cells. The Humoral Immunological Index represented absolute concentration and percentage of B cells, concentrations of IgG, IgM, IgA, and an index of neutrophilic myeloperoxidase activity.

Differences in emotion-immune interactions between males and females were demonstrated. Results indicated a positive

relationship between Trait Anger and the Cell-Mediated Immunological Index for the females. A negative relationship was found to exist for the males between Anxious Depression and the Humoral Immunological Index. Particular criticisms of previous psychoneuroimmunological research were met by addressing sex differences and differences in various conditions of anger and depression, as well as through assessment of cumulative effects of negative emotions on immune system status. Directions for future research in addressing similar issues are suggested. In general, results provide support for validity of mindbody interactionism and imply the need for revision of standard medical and psychological treatment.

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TABLE OF CONTENTS

LIST OF TABLES

NEGATIVE PSYCHOLOGICAL STATES: PREDICTORS FOR IMMUNOLOGICAL HEALTH

Conceptualization of Cartesian dualism appeared to have developed during a time of mechanistic thought and strict reductionistic approaches to scientific inquiry (Schultz & Schultz, 1987). Acceptance of this viewpoint directed science away from holistically approached investigations, so that the traditional Western view of health and disease evolved from a biased information base. Holistic beliefs have since been rejected in favor of "scientifically" established information, and investigations not founded in dualistic principles have largely been disregarded as valid additions to contemporary data. (Achterberg, 1985, Achterberg & Lawlis, 1980).

Multidisciplinary research, however, has challenged the disintegration of human processes and scientific fields of study by producing evidence in support of mindbody unity (Achterberg & Lawlis, 1984). The areas of Behavioral Medicine and psychoneuroimmunology have been remarkably productive in demonstrating the intricacies of disease etiology and progression (Ader, 1981). The basic premise of psychoneuroimmunology was founded on the existence of complex interrelationships within all illnesses, both physical and mental (Solomon, 1985). Thus, as this field has evolved into a viable discipline, seemingly novel conceptualizations of disease and health have been introduced into mainstream science (Lloyd, 1987). Research based on such

interactive and interdependent principles has repeatedly implicated psychological factors as integral components in disease processes, particularly those associated with immune competence (Ader, 1981, Lloyd, 1987).

The consideration of emotionality as an independent variable in disease processes began to gain increasing validation with the advent of psychoneuroimmunology (Levy, 1984, Lloyd, 1987). The concept that specific personality types exist (in terms of emotional make-up) that predispose an individual to particular illnesses has been proposed by several researchers; however, meta- and cluster analytic investigations have failed to support this contention (Eysenck, 1988, Friedman & Booth-Kewley, 1987, Stanwyck & Anson, 1986). Consistently, though, evidence for a "generic disease-prone personality" associated with illnesses such as cancer, heart disease, headaches, asthma, and arthritis has been found (Thomas, 1988).

Eysenck (1988) extended the role of emotions by focusing on their efficacy in management of interpersonal stress and found that personality variables then became successful predictors of death from cancer and cardiac heart disease. In his research, negative emotions such as depression and anger were predominately associated with deleterious health outcomes. Other investigators have consistently found similar results, particularly with regard to general health. Successful predictions of general health and mortality for large numbers of subjects have been made based on negative emotions and attitudes (Barefoot, Siegler, Nowling, Peterson, Haney, & Williams 1987). More specifically, anger has

consistently and independently correlated with general health problems in large samples as well (Broman & Johnson, 1988). Extremes in anger expression have also been proposed to account for negative health consequences; however, suppression of emotional reactions has also been linked to diseases involving immune competency such as cancer and auto-immune type illnesses such as rheumatoid arthritis and diabetes (Achterberg-Lawlis, 1982, Achterberg & Lawlis, 1984, Baltrusch & Waltz, 1985, Cox & MacKay, 1982, Daltore, Shontz, & Coyne, 1980, Eysenck, 1988, Grossarth-Maticek, Bastiaano, & Kanazir, 1985, Morris, Greer, Pettingale, & Watson, 1981, Plaut & Friedman, 1981, Solomon, 1981).

Depression and anger has often been associated with cancer and frequently with higher incidences of respiratory tract infections, infectious mononucleosis, and certain other viral illnesses (Dorian & Garfinkel, 1987, Jemmott & Locke, 1984). Studies investigating possible relationships between depression and anger and other immune related illnesses such as genital herpes, recurrent herpes labialis, essential dyspepsia, chronic duodenal ulcer, and bronchial asthma, however, have yielded equivocal results (Agarwal & Sethi, 1978, Creer, 1986, Holleander & Florin, 1983, Kemeny, Cohen, Zegans, & Conant, 1989, Schmidt, Zyzanski, Ellner, Kumar, & Arno, 1985, Solomon, 1981, Spittle & Sears, 1984, Talley, Ellard, Jones, Tennant, & Piper, 1988, Thompson & Thompson, 1985).

Anger Conceptualization

Critics of psychoneuroimmunological research have often focused on difficulties in experimental design, particularly the lack of consistency with which variables have been defined. (Plaut & Friedman, 1981). Ambiguity has been particularly evident within conceptualization and measurement of anger, hostility, and aggression (Spielberger, Johnson, et al., 1985). In their analysis of anger conditions, Riley and Treiber (1989) determined the existence of three factors, anger experience/hostility, verbal/adaptive anger expression, and physical/maladaptive anger expression. Within their work in developing an anger scale, Spielberger, Jacobs, Russell, & Crane (1983) considered anger as an emotional condition possessing variations in intensity of feeling, on a continuum from annoyance to rage. They were able to identify distinct anger conditions such as state anger, trait anger, anger in, anger out, anger control, and anger expression, as well as two separate components of trait anger (angry temperament and angry reaction).

Other aspects of this emotion, such as the importance of social roles, have been considered, as in Averill's (1982) definition of anger as an emotion rising out of frustration from disregard of expectations and desires. Along these same lines, Frijda (1986) contended that anger provocation relies on such aspects as intentionality and controllability, whereas Rolls (1986) felt that anger was associated with discontinuation or omission of positive reinforcement. Stein and Levine (1990) advocated a goal-oriented

approach in defining anger whereby a person responds with anger due to goal blockage and an accompanying perception that the goal can be restored.

Plutchik (1984) stated that reliance on subjective reporting has produced serious limitations in accurate measurement of emotional status. He suggested that a more rigorous definition be obtained through inclusion of additional components such as physiological changes, attitudes toward self, and impulses to action. Others have also believed that physical and subjective features as well as cognitive aspects are important for more comprehensive conceptualization and measurements of anger (Radke-Yarrow & Kochanska, 1990, Lazarus, Coyne, & Folkman, 1984). For example, Averill (1990) contended that structural and functional elements of emotionality be analyzed through biological, psychological, and social perspectives. Tavris (1989) emphasized the combination of physiological arousal and cognitive perceptions in defining anger. Thompson (1988) felt that anger was best represented as a combination of emotion and motivation that was characterized by desire and action to eliminate the cause of unpleasant physiological arousal.

Lack of consistency within anger conceptualization and operational definitions has been proposed to account for discrepancies in results between various studies of associated physiology (Biaggio & Maiuro, 1985). Although Ax's (1953) research demonstrated that cardiovascular changes associated with anger were indicative of mixed epinephrine-norepinephrine reactions,

other attempts to replicate his findings have failed (Weerts & Roberts, 1976). Researchers have more consistently identified only norepinephrine elevations during anger reactions (Elmadjean, Hope, & Lamson, 1957). Evidence for elevations in serum cortisol concentrations in association with anger has also been in disagreement (Franks, et al., 1991, Persky, et al., 1958). Most researchers have agreed that the anger response is generally associated with central nervous system and neuroendocrine activity and thus reflects involvement in the integration of neural, endocrine, and immune systems (Diamond, 1982, Thompson, 1988).

Depression Conceptualization

Depression has seemed to have been more thoroughly conceptualized, and most theoretical perspectives have been fairly consistent in viewing the syndrome as encompassing affective, cognitive, and vegitative signs (Millon & Kotik, 1985). Cognitive theorists have considered distorted, negative views of the self, future, and world as central to development of depression, but has acknowledged a role for interpersonal processes (Sacco & Beck, 1985). Seligman's cognitive-behavioral theory emphasized learned helplessness in the development of a negative cognitive set which then may lead to depression (Peterson & Seligman, 1985). Behavioral perspectives which have focused on reinforcement history have been viewed within the context of social learning theories in explaining development and maintainence of depression. The combination of inadequate rates of reinforcement, low frequency of social activity, deficient social skills, and the

tendency to pull for rejection and negative affect from others have been thought integral to the process. (Hoberman & Lewinsohn, 1985). Psychoanalytic theorists have generally viewed the tendency toward depression as deeply embedded within personality structure, so that the person is continually at risk for developing the syndrome (Benporad, 1985). Millon and Kotik (1985) have generally agreed that characterological factors may predispose a person to depression by reducing adaptive flexibility, thus promoting self-defeating behaviors and poor stress tolerance.

Somatic approaches to understanding the process of depression have proposed that underlying biological mechanisms lead to disruptions in mood. Current theories have depended on understanding the mechanisms of action and therapeutic effects of antidepressant medications. Tricyclic antidepressants have been known to prevent reuptake of norepinephrine, while monoamine oxidase inhibitors have been recognized as providing more monoamine neurotransmitters through delay of enzymatic destruction. Thus, the catecholamine hypothesis of depression has proposed that deficiencies of catecholamines underly depression, while the indoleamine hypothesis has proposed a functional deficiency in serotonin (Noll, Davis, & DeLeon-Jones, 1985).

Biopsychological theories of depression have generally adhered to a medical model, yet have emphasized the importance of psychological processes in maintainance of depression (Rounsaville, Klerman, Weissman, & Chevron, 1985). More recently, Fisher (1990) has proposed a psychobiological model of negative emotions which

is based in personal construct theory. Within his model, depression is viewed as a function of a primitive construct (loss of attachment) and thus associated with activity in the pituitary-adrenal cortical system. Physiological changes associated with depression are then posited to be the result of activity within this physiological system. This model has provided a useful framework with which to investigate immune-emotion interactions (Franks, et al., 1992).

Interaction of Systems

The Immune System

The immune system has played a major role in protection of the host by combating foreign pathogens through recognition and destruction/elimination. The cellular constituents of the immune system have been known to include neutrophils, lymphocytes, monocytes/macrophages, eosinophils, and basophils. Neutrophils have provided non-specific protection for the host and average approximately 59% of leukocytes, with an interval of 1.1 to 7.0×10^9 in adults (Nelson & Morris, 1991). Functional activity of these cells has been demonstrated and include chemotaxis, phagocytosis, and enzymatic activity (Nelson & Davey, 1991). Various enzymes, including peroxidase, have been found in the granules and empty into phagocytic vacuoles to produce bactericidal action (Boxer & Smolen, 1988). Enzymes released outside the neutrophil have been shown to produce tissue injury, necrosis, and inflammation (Jandl, 1987). Neutrophilia has occurred in response to various factors such as severe exercise, stress, epinephrine, corticosteroids, systemic infections, pain, fear, and anger (Davey &

Nelson, 1991). Functional ability of neutrophils has been assessed through studies of myeloperoxidase activity, chemotaxis, and bacterial killing. Myeloperoxidase has been reported as critical for the intracellular killing of *Candida* species, and has been thought to be important in the killing of *Staphyolococci* as well (Klempner, Styrt, & Ho, 1989). The significance of decreases in myeloperoxidase activity has not yet been elucidated, as this has been shown to be present in both asymptomatic and infection-prone individuals (Lehrer & Cline, 1969, Parry, Root, Metcalf, Delaney, Kaplow, & Richar, 1981). Comparison of patients with complete and partial myeloperoxidase deficiencies, however, has suggested that as activity decreases, the functional ability of neutrophils under certain conditions may be reduced (Klempner, Styrt, & Ho, 1989).

Eosinophil numbers have been assessed, and have been known to constitute approximately 3% of leukocytes, ranging from 40/μL to 350/μL in non-allergic individuals (Nelson & Morris, 1991). Although their function has not been very well understood, their participation in inflammatory conditions such as allergic reactions and asthma, their ability to respond to immunologic stimuli from some antigens and cells, and their ability to phagocytize has been demonstrated (Nelson & Davey, 1991). During acute stress, a temporary decrease in eosinophils has been shown to occur due to the release of epinephrine and glucocorticoids, followed by T lymphocyte mediated regeneration (Davey & Nelson, 1991).

Basophils have been known to make up the smallest percentage of leukocytes, with approximately 0.5% of the total and ranging

from about 0.0 to 0.2 x 10^9/L (Nelson & Morris, 1991). Heparin, histamine, and peroxidase were shown to be contained within their granules, and their ability to synthesize histamine, eosinophil chemotactic factor of anaphylaxis, and platelet activating factor has been demonstrated (Dvorak & Dvorak, 1975, Nelson & Davey, 1991). Basophil response to corticosteroids (leaving the circulating blood pool) has been demonstrated as well as their diurnal variation (Davey & Nelson, 1991, Nelson & Davey, 1991).

Monocytes/macrophages have been found to function similarly to neutrophils through chemotaxis and phagocytosis, but have also played a more integral role in the immune response. Assessment of reference values have determined that monocytes average approximately 4% of leukocytes, ranging from 0.0 to 0.8 x 10^9/L and are transformed into macrophages following migration into the tissues (Nelson & Davey, 1991, Nelson & Morris, 1991). It has been demonstrated that these cells become motile in response to lymphokines and complement components, become immobile in response to lymphocyte migration-inhibition factor, and following processing of antigens, present determinants to lymphocytes (Nelson & Davey, 1991). Their cytotoxic capabilities have also been revealed (Mavier & Edgington, 1984). Substances synthesized within macrophages have included complement components, transferrin, muramidase, interleukin-1, tumor necrosis factor, and interferon (Nelson & Davey, 1991).

Although the necessity of macrophages for antigen processing and cellular interactions has been understood, lymphocytes have

been known to be responsible for the specificity of the immune response. Research has shown that lymphocytes constitute approximately 34% of leukocytes and normally range from 1.5 to 4.0 x 10^9/L (Nelson & Morris, 1991). It has been suggested that as values approach 4.0 and exceed 5.0, the presence of infectious diseases should be suspected. For values above 10.0, it has been recommended that patients be evaluated for chronic lymphocytic leukemia. Clinical lymphocytopenia has been identified with values below 1.5 and has been associated with a number of disease states, including immunodeficiency syndromes, renal failure, congestive heart failure, tuberculosis, pneumonia, lymphoma, and systemic lupus erythematosus (Statland, 1987, Williams, Beutler, Erslev, & Lichtman, 1990). Persistant lymphocyte counts of less than 1.2 have been associated with increased mortality among hemophiliac patients (Eyster, et al., 1985). Occurrances of lymphocytopenia in response to increased levels of corticosteroids has also been demonstrated (Davey & Nelson, 1991).

Schliefer, Scott, Stein, and Keller (1986) stated that the immune system functions through the actions and interactions of two major divisions: cell-mediated and humoral immune processes. T lymphocytes have been described as involved in cell-mediated immunity, while B lymphocytes have been active in humoral immune processes (Rowlands, Wiener, Bolton, & Muus, 1991). T cells have been found to make up about 70% of the total circulating lymphocyte population and to contain subsets that can be identified based on surface markers. In general, these cells have been responsible for recognition of antigens, cytotoxicity, and

modulation of the immune response (Rowlands, Wiener, Bolton, & Muus, 1991). Research has determined that differentiation and functional maturation of these subsets occur in the thymus and include T-suppressor cells, T-helper cells, T-cytotoxic cells or killer cells, and T-delayed hypersensitivity cells (Sell, 1987). Suppressor-T cells have functioned in limiting and controlling the immune response, sensitized cytotoxic-T cells have been shown to lyse target cells, and delayed hypersensitivity-T cells have been shown to mediate the delayed hypersensitivity reaction. The function of helper-T cells in interacting with macrophages and B cells to induce antibody formation has been demonstrated. Natural killer cells are a lymphocyte subpopulation that have demonstrated cytolytic ability for a variety of cell types, including cancer and virally infected cells (Schliefer, Scott, Stein, & Keller, 1986).

Some researchers have reported that the number of total lymphocytes and T cells decrease with age while others have failed to find such changes (Davey & Huntington, 1977, Diaz-Jouanen, Strickland, & Williams, 1975, Smith, Evans, & Steele, 1974, Weksler & Hutteroth, 1974). B lymphocyte number, however, has been shown to remain stable throughout life (Davey & Huntington, 1977). Technicon Instruments Corporation (1989) has suggested a range of 66 to 87% for total circulating mature and immature T lymphocytes, 27 to 58% for helper-T cells, and 13 to 40% for suppressor-T cells. In evaluating lymphocyte subsets, it has been suggested that both absolute and percentage values be taken into consideration.

The ratio of helper- to suppressor-T cells has also been used with the absolute values of these cells in order to more fully assess health status (Rowlands, Wiener, Bolton, & Muus, 1991). This method of assessment has been important in many autoimmune disorders in that increases in helper to suppressor ratios have been typical of autoimmune illnesses and have been thought to be partly responsible for the associated increase in immune activity. Suppressor-T cells have been typically shown to be decreased during a number of these illnesses, and sometimes may be used to predict symptom progression (Isenberg, Shoenfeld, & Schwartz, 1984). However, studies of some autoimmune disorders, such as systemic sclerosis, lupus, and rheumatoid arthritis, have demonstrated increased helper-T cell populations (Janossy, et al., 1981, Schoenfeld & Schwartz, 1984).

Decreases in the helper to suppressor ratio below about 0.41 have been noted to correlate with extent of clinical illness and course of infection from several bacterial and viral infections (Blumberg & Schooley, 1985). Patients who have been infected with *Human Immunodeficiency Virus* (HIV) usually exhibit a decrease in this ratio due to destruction of helper-T cells by the virus and normal or increased levels of suppressor-T cells (Rowlands, Wiener, Bolton, & Muus, 1991). Many patients who have been seropositive for HIV but have not yet developed AIDS have been found to have low helper to suppressor ratios due to elevated suppressor-T cell numbers, whereas diminished helper-T cells have been recognized as producing the decreased ratio for those who

have developed AIDS-related complex (Pinching, 1985, Zolla-Panzer, 1986). Ratios for patients with AIDS-related Kaposi's sarcoma and those with AIDS-related complex have been noted to average from 0.46 to 0.80 (Zolla-Panzer, 1986). Helper to suppressor ratios have also been utilized in cases of renal transplants in order aid immunosuppressive therapy and to detect rejection (Giorgi, 1986). Ratios of less than 1.0 have been observed in infectious processes related to graft rejection; however, a high incidence of viral infections in these patients have been associated with ratios of less than 1.5 (Blumberg & Schooley, 1985, Stoolman, 1989). Ratios of 0.5 to 1.0 have been associated with chronic lymphocytic leukemia (Williams, Beutler, Erslev, & Lichtman, 1990).

Appropriate interactions between helper-T cells and suppressor-T cells have been thought to be responsible for adequate activation of B lymphocytes. Helper-T cells then become active in modulating humoral immunity, while suppressor-T cells have suppressed this activity (Rowlands, Wiener, Bolton, & Muus, 1991). B cells, derived from the bone marrow in adults, and constituting 4 to 16% of total circulating lymphocytes, have been shown to undergo differentiation in two stages. The first stage was exhibited to be independent of antigen; otherwise, proliferation, differentiation, and plasma cell formation are regulated by antigen activation and interactions of T cells, macrophages, and growth factors (Cooper, 1987). Evidence has been demonstrated in support of the association of increasing B cell activation with severity of illness

in AIDS, and a high frequency of B-cell lymphomas has been documented in these patients (Birx, Redfield, & Tosato, 1986, Ziegler, Beckstead, & Valberding, 1984, Zolla-Pazner, 1986). Decreases in B-cell production have been associated with hypogammaglobulinemias (Grieco & Meriney, 1983)

Depending on the commitment of the B cells, plasma cells have synthesized IgM, IgD, IgG, IgA, or IgE; however, all initially produce IgM and some of these have been shown to co-express IgD. IgM has provided the initial defense against bacteremia and functions in cross-linking antigen and in complement activation (Ricardo & Tomar, 1991). It has been suggested by Statland (1987) that concentrations of approximately 50 to 270 mg/dL be considered normal. Values below 40 have been associated with immunodeficiency, Celiac-sprue disease, leukemia, malignant melanoma, and monoclonal gammopathy of IgA or IgG. Statland has also recommended that IgM monoclonal gammopathy be suspected at values above 300, and particularly so when exceeding 1000. Other causes of increased values greater than 300 were cited, including infectious processes, liver diseases, autoimmune disorders, and nephrotic syndromes.

Assessments of IgG have found that its concentration normally ranges from about 538 to 1400 mg/dL, making up 80% of total immunoglobulin. Its abilities to pass into extravascular spaces, bind to phagocytic cells to enhance their efficiency, and bind to and activate complement have been demonstrated. (Ricardo & Tomar, 1991). Values below 600 have been associated with leukemia, immunodeficiency, nephrotic syndrome, nephrotic syndrome, and

monoclonal gammopathy of IgM or IgA, while values above 1700 have indicated possible IgG monoclonal gammopathy and have been associated with liver disease, autoimmune diseases, infectious processes, and cystic fibrosis. It has been demonstrated that IgG monoclonal gammopathy is strongly suggested at values above 5000 (Statland, 1987).

IgA has been found to be present in serum in concentrations of about 44-360 mg/dL but to function primarily with the addition of a secretory component for protection of external body surfaces. Thus, serum IgA has been found in milk, saliva, tears, and respiratory and intestinal secretions and has been thought to function through prevention of adherence of microorganisms to mucosal cell surfaces. IgA has also been thought to play a role in preventing allergic reactions to food by preventing the absorption of their antigens into the bloodstream. Values below 40 have been associated with immunodeficiency or monoclonal gammopathy of IgM or IgG. Other causes of decreased values have included nephrotic syndrome, leukemia, and typhoid fever. Possible causes of levels above 450 have included infectious processes, liver diseases, autoimmune diseases, cystic fibrosis, and celiac disease. It has been recommended that IgA monoclonal gammopathy be suspected at values above this level; however, this is more strongly suspected when IgA exceeds 1000 (Statland, 1987).

IgD has been shown to be relatively less concentrated in serum and only comprises 1% of total immunoglobulin. Its presence on the membrane surface of B cells in high proportion and its function as

an antigen receptor for these cells has been demonstrated. The smallest concentration of immunoglobulin, at 17 to 450 ng/mL, and less than 1% of the total, has been found to be IgE. It has been primarily involved in allergic reactions and parasitic infections. IgE has been shown to have the ability to bind to basophils and mast cells and to be produced in respiratory and intestinal tract linings (Ricardo & Tomar, 1991).

A number of diseases have been associated with polyclonal hyperimmunoglobulinemia, including AIDS and autoimmune disorders such as systemic lupus erythematosus, rheumatoid arthritis, scleroderma, and thyroiditis. The immunoglobulins in these instances have not seemed to be directed toward specific antigens but may instead be related to chronic general antigenic stimulation or disruption of regulation by T cells (Ricardo & Tomar, 1991, Zolla-Pazner, 1986).

The overall efficiency of the immune response has been recognized as dependent on the combination of lymphocyte subpopulations and their functional abilities as well as their products of self-regulation, the lymphokines (Schliefer, Scott, Stein, & Keller, 1986). Interleukin-1 and interleukin-2 have been described as two of five interleukins that are considered one class of lymphokines. Macrophages have been shown to produce interleukin-1, which functions to enhance thymocyte and T cell growth by inducing T cells to produce interleukin-2. Interleukin-1 has had a variety of other biological functions, including pyrogenic activity, increasing white blood cell count, sleep induction, and

acting as a co-factor in B cell activation. Macrophages have also been stimulated to produce prostaglandin-2, which then inhibits the effects of interleukin-1. It has been determined that interleukin-2 is produced by T lymphocytes and can stimulate proliferation and differentiation of both T and B cells (Katzen, et al., 1985). Interleukin-3, produced by activated T cells, has demonstrated the ability to stimulate growth in each hematopoietic cell line (Zoumbos, Raefsky, & Young, 1986). Another factor known to be produced by activated T cells is interleukin-4, which can induce B cell proliferation and enhance IgE, IgG1, T cell and mast cell growth factor production (Rowlands, Wiener, Bolton, & Muus, 1991). Interleukin-5 has been known to function in enhancing proliferation of B cells as well as the in the acquisition of secretory activity of IgA (Webb, Pierce, & Cohen, 1987).

Other lymphokine classes have included the interferons, tumor necrosis factor, macrophage/monocyte activating factor, macrophage inhibitory factor, leukocyte migration inhibitor factor, eosinophil chemotactic factor, neutrophil chemotactic factor, and B cell growth and differentiation factors. Three groups of interferons have been known to exist, and all have demonstrated antiviral and antiproliferative activity. All have also been shown to enhance certain antigen class activity as well as increasing plasma cell maturation and secretion of antibodies (Webb et al., 1987).

Neuroendocrine Mediation

With the advent of more holistic approaches to human functioning, many investigations of emotionality were directed toward elucidating the mechanism of their intermediary role. Such studies of emotionality have consistently implicated the neuroendocrine system as the primary connection through which emotions mediate immune function (Ader, 1981). The pituitary, through its connections to various neural structures and as the director of the endocrine response, has been identified as crucial to the integration of these systems (Lloyd, 1987). Regulation of the pituitary during stress states by secretion of corticotropin releasing factor from the hypothalamus has been recognized (DeSouza, 1989). The ability of this substance to alter pituitary secretion of adrenocorticotropin hormone (ACTH), leutinizing hormone, and growth hormone has been demonstrated (River, Petraglia, Walker, & Vale, 1989). Other autonomic effects reported for corticotropin releasing factor include elevations in circulating catecholamines (DeSouza, 1989).

The pituitary's ability to receive information from a variety of areas, including the neocortex, thalamus, limbic structures, midbrain, preoptic area, and brainstem has been reported (Renaud, Pittman, & Blume, 1979). Of these, neocortical and limbic structures have been found to be of particular importance in directing the emotional response. Activity of the limbic-hypothalamic-pituitary axis has been shown to initiate release of substances from the pituitary by which peripheral endocrine organ

secretion is directed (Holsboer, 1988). For example, synthesis and secretion of glucocorticoids from the adrenal cortex has been known to be promoted by pituitary release of ACTH. Additionally, descending fibers from the hypothalamus into the spinal cord and their subsequent innervation into the adrenal medulla have been recognized as potentiators of catecholamine release through emotion-initiated sympathetic nervous system activity (Diamond, 1982, Kelly, 1985, Tecoma & Huey, 1985).

The role of glucocorticoids and catecholamines in immunomodulation has been extensively studied (Dienstbier, 1989, Guyre, Girard, Morganelli, & Manganiello, 1988, Tecoma & Huey, 1985). Responses of the immune system to catecholamines, however, have been difficult to delineate due to their complexity; thus enhancement as well as suppression has been reported (Dienstbier, 1989). Immune functions shown to be suppressed by catecholamine exposure have included chemotactic and phagocytic activities of monocytes and neutrophils, and proliferation, cytotoxicity, and secretory activity (immunoglobulin and interferon synthesis) of lymphocytes (Fuchs, Campbell, & Munson, 1988, Jemmott, 1985, Tecoma & Huey, 1985). In addition to its role as an anti-inflammatory agent, cortisol has been thought to exert its influence on cellular immune processes through modulation of catecholamine immunosuppression (Guyre, Girard, Morganelli, & Manganiello, 1988, Tecoma & Huey, 1985). In their review of the literature, Guyre et al. proposed that cortisol can also inhibit various cytokine production.

Neuropeptides

The ability of some neuropeptides to alter central nervous system activity through neurotransmitter or neuromodulatory activity and thus their integral performance in such processes as memory, learning, perception, mood, behavior, and emotion has been described (Ruff, Sacerdote, Wiedermann, & Pert, 1989). Based on structural similarities, neuropeptides have been categorized into several major classes such as opioids, insulins, neurohypophyseals, tachykinins, secretins, somatostatins, and gastrins (Schwartz, 1985). Relatively few of the identified neuropeptides have demonstrated autonomic nervous system regulatory activity or have been extensively studied within the context of immune system modulation (Ruff, Sacerdote, Wiedermann, & Pert, 1989).

Two opioid systems, distinct both functionally and anatomically, have been elucidated. The first has been associated with neuronal cells of the central and peripheral nervous systems and the second with neurosecretory cells of endocrine organs. Centrally, opioid peptides have been reported to function as neuromodulators and because of their axonal projections, have appeared to be important in regulating autonomic and endocrine functions, pain perception, and behavior (Holaday & Malcolm, 1987). Evidence has also pointed to their role in limbic system functioning (Gallagher, Meagher, & Decker, 1989) Precursors for opioid peptides, which vary in neural distribution and synthesis sites, have included proenkephalin A, proenkephalin B and pro-opiomelanocortin (Lynch & Snyder, 1987). Pro-opiomelanocortin has been identified as a β-endorphin,

met- and leu-enkephalin as proenkephalin-A, and dynorphins as proenkephalin-B. It has been reported that the primary source for circulating β-endorphin is the pituitary, and for enkephalins is the adrenal medulla; however, these substances have also been identified in the pancreas, gastrointestinal tract and placenta. The hormonal nature of their physiological function has been described because of their release into the bloodstream during stress states (Holaday & Malcolm, 1987). It has also been suggested that research supports their role in immune functioning (Holaday & Malcolm, 1987, Ruff, Sacerdote, Wiedermann, & Pert, 1989).

Tachykinins have been identified as a group of neuropeptides that have the ability to induce tachycardia by lowering blood pressure. Substance P has been recognized as a member of this group with its powerful vasodilating ability (McGillis, Mitsuhashi, & Payan, 1990) Within the central nervous system, it has been shown to coexist with serotonin (Schwartz, 1985). Evidence has been reported for the role of substance P in regulation of autonomic nervous system activity, including associated increases in adrenal nerve activity and in circulating levels of epinephrine and norepinephrine (Brown, 1989). In addition to central nervous system activity, the identification of substance P in sensory neurons of the peripheral system, including the skin, vasculature, gastrointestinal tissue, mucosal tissue, and around joints has been reported (Pernow, 1983). It has also been suggested that adequate evidence exists for the role of substance P in modulating immune and inflammatory processes (McGillis, Mitsuhashi, & Payan, 1990).

Vasoactive intestinal peptide has been identified as one of a number of peptides classified as secretins, which has been found in the central and peripheral nervous systems as well as in the gut. It has been described in highest distributions in the cerebral cortex, hypothalamus, amygdala, hippocampus and corpus striatum. It has also been reported to act synergistically with norepinephrine, to coexist with acetylcholine, and to be imperative for normal brain function. It has been recognized as a principal component in vasodilation, cardiac output, hyperglycemia, smooth muscle relaxation, liver glycogenolysis, and gastrointestinal secretory processes (Gozes, 1987, Schwartz, 1985). The function of vasoactive intestinal peptide in communication between the nervous and immune systems has also been reported (Sirianni, et al., 1990).

Although the full physiological role of nerve growth factor in the central nervous system has not yet been elucidated, it has been recognized as necessary for the development and maintenance of neurons in peripheral sympathetic and sensory nervous systems (Bard, Edgar, & Thoenen, 1987). The ability of nerve growth factor to influence both cellular and humoral immune processes has also been described (Thorpe, Jerrells, & Perez-Polo, 1990).

Somatostatins are another group of peptides that have been recognized as exerting autonomic nervous system regulation (Brown, 1989). Secretion has been shown to be stimulated by corticotropin releasing factor and they have appeared to produce a decrease in ACTH production (DeSouza, 1989, Brown, 1989).

Somatostatins are also the only peptides that have been identified as having a diminishing effect on circulating epinephrine levels (Brown, 1989).

Evidence for peptide involvement in communication between nervous, endocrine and immune systems has been extensive, but because of the nature of the research, the information has been generally dispersed and thus difficult to collate (Ruff, Sacerdote, Wiedermann, & Pert, 1989). The potential ability of these substances for direct modulation of immune function has come from studies demonstrating their direct innervation of primary (thymus) and secondary (spleen, lymph nodes, gut-associated lymphoid tissue) lymphoid organs. Nerve fibers for neuropeptide Y and calcitonin gene related peptide have been found in the spleen, thymus, and lymph nodes, with neuropeptide Y co-localizing with noradrenergic fibers in latter of these two organs (Bellinger, et al., 1990, Felten, Felten, Carlson, Olschowka, & Livnat, 1985, Fink & Weihe, 1988, Popper, Mantyh, Vigna, Magioos, & Mantyh, 1988). Enkephalin fibers have been demonstrated in the thymus and spleen and vasoactive intestinal peptide in the thymus, lymph nodes, and gut associated lymphoid tissue (Ekblad, Winther, Ekman, Hakanson, & Sundler, 1987, Felten & Felten, 1990, Felten, Felten, Carlson, Olschowka, & Livnat, 1985, Popper, Mantyh, Vigna, Magioos, & Mantyh, 1988). Cholecystokinin and substance P fibers have been localized in all four lymphoid organs (Bellinger, et al., 1990, Ekblad, Winther, Ekman, Hakanson, & Sundler, 1987, Felten & Felten, 1990, Felten, Felten, Carlson, et al., 1985, Kurkowski, Kummer, & Heym,

1990, Popper, Mantyh, Vigna, Magioos, & Mantyh, 1988). Furthermore, close contact between substance P nerve fibers and mast cells has been discovered in the rat jejunum intestinal mucosa (Stead, Tomioka, et al., 1987). Additionally, nerve fibers for neurotensin have been discovered in parts of the spleen, and for somatostatin, endorphins, vasopressin, and pancreatic peptide in the thymus (Felten & Felten, 1990, Felten, Felten, Carlson, et al., 1985).

Alternatively, neuropeptides have been thought to modulate immune changes through more direct interactions with the cells themselves. Receptors for many neuropeptides have been discovered on various cells of the immune system. Studies have demonstrated lymphocyte receptor sites for nerve growth factor, substance P, opioid peptides, prolactin, cholecytsokinin, somatostatin, and vasoactive intestinal peptide (Goetzl, Grotmol, et al., 1989, Goetzl, Turck, & Sreedharan, 1990, McMillen, et al., 1990, Morgan, Thorpe, Marchetti, & Perez-Polo, 1989, Payan, Brewster, Missirian-Bastian, & Goetzl, 1984, Robb, Munck, & Smith, 1981, Russell, et al., 1988). Receptors for opioid peptides have also been reported for monocytes and granulocytes, and the existence of substance P and calcitonin gene-related peptide receptors on non-human macrophages has been documented (Abello, Kaiserlian-Nicolas, Cuber, Revillard, & Chayvialle, 1990, Goetzl, Turck, & Sreedharan, 1990, Hartung, Wolters, & Toyka, 1986). Research has also demonstrated the presence of two types of interleukin-1 receptors on leukocytes (one for modulation of fever and one for

modulation of C-reactive protein and leukocytosis), both of which appear to be influenced by α-melanocyte stimulating hormone (Dao, Bell, Feng, Jameson, & Lipton, 1988).

Studies examining the effects of various peptides on health status and functioning of leukocytes have provided indirect evidence of interactions at the cellular level. Morley, Kay, and Solomon (1989) stated that chronic opiate ingestion has been associated with a higher incidence of infectious diseases from decreased immunocompetence. Research of opioid peptides and the immune system, however, have produced inconsistent as well as conflicting results (Fischer, 1988, Tecoma & Huey, 1985). Significantly decreased levels of β-endorphin have been reported for patients with rheumatoid arthritis (Fischer, 1988). Although β-endorphins have been shown to suppress activation of B cells, no effect on antibody formation has been noted (Fischer, 1988, Morgan, Janda, McClurg, & Buchner, 1990). Other effects of opioid peptides have included enhancement of natural killer cell activity, stimulation of suppressor-T cell populations, decreases and increases in rosette formation, reduction of cytotoxicity, chemotactic activation of mononuclear cells, histamine release from mast cells, increases in interferon-γ, interleukin-2 and superoxide production (Ottaviani, et al., 1990, Morley, Kay, & Solomon, 1989). Beta-endorphin has been associated with suppression of antigen-stimulated T cells and enhancement of mitogen-stimulated proliferation, but has also demonstrated no modulatory effect (Fischer, 1988). Other neuropeptides reported to

affect lymphocyte proliferation include neuropeptide Y, substance P, vasoactive intestinal peptide, nerve growth factor, and somatostatin (Bonneau, Kiecolt-Glaser, & Glaser, 1990, Jones, James, & Mansour, 1990, Pallone, et al., 1990, Thorpe, Jerrells, & Perez-Polo, 1990).

Substance P has been implicated in the rheumatoid arthritic process, and has been reported to regulate cytokine production by macrophages, stimulate macrophage function, and activate histamine secretion from mast cells (Hartung & Toyka, 1983, Kimball, 1990, Lotz, Vaughn, & Carson, 1988). Nerve growth factor has also been known to enhance inflammatory processes, through chemoattraction of leukocytes and degranulation of mast cells (Boyle, Lawman, Gee, & Young, 1985, Stead, Bienenstock, & Stanisz, 1987).

Prolactin has been found to reduce cytolytic activity of natural killer cells at high concentrations, but at lower concentrations has enhanced this function (Matera, Cesano, Veglia, & Muccioli, 1990). Vasoactive intestinal peptide has also been shown to interfere with natural killer cell lysis (Pallone, et al., 1990, Sirianni, et al., 1990). Evidence has implicated the role of cholecystokinin in co-modulation of lymphocyte activation (McMillen, et al., 1990). The role of calcitonin gene-related peptide in the inhibition of superoxide ion production and antigen presentation in macrophages has been reported (Abello, Kaiserlain-Nicolas, Cuber, Revillard, & Chayvialle, 1990).

Bidirectional Communication

It has been suggested that the relationship between immunological and behavioral processes is one of reciprocity, so that maintenance of homeostasis is an interdependent process (Ader, 1990). Ader's conditioning studies, in which learning has significantly influenced immune competence and conversely immune status has influenced behavior, have supported this contention Furthermore, studies that have involved administration of lymphokines (including interferons, interleukin-2, and tumor necrosis factor) in high concentrations to cancer patients have documented accompanying psychological and neurocognitive symptomology such as depression, anxiety, confusion, visual hallucinations, disorientation, and agitation (Triozzi, Kinney, & Rinehart, 1990).

Evidence has also been presented for the availability of neuropeptides and hormones through synthesis and secretion by the immune cells themselves (Blalock, Harbour-McMenamin, & Smith, 1985, Goetzl, Turck, & Sreedharan, 1990). In their review of the literature, Tecoma and Huey (1985) found suggestions of an integrative role for the immune system in which information is relayed centrally during infections to provide unity of response. Lymphocytes have been reported to produce ACTH, corticotropin releasing factor, β-endorphin, thyrotropin, growth hormone, lutenizing hormone, chorionic gonadotropin, and prolactin (Goetzl, Grotmol, et al., 1990, Weigent, Baxter, Guarcello, & Blalock, 1990). Corticotropin releasing factor has been reported to activate the

secretion of lymphocyte-synthesized pro-opiomelanocortin (precursor of endorphins) with subsequent elevations in ACTH and β-endorphin levels (Galin, LeBoeuf, & Blalock, 1990). It has also been reported that ACTH expressed by virally activated lymphocytes can produce increases in cortisol secretion and that interleukin-1 can potentiate ACTH release from the pituitary (Tecoma & Huey, 1985). Other pituitary effects from immune activation have been reported, including suppression of release of thyroid stimulating hormone (Scarborough, 1990). Mast cells and basophils have been found to be capable of producing various types of vasoactive intestinal peptides (Goetzl, Grotmol, et al., 1989).

Studies of bidirectional communication between systems have also implicated the involvement of various cytokines. Scarborough (1990) has even suggested that, although the primary route of influence on the pituitary is most likely through the hypothalamus, cytokines provide the underlying mechanism for pituitary influence from immune activation. Several mechanisms of action have been considered, such as stimulation of endocrine organs from cellularly derived cytokines, stimulation of afferent nerves, and production of cytokines by the hypothalamus or pituitary (Scarborough, 1990). Indirect modulation of the pituitary by interleukins through changes in circulating cortisol, thyroxine, and gonadal steroids has been demonstrated (River & Vale, 1989). It has also been reported that administration of tumor necrosis factor in animals increases circulating catecholamine and cortisol levels and induces ACTH secretion (Ricciardi-Castagnoli, et al., 1990).

The idea that cytokines may act intrinsically to modulate hypothalamic and pituitary processes has been supported by research describing the presence of these substances in such brain structures (Scarborough,1990). Merrill (1990) has also described the ability of both glial and neuronal cells to produce and be affected by interleukin-1, -3, and -6. Furthermore, the ability of interleukin-2 to affect these cells as well as enhancing the production of pro-opiomelanocortin and corticotropin releasing factor in the pituitary has been described (Merrill, 1990).

Emotions and Immunology

Studies that have focused on relationships between negative emotionality and immune parameters have substantiated a dynamic interaction between the two processes (Lloyd, 1987). For example, studies have indicated poorer consequences for immune status with suppression of negative emotionality. Decreased natural killer cell activity, diminished differentiation of lymphocyte subpopulations, and decreased levels of circulating monocytes in association with emotional suppression has been shown (Beutler, Engle, Oro-Beutler, Daldrup, & Meredith, 1986, Jamner, Schwartz, & Leigh, 1988). Conversely, release of negative emotions has been shown to enhance immune functioning by increasing responsiveness of T cells to mitogen stimulation (Pennebaker, Kiecolt-Glaser, & Glaser, 1988).

In general, investigations of the the association between depression and the immune competence have consistently demonstrated reduced mitogen responsiveness (Darko, Gillin, Christian, Risch, & Bulloch, 1989, Dorian & Garfinkel, 1987,

Kiecolt-Glaser & Glaser, 1986, Kronfol & House, 1989, Linn, Linn, Bernard, & Jensen, 1984, Tecoma & Huey, 1985). Although few other immune parameters have typically been studied, O'Neill and Leonard (1986) reported a reduction in phagocytic activity of neutrophils in depressed patients which returned to normal in response to treatment. Additionally, a significant negative correlation between the depression scale of the MMPI and natural killer cell activity in a sample of college students has been found (Heisel, Locke, Kraus, & Williams 1986). Decreased populations of natural killer cells, total T lymphocytes, and circulating T and B cells have been also been reported with depression (Denney, Stephenson, Penick, & Ronald, 1988, Dorian & Garfinkel, 1987, Evans, Pederson, & Folds, 1988, Kiecolt-Glaser & Glaser, 1986, Kronfol & House, 1989, Kronfol, Turner, Nasrallah, & Winokur, 1984). However, others have failed to find similar changes in T and B cell populations (Kronfol, et al., 1984, Tecoma & Huey, 1985). Studies focusing on subpopulations of T lymphocytes have also yielded conflicting results. Decreases, increases, and no changes in numbers of suppressor-T cells have been noted (Denney, Stephenson, Penick, & Weller, 1988, Krueger, Levy, Cathcart, & Fox, 1984, Tondo, Pani, Pellegrini, Bettoli, & Milia, 1988, Wilson, Surman, Colvin, & Ozonoff, 1990). Helper-T cells have also been reported as decreased or increased with depression (Denney, et al., 1988, Krueger, et al., 1984, Tondo et al., 1988). No changes in the ratio of helper-T to suppressor-T cells has also been determined (Denney, Stephenson, Penick, & Weller, 1988). The idea that glucocorticoid

receptor sites are particularly important in mediating psychogenic immunological changes was supported by the observation that the number of these receptor sites on lymphocytes was state dependent, returning to normal in those patients who had recovered from depression (Hunter, Dick, Christie, & Goodwin 1988). Although the production of information focused on depression in negative emotion/immune system relationships has been fairly steady, similar research utilizing anger has been exceedingly sparse. Higher serum levels of IgA in those women with breast cancer who suppressed anger has been reported (Pettingale, Philalithis, Tee, & Greer, 1981). Additionally, increased aggressiveness has been found to be significantly associated with decreased β-adrenergic receptor density on lymphocytes (Moises, Bering, & Muller, 1988).

The most controversial issue within these types of investigations has been whether the diminished immune status observed in association with negative emotionality ultimately results in poorer health conditions (Bonneau, Kiecolt-Glaser, & Glaser, 1990). Dorian and Garfinkel (1987) have contended that enough evidence exists to strongly suggest that immune competence may be altered toward immunosuppression in association with psychological factors that are involved with adaptation to the social environment, and Eysenck (1988) has contended that emotions provide this function. However, inconsistent results within psychoneuroimmunological research have abounded, and a number of criticisms have been directed toward various methodologies utilized (Dorian & Garfinkel, 1987). Suggestions for

designing future research to facilitate understanding the various interactions have been few; however, Dorian and Garfinkel (1987) proposed assessing multiple aspects of immunological functioning within a single research design in order to produce a general index of immune competence. Quantitation of T-lymphoctyes has been an effective method by which to determine the functional state of the cell-mediated branch of the immune system, while quantitation of B-lymphocytes has been correlated with the functional state of the humoral system. It has also been suggested that comparisons between males and females be incorporated into future designs, as previous research has indicated that psychoneuroimmunological relationships may differ between these two groups (Franks, et al., 1991).

The purpose of the present study was to explore relationships between negative emotional states and general immunological status of both cell-mediated and humoral systems. A more novel approach to exploring such interactions would be to utilize immune indexes to better facilitate representation of the overall status of this system. Such indexes may be able to take into account the unique variability of each individual parameter and thus better reflect their outcome on general immune status. With this in mind, several hypotheses were generated: (1) anger conditions would be associated with changes in Cell-Mediated and Humoral Immunological Indexes, (2) depression conditions would be associated with changes in Cell-Mediated and Humoral Immunological Indexes, and (3) males and females would differ in immune-emotion relationships.

Method

Subjects

Subjects were drawn mainly from a psychology graduate student population, but also included some from staff, faculty, and others outside the university. There were 71 subjects comprised of 36 males and 35 females. Ages ranged from about 25 to 55 years old. Prospective subjects completed a health questionnaire to gather demographic information and to screen for the presence of general health problems

Instruments

Clinical Analysis Questionnaire (CAQ). The CAQ was developed to measure normal and pathological personality factors (Krug, 1980). Reliability and validity across all scales are reported to range from 0.51 to 0.90 and 0.45 to 0.86, respectively (Krug, 1980). Five clinical scales of the CAQ were used to determine the presence and extent of depression: Agitated Depression, Anxious Depression, Low Energy Depression, Guilt and Resentment, and Boredom and Withdrawal.

State-Trait Anger Expression Inventory (STAXI). The transitory experience of anger was measured as State Anger. The Trait Anger scale was used to reflect individual differences in anger proneness. There are two subscales within Trait Anger; one (Angry Temperament) which measured the tendency to express anger without provocation, and another (Angry Reaction) which measured the tendency to express anger when criticized or treated unfairly. Validation studies have indicated State Anger and Trait Anger are

highly valid and reliable measures (Spielberger, 1988). Three additional scales were utilized to determine the expression of anger: Anger-In, defined as suppressed anger, Anger-Out, defined as anger expressed outward, and Anger Control, defined as attempts to control anger. A fourth scale of the STAXI was intended to measure Anger Expression or the frequency of occurrence. Anger expression subscales reliabilities have been reported to range from 0.70 to 0.73 and validities from 0.22 to 0.52 (Knight, Chisholm, Paulin, & Waal-Manning, 1988).

Technicon H*1 Analyzer. (Technicon Instruments Corporation, 1985). The Technicon H*1 is an automated flow cytometer that provided complete blood counts and indexes of white blood cell enzymatic activity. Complete blood counts were performed to assay the general health of each subject. Results included an index of peroxidase activity of the white blood cells for each sample. The instrument also provided lymphocyte subset determination following manual preparation of blood samples.

Beckman Array Protein System. (Beckman-Dickinson Diagnostics, 1989). The Array Protein system is a rate nephalometer and was used to determine immunoglobulin levels (IgM, IgG, and IgA).

Immunological Indexes. The Cell-Mediated Index was created from absolute values of total lymphocytes, absolute values and percentages of total T-lymphocytes, suppressor-T lymphocytes, helper-T lymphocytes, and the ratio of helper-T to suppressor-T lymphocytes to indicate the general status of the cellular immune

system. The Humoral Index was created from white blood cell peroxidase activity, absolute values and percentages of B lymphocytes, and immunoglobulin levels (IgG, IgA, and IgM) to reflect the general status of the humoral immune system. Various ranges for each parameter were assigned a numerical value in ascending order to reflect their desirability for immunological health (low numbers being low desirability, higher numbers being more optimal). Addition of values resulted in two immune indexes for each subject; the higher the numbers reflecting more immunocompetence. The cut-offs for assignment of scaled scores for individual immune parameters may be seen in Appendices A and B.

Procedure

All subjects were administered the CAQ and STAXI according to standard procedures. Three to four days later, early morning blood samples were drawn, including 5 ml in EDTA and 7 ml in a serum separator tube. All subjects were instructed to refrain from taking medications or consuming alcohol for 24 hours prior to blood sampling. Samples were transported and complete blood counts and lymphocyte subset assays were begun within four hours of collection. Blood samples for immunoglobulin assays were centrifuged and the serum removed and frozen at -70°C for later testing.

Complete Blood Counts with Differential and Peroxidase Index. Following confirmation of instrument reliability, each sample was adequately mixed and aspirated through the Technicon H*1 Analyzer according to standard techniques (Technicon Instruments

Corporation, 1985), producing complete blood counts and an index of white blood cell peroxidase activity. All subjects included in the analysis fell within the normal range for white blood cell counts, thus ruling out the presence of infection.

Lymphocyte Analysis. For the enumeration of B cells, total T cells and their subtypes, suppressor-T and helper-T cells, each blood sample was prepared manually prior to aspiration and assayed according to standard techniques (Hickey & Gannon, 1987, Technicon Instruments Corporation, 1989).

Immunoglobulin Analysis. Prior to analysis, each sample was allowed to thaw to room temperature and thoroughly mixed. Instrument reliability was confirmed and samples were assayed according to standard techniques (Beckman-Dickinson Diagnostics, 1989).

Results

Data were analyzed by Pearson product moment correlation and t-test. Analyses were performed for males and females, $n = 40$ and 35 respectively. Descriptive information was calculated for psychological data (see Table 1) and immunological scaled scores (see Table 2).

The Cell-Mediated Immunological Index ranged from 20 to 32 for males and from 15 to 32 for females. The Humoral Immunological Index ranged from 1 to 25 for males and from 8 to 25 for females. Comparison by t-test revealed no differences in Cell-Meditated nor Humoral Immunological Indexes between males and females (see Table 3).

For the female group, results indicated that a significant relationship exists between Trait Anger and the Cell-Mediated Immunological Index, $r(35) = .35$, $p < .05$. No significant correlation was found for any anger condition with either index for the males (see Table 4).

No significant correlation was found for depression conditions with either index for the females. For the males, results indicated a significant relationship between Anxious Depression and the Humoral Index, $r(36) = -0.38$, $p < .05$ (see Table 5).

Table 1

Mean Scores and Standard Deviations for Psychological Data

	Total		Males		Females	
	Mean	SD	Mean	SD	Mean	SD
Anger						
State	53.75	8.67	55.39	7.16	52.06	10.15
Trait	52.41	11.19	53.79	10.20	50.40	12.27
Temperament	54.78	10.06	55.71	8.87	53.26	11.35
Reaction	51.05	10.57	50.89	9.54	50.94	11.98
In	54.38	10.07	53.66	9.37	54.77	10.08
Out	53.65	11.21	54.87	9.21	51.60	12.89
Control	48.40	13.01	43.76	13.95	53.00	10.48
Expression	52.36	14.05	57.95	12.56	45.74	13.10
Depression						
Agitated	11.61	3.99	12.76	3.62	10.41	3.79
Anxious	7.33	4.05	6.42	3.57	8.02	4.26
Low Energy	7.78	6.19	6.90	5.44	8.64	6.87
Guilt and Resentment	6.90	5.59	5.37	4.72	8.31	6.06
Boredom and Withdrawal	4.60	3.79	4.37	2.95	4.87	4.59

Table 2

Mean Scores and Standard Deviations for Immunological Scaled Scores

	Total		Males		Females	
	Mean	SD	Mean	SD	Mean	SD
Cell-Mediated						
Total Lymphocytes*	2.85	1.52	3.03	1.37	2.73	1.59
T-cells*	2.94	1.52	3.05	1.36	2.90	1.61
Suppressor T-cells*	2.99	1.52	3.10	1.39	2.95	1.58
Helper T-cells*	3.25	1.50	3.48	1.28	3.13	1.59
HS Ratio	2.33	1.44	2.60	1.46	2.13	1.38
T-cells (%)	3.04	1.48	3.05	1.32	3.00	1.62
Suppressor T-cells(%)	2.82	1.72	3.10	1.57	2.60	1.81
Helper T-cells(%)	3.28	1.46	3.40	1.34	3.18	1.57
Humoral						
B-Cells*	3.21	1.52	3.35	1.37	3.18	1.58
B-Cells(%)	2.98	1.73	2.90	1.77	3.13	1.65
IgG	3.26	1.50	3.45	1.36	3.10	1.61
IgM	3.31	1.49	3.50	1.34	3.15	1.61
IgA	3.31	1.50	3.45	1.36	3.20	1.62
MPXI	3.21	1.62	3.20	1.45	3.20	1.77

*absolute concentration (μL)

Table 3

Mean Scores, Standard Deviations, and t-Values for Cell-Mediated and Humoral Immunological Indexes

Immunological Index	Males		Females		
	Mean	SD	Mean	SD	t-value
Cell-Mediated	24.80	9.24	22.60	11.39	1.52
Humoral	19.85	7.10	18.95	9.25	1.70

Table 4

Correlation of Anger Scores and Immunological Indexes

	Cell-Mediated Index		Humoral Index	
	Males	Females	Males	Females
State Anger	0.03	0.09	-0.03	-0.07
Trait Anger	-0.14	0.35*	-0.18	0.27
Angry Temperament	-0.12	0.28	-0.20	0.13
Angry Reaction	-0.02	0.29	0.02	0.22
Anger In	0.04	0.28	0.03	0.22
Anger Out	0.03	0.24	-0.09	0.08
Anger Control	0.01	-0.06	0.03	-0.05
Anger Expression	0.03	0.28	-0.02	0.16

*p < .05 (two-tailed)

Table 5

Correlation of Depression Scores and Immunological Indexes

	Cell-Mediated Index		Humoral Index	
	Males	Females	Males	Females
Agitated Depression	0.19	-0.18	0.14	-0.21
Anxious Depression	-0.30	0.06	-0.38*	-0.01
Low Energy Depression	0.07	0.20	-0.05	0.17
Guilt and Resentment	-0.13	0.21	-0.19	0.16
Boredom and Withdrawal	-0.20	0.21	-0.28	0.19

*p < .05 (two-tailed)

Results of raw correlations of individual immunological scaled scores with anger and depression may be seen in Appendices C and D respectively.

Discussion

Firm support was found for the third hypothesis, indicating that men and women differ in immune-emotion relationships. It appears that depression and anger have different implications with males and females for immunological competence. For females, immune-emotion interactions appear to be more intricately connected to anger conditions, while depression seems to have a more significant relationship for males. It is possible that males and females differ intrinsically in physiological responding to negative emotional states. This may be related to inherent differences in sex-related hormonal status which might predispose males and females toward distinct psychophysiological interactions. It may also be possible that through psychological processes, particular emotional states tend to provide separate cognitive representations for males and females. These might underly self-efficacy and coping beliefs which then interact at a neurochemical level during the experience of anger and depression, with distinct outcomes for men and women in psychoneuroimmunological relationships. Thus, differences in biochemical responsiveness could potentially influence particular immune parameters via receptor sites on cells.

Results indicate that males and females tend to differ in types of general immune processes associated with anger and depression. For females, immune-emotion interactions appear to involve the cell-mediated branch of the immune system, while humoral immune processes seem more involved for males. For the females, the Cell-Mediated Index appears to be significantly related to Trait Anger,

which represents a general tendency to respond with anger over a wide variety of situations. The percent of females who significantly elevated the Trait Anger scale, however, was relatively small, so that scores falling within the upper ranges of the sample may also represent women who perceive themselves more characteristically assertive than necessarily angry. For these women, it appears that this personality trait is influential in upgrading cell-mediated immune status. It may be that an ability to effectively anticipate and respond to anger-provoking situations is beneficial toward processes necessary for appropriate regulation of the entire immune system. This could represent an adaptive readiness, mediated through psychoneuroimmunological processes, to defend against potential assaults from the environment.

These results have particular implications for passive, unassertive women and for those who are unable to characteristically respond with anger in an ego-syntonic manner. Such females may be diminishing cell-mediated immune status and thus could potentially be placed at risk for disorders related to disruption of this system. This may include autoimmune-type illnesses such as rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis, but could potentially influence the ability of the humoral system to respond effectively to various types of infectious processes. Thus, perceived ability to readily and effectively respond to threat and conflict with minimal anxiety or negative self-attribution may play an important role in

mediation of anger and immune system readiness. Future research should address the role of other cognitive processes in immune-emotion interactions.

Other anger conditions, including the manner of anger responding, do not appear associated with cell-mediated immune status for women. It may be that although particular paramaters could be related in isolation to various types of anger, such changes are not remarkable enough to significantly alter overall immune status. There may also be additional influences from such variables as timing, duration, intensity, and frequency of emotional responding on immunological processes, which should be considered in future investigations.

For the males, the Humoral Index appears to be significantly related to Anxious Depression, which represents a depressive state that has components of shakiness, confusion, nervousness, low self-confidence, and diminished coping. For these men, it seems that as this state of depression intensifies, the ability of the humoral immune system to provide appropriate surveillance and effective defense against biological incitants is potentially diminished. Thus, depressed males who exhibit associated feelings of anxiety may be at risk for a variety of infectious processes. This may be particularly significant for those with compromised immune systems, such as AIDS patients, who often experience profound depressive states with nervousness, confusion, and diminished coping and for whom minor illnesses potentially have significant health consequences. The effects of addressing

depressive symptomology, anxiety, and coping on general health status and symptom progression for these patients should be investigated.

Other depressive states do not appear associated with humoral immune status for men. Although these conditions might possibly be related to individual parameters of the humoral immune system, when taken as a whole, they do not appear significant enough to change general immune status. Neuroendocrine activity occurring during conditions of anxiety may be increased over other depressive states, so that higher levels of substances mediating immune processes are produced or are sustained over a longer period of time. It is also possible that different types of depression are subtly but distinctly represented neurochemically. The production of different neuropeptides during individual depressive states could differentially affect humoral immune parameters via receptor sites on cells. Additionally, other factors such as timing, duration, frequency, and intensity of emotional responding may influence which depressive conditions tend to significantly alter immunological processes, and should be taken into account in future research.

Results provide mixed support for the first two hypotheses. Anger and depressive states were expected to be associated with changes in both cell-mediated and humoral immune status. However, anger appears associated with only cell-mediated status and depression with only humoral status. This may be due to emotion-immune interactions that could be dependent on underlying

gender-related hormonal status. It may also be possible that receptor sites on individual components of these two systems differ enough so that even if neuroendocrine and neuropeptide responses were consistent for a particular negative emotion, only one branch of immune system functioning would be significantly altered. Additionally, other factors such as timing, duration, intensity, and frequency of a particular class of emotional experience may have differential effects on cell-mediated and humoral immunological processes and should be considered in future investigations. There may also be the need to further study emotionality in groups of patients with various types of medical disorders, as well as the effects of different psychotherapeutic approaches on the progression of particular disease states.

The implications of these results are relevant for all health-related fields, and underscore the importance of understanding patients and clients within a more holistic framework. Mental health workers need to become aware of the potential impact of negative emotional states for the physical well-being of clients. Based on this investigation, it appears advisable to moniter individual states of depression in relation to possible health risks, particularly for male clients. Lack of assertiveness or ability to appropriately express anger should similarly be addressed with female clients.

In general, client education regarding the relationship between emotions, immune system functioning, and general health should be routinely incorporated in treatment protocols. A thorough client and

family health history should be obtained as well, in order to become aware of potential risks and benefits of psychotherapy. Therapeutic approaches may need to be generally recommended for particular groups of patients as well.

For the physician, and others who work within the medical arena, an awareness of the psychological state of a patient needs to be maintained and monitered over the course of an illness. A thorough psychological history should be obtained in order to clarify those patients who may be more at risk. Physicians should readily recommend some form of psychotherapy when appropriate, and may need to routinely provide appropriate referrals for patients with certain medical disorders. Physicians should also inform patients of the potential risks of emotional difficulties and the possible benefits of emotional well-being, and encourage patients to discuss such needs.

In general, the results of this study add to the growing body of science that has been prolific in effectively supporting the validity of the field of psychoneuroimmunology. This investigation is unique, however, in that it effectively addresses criticisms of previous research in which negative emotionality has been associated with changes in particular parameters of immunological functioning without an indication of the cumulative effect of these changes on immune system status. Through the novel use of indexes representing multiple aspects of immunity, an indication of the general status of cell-mediated and humoral immune systems can be obtained, which better reflect the contribution of unique variability of individual parameters. Another possibility would be

to utilize a total index taking into account parameters from both cell-mediated and humoral immune systems; however, this was looked at within this study and appears to inaccurately represent contributions of changes in each toward overall immune status. Utilization of such an index would not provide adequate information as to the mediating influences of emotions on health and well-being.

This study also addresses the tendency of previous investigators to fail to account for possible differences in various conditions of anger and depression, as well as differences between males and females in immune-emotion relationships. One might also consider that individual combinations of psychological scales would make a difference in such relationships; however, many of these scales are highly intercorrelated, so that such analyses as multiple regressions are not warranted.

Interactionism between mind and body has been consistently demonstrated throughout the area of psychoneuroimmunology; however, it is becoming more evident that many of the criticisms directed toward the field are well-founded. Until research begins to respond to such challenges by creating new designs that address these and related issues, the goal of incorporation of underlying principles and their implications within the general health care system may remain elusive.

APPENDIX A

RATINGS FOR CELL-MEDIATED IMMUNOLOGICAL INDEX

APPENDIX A

RATINGS FOR CELL-MEDIATED IMMUNOLOGICAL INDEX

	1	2	3	4
Total Lymphocytes*	<1200 >10,000	1200-1500 5000.0-10,000	1500-1800 4000-5000	1800-4000
Total T-cells*	<791.5 >8700.5	791.5 - 990.6 4350.9-8700.5	990.6-1188.6 3480.9-4350.9	1188.6-3480.9
Suppressor T-cells*	<155.5 >4000.5	155.5 - 195.1 2000.3-4000.5	195.1 - 234.1 1600.4-2000.3	234.1-1600.4
Helper T-cells*	<323.5 >5800.5	323.5 - 405.3 2900.6-5800.5	405.3 - 486.3 2320.6-2900.6	486.3-2320.6
HS-Ratio	< 0.41 >3.30	0.41-0.63 3.06-3.30	0.64-1.45 2.25-3.06	1.45-2.25
Total T-cells (%)	>22 >96	22-44 92-96	44-65 88-92	65-87
Suppressor T-cells (%)	<5 >80	5-10 60-80	10-13 40-60	13-40
Helper T-cells (%)	<9 >86	9-18 72-86	18-26 58-72	26-58

*absolute concentration (μL)

APPENDIX B

RATINGS FOR HUMORAL IMMUNOLOGICAL INDEX

APPENDIX B

RATINGS FOR HUMORAL IMMUNOLOGICAL INDEX

	1	2	3	4
B-Cell*	<47.5 1600.5	47.5 - 60.0 800.2-1600.5	60.0 - 72.0 640.2-800.2	72.0-640.2
B-Cell (%)	<2 >73	2-4 45-72	16-45	4-16
IgG**	>5000	<538 1700-5000	538 - 600 1381-1700	600-1381
IgM**	>1000	<40 300-1000	40 - 50 272-300	50-272
IgA**	>1000	<40 450-1000	40 - 44 360-450	44-360

*absolute concentration (μL)

**mg/dL

	1	2	3	4	5	6	7
MPXI	<-25.4	-25.4--19.3	-19.3--13.3	-13.3--1.2	-1.2-4.8	4.8-10.9	>10.9

APPENDIX C
CORRELATION OF PSYCHOLOGICAL SCORES AND CELL-MEDIATED SCORES

APPENDIX C

CORRELATION OF PSYCHOLOGICAL SCORES AND CELL-MEDIATED SCALED SCORES

All Subjects

	Total Lymphs	Total T	Sup T	Help T	HS Ratio	Total T(%)	Sup (%)	Help (%)
Anger								
State	0.08	0.08	-0.01	-0.03	-0.02	0.11	0.15	0.13
Trait	0.09	0.12	0.06	0.11	0.17	0.01	0.12	0.00
Temperament	0.07	0.05	-0.03	0.02	0.07	0.13	0.13	0.09
Reaction	0.11	0.14	0.11	0.13	0.15	-0.02	0.12	0.03
In	0.14	0.04	0.02	0.14	0.13	0.02	-0.02	0.04
Out	0.09	0.10	0.01	0.03	0.06	0.09	0.22	0.11
Control	-0.09	-0.05	0.02	-0.04	-0.12	-0.05	-0.11	-0.01
Expression	0.14	0.08	-0.01	0.07	0.14	0.11	0.16	0.10
Depression								
Agitated	-0.00	-0.07	-0.08	-0.06	0.04	-0.07	0.01	-0.06
Anxious	-0.13	-0.16	-0.14	-0.07	0.07	-0.17	-0.02	-0.13
Low Energy	0.06	0.06	0.07	0.06	0.21	0.07	0.09	0.06
Guilt and Resentment	-0.02	0.03	-0.00	-0.02	0.08	0.07	0.04	0.03
Boredom and Withdrawal	0.00	0.03	0.06	0.09	0.14	0.06	0.03	0.08

Males

	Total Lymphs	Total T	Sup T	Help T	HS Ratio	Total T(%)	Sup (%)	Help (%)
Anger								
State	0.05	0.15	0.05	-0.05	0.01	0.00	-0.01	0.00
Trait	-0.15	-0.06	-0.18	-0.18	-0.01	-0.16	-0.10	-0.10
Temperament	-0.10	-0.06	-0.18	-0.17	-0.03	-0.06	-0.09	-0.12
Reaction	-0.02	0.04	-0.04	-0.03	0.05	-0.14	0.04	-0.01
In	0.11	-0.06	-0.11	-0.04	0.15	0.09	-0.02	0.13
Out	-0.00	0.10	-0.03	-0.01	0.09	0.00	0.01	0.08
Control	-0.03	-0.02	0.09	0.06	-0.01	-0.07	0.01	0.03
Expression	0.07	0.04	-0.11	-0.04	0.07	0.13	-0.01	0.08
Depression								
Agitated	0.25	0.18	0.17	0.10	0.24	0.11	0.12	0.13
Anxious	-0.27	-0.37*	-0.37*	-0.37*	0.06	-0.32*	-0.17	-0.23
Low Energy	0.08	-0.04	0.05	-0.08	0.29	-0.03	0.14	0.03
Guilt and Resentment	-0.13	-0.20	-0.18	-0.27	0.07	-0.10	-0.03	-0.07
Boredom and Withdrawal	-0.25	-0.33*	-0.15	-0.22	0.08	-0.27	-0.10	-0.14

* $p < .05$

Females

	Total Lymphs	Total T	Sup T	Help T	HS Ratio	Total T(%)	Sup (%)	Help (%)
Anger								
State	0.09	0.03	-0.04	-0.05	-0.07	0.19	0.22	0.22
Trait	0.33*	0.33*	0.34*	0.39*	0.44*	0.21	0.31	0.15
Temperament	0.23	0.19	0.13	0.19	0.24	0.32	0.33*	0.31
Reaction	0.28	0.29	0.31	0.33*	0.33*	0.13	0.25	0.12
In	0.36*	0.31	0.33*	0.31	0.22	0.14	0.16	0.15
Out	0.21	0.16	0.12	0.12	0.13	0.23	0.41*	0.23
Control	-0.06	-0.01	0.00	-0.04	-0.18	-0.00	-0.15	0.04
Expression	0.28	0.22	0.19	0.21	0.22	0.24	0.37*	0.23
Depression								
Agitated	-0.17	-0.22	-0.24	-0.16	-0.11	-0.15	-0.09	-0.17
Anxious	0.03	0.01	0.07	0.03	0.14	-0.05	0.18	-0.00
Low Energy	0.13	0.20	0.16	0.24	0.22	0.20	0.15	0.16
Guilt and Resentment	0.13	0.23	0.18	0.22	0.17	0.23	0.19	0.17
Boredom and Withdrawal	0.13	0.21	0.16	0.25	0.18	0.22	0.11	0.19

*p < .05

APPENDIX D

CORRELATION OF PSYCHOLOGICAL SCORES AND HUMORAL SCALED SCORES

APPENDIX D

CORRELATION OF PSYCHOLOGICAL SCORES AND HUMORAL SCALED SCORES

All Subjects

	Total B-cell	B-cell (%)	IgG	IgM	IgA	MPXI
Anger						
State	-0.04	0.19	-0.04	-0.02	-0.03	-0.16
Trait	0.04	0.07	0.04	0.06	0.05	-0.06
Temperament	-0.03	-0.04	-0.05	-0.02	-0.02	-0.06
Reaction	0.08	0.12	0.12	0.12	0.10	-0.05
In	0.15	0.17	-0.02	0.04	0.07	-0.08
Out	-0.05	-0.05	-0.02	-0.01	-0.02	-0.06
Control	-0.03	-0.04	-0.04	-0.05	-0.05	-0.09
Expression	0.01	0.02	0.02	0.05	0.06	-0.04
Depression						
Agitated	-0.03	-0.04	-0.15	-0.11	-0.12	-0.06
Anxious	-0.20	0.00	-0.20	-0.18	-0.16	-0.19
Low Energy	0.06	0.18	-0.01	0.03	0.04	-0.03
Guilt and Resentment	-0.01	0.16	-0.10	-0.05	-0.04	-0.00
Boredom and Withdrawal	0.05	0.18	-0.05	-0.00	-0.01	0.03

Males

	Total B-cell	B-cell (%)	IgG	IgM	IgA	MPXI
Anger						
State	-0.04	0.15	0.01	-0.01	-0.01	-0.27
Trait	-0.20	-0.06	-0.10	-0.13	-0.12	-0.25
Temperament	-0.21	-0.11	-0.19	-0.19	-0.14	-0.16
Reaction	-0.06	0.04	0.13	0.10	0.09	-0.20
In	-0.05	0.17	0.13	0.16	0.13	-0.21
Out	-0.15	-0.01	-0.05	-0.10	-0.08	-0.09
Control	0.06	0.04	0.10	0.09	0.05	-0.19
Expression	-0.07	0.07	-0.05	-0.04	0.03	-0.05
Depression						
Agitated	0.26	0.24	-0.06	-0.03	-0.01	0.25
Anxious	-0.34*	-0.06	-0.40**	-0.37*	-0.33*	-0.44**
Low Energy	-0.06	0.14	-0.09	-0.07	-0.03	-0.17
Guilt and Resentment	-0.24	0.02	-0.28	-0.22	-0.18	-0.09
Boredom and Withdrawal	-0.32*	0.04	-0.32*	-0.35*	-0.33*	-0.19

*$p < .05$, **$p < .01$

Females

	Total B-cell	B-cell (%)	IgG	IgM	IgA	MPXI
Anger						
State	-0.06	-0.05	-0.10	-0.06	-0.07	-0.07
Trait	0.30	0.34*	0.21	0.26	0.23	0.17
Temperament	0.16	0.14	0.09	0.13	0.12	0.07
Reaction	0.26	0.29	0.18	0.21	0.19	0.12
In	0.27	0.26	0.13	0.21	0.20	0.19
Out	0.09	0.07	0.06	0.10	0.09	0.05
Control	-0.06	0.02	-0.08	-0.10	-0.08	0.00
Expression	0.17	0.14	0.13	0.19	0.17	0.12
Depression						
Agitated	-0.21	-0.12	-0.23	-0.21	-0.18	-0.23
Anxious	-0.07	0.00	-0.00	0.03	0.02	-0.00
Low Energy	0.21	0.22	0.11	0.18	0.15	0.10
Guilt and Resentment	0.21	0.24	0.09	0.15	0.12	0.09
Boredom and Withdrawal	0.25	0.25	0.09	0.18	0.15	0.13

*p < .05

APPENDIX E

INFORMED CONSENT

APPENDIX E

INFORMED CONSENT

I, _____ wish to participate in a research project being conducted under the supervision of Dr. J. R. Butler. I understand that the primary purpose of this research is to demonstrate the existence or nonexistence of a relationship between certain psychological factors (e.g., hostility, tension, etc.), various immune system parameters, and endocrinological functions. I understand that all blood will be drawn by a trained phlebotomist and that J. R. Toledo, M.D., or other licensed physician, will provide medical supervision. I understand that I will be required to take paper and pencil psychological tests 3 or 4 days prior to the blood sample being taken.

I understand that all test results, both psychological and biological, will be coded to ensure confidentiality and that feedback will be provided upon completion of the study. I understand that my participation in this study is completely voluntary and that I may withdraw at any time without jeopardy. I understand that the investigator may drop me from the study as long as this action is not detrimental to me.

I, _____, hereby release the University of North Texas, the Department of Psychology, and the Psychology Clinic from all claims, demands, damages, actions, or causes of action, costs, loss of services and expenses resulting from research that will include blood draws to be taken to measure immune system parameters and endocrinological functions and the administration of psychological questionnaires. It is understood that I may withdraw from participation in this research at any time.

This research project has been fully explained to me and I have read and fully understood this agreement. Therefore, I voluntarily agreed to participate in this research project.

Signed _____

Participant

Signed _____

Witness

Date _____

APPENDIX F

HEALTH INVENTORY

APPENDIX F

HEALTH INVENTORY

Name__(ID number)_____ Today's date_____

Address_____

Residence Phone no._____

Business/other phone_____

Date of birth_____ Sex_____ Race_____

Marital Status_____ Other employment_____

Where employed_____

Program at UNT_____ Do you feel any pronounced stress at this time?_____ If yes, describe the nature of the stress: _____

_____

Do you consider yourself generally optimistic__pessimistic__

What are your primary foods and drink (please list)_____

_____

Do you take nutritional supplements? List them. How often? How much?_____

_____

How much do you exercise? Daily? Weekly?_____

Describe the exercise_____

_____

Average number of drinks daily_____ Weekly_____

Do not drink alcohol at all_____ (no alcohol is permitted 24 hours before blood samples are taken). What is your height?_____Weight?_____

Last taken blood pressure_____/_____

Have you ever had: Anaphylaxis_____ Arthritis_____

Emphysema_____ Paralysis_____ Peptic ulcer_____

Stroke_____ Tuberculosis_____ Convulsions_____

Diabetes_____ Heart attack_____ Severe dizzy spells____

High blood pressure_____ Laryngeal edema_____

Loss of consciousness_____ Psychiatric care_____

Pneumonia_____ Severe reactions to allergy tests or allergy injections_____ What is the worst allergic reaction you have ever had?_____

Have you ever had a severe exposure to chemicals, for example, to pesticides?_____ If so describe. When, Where, etc._____

_____

Are you chronically being exposed to any chemicals now? ___

If so, describe_____

_____

Drug History

Check drugs taken on a regular basis:

Cortisone_____Phenobarbital_____Tranquilizers_____

Penicillin_____Demerol_____Digitalis_____

Marijuana_____Sleeping Pills_____Sulfa Drugs_____

Insulin_____Street Drugs_____Paregoric_____

Nose Drops_____Mycin Drugs_____A.C.T.H._____

Hormones_____Aspirin_____Antihistamines_____

Adrenalin_____Tylenol_____Dilantin_____

Cough Medicine_____Blood Pressure Med___Laxatives_____

Antibiotics_____Codeine_____Birth Control Pills_____

Metaprel_____Susphrine_____Alupent_____

Brondecon_____Decadron_____Potassium Iodine_____

Theokin_____Aminodur_____Bronkephrine_____

Deconamine_____Theophylline_____Aminophyllin_____

Bronkodyl_____Elixophyllin_____Vanceril_____

Verequad_____Bronkometer_____Ephedrine_____

Aerosols_____Prednisone_____

Others_____

_____

Do you require: normal___ low____high___doses of drugs as a rule? Explain_____

Do you require frequent use of antibiotics? Yes___No___

Which_____

Do you get colds or other upper respiratory ailments frequently? Explain_____

Indicate your choice of day and time when you would be able to take part in this study.

First choice: Day_____Time:_____

2nd choice: Day_____Time:_____

3rd choice: Day_____Time:_____

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