Psychosocial Predictors of Survival in Persons with HIV or AIDS

Carlos A. Escoto

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Psychosocial Predictors of Survival in Persons with HIV or AIDS

by

Carlos A. Escoto

A Dissertation submitted in partial satisfaction of the requirements for the degree of Doctor of Philosophy in Psychology

December 2002
Each person whose signature appears below certifies that this dissertation in his/her opinion is adequate, in scope and quality, as a dissertation for the degree Doctor of Philosophy.

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ABSTRACT OF THE DISSERTATION

Psychosocial Predictors of Survival in Persons with HIV or AIDS

by

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Doctor of Philosophy, Graduate Program in Psychology
Loma Linda University, December 2002
Dr. Kiti Freier, Chairperson

The HIV pandemic is in its second decade of existence. HIV has distinguished itself by effecting every part of the globe. It is estimated that there are currently over 40 million people living with HIV or AIDS diagnoses in the world today. Great strides have been made in the treatment of HIV and AIDS. Combination therapy of drugs has been shown to keep viral replication at very low levels. The result of drug therapies has resulted in keeping persons with HIV from progression to full blown AIDS. Also, drug therapies are responsible for a significant drop in mortality rates from AIDS. However, persons with AIDS have a second medical issue that must be addressed, specifically the rebuilding of immune system. Both HIV and AIDS have a variable course in disease progression. The field of Psychoneuroimmunology proposes a mechanism by which psychosocial variables could impact immune function and may serve to exacerbate or be protective of disease.

The present study assessed the psychosocial variables (depression, stress and negative explanatory style) which research has shown to effect immune status. However, this study differs from other studies in that Hierarchical Linear Regression will be used to assess immune function as a mediating factor between psychosocial variables and survival. The mediational model was not supported. Results indicate that psychosocial
variables did not impact survival through the immune system in this sample of persons with HIV and AIDS. Only measures of immunity were shown to impact survival.
Psychosocial Predictors of Survival in Persons with HIV or AIDS

HIV/AIDS

Acquired Immunodeficiency Syndrome (AIDS) was first discovered in 1981. The search for the cause of AIDS; led to the discovery of the human immunodeficiency virus (HIV). HIV falls under the classification of a retrovirus. Like other viruses, HIV relies on a host cell for replication. However, HIV has in its' nucleus, viral RNA. Other viruses, have viral DNA in their nucleus. HIV incorporates its genes into the host cell or T-helper cells. The T-helper cell is forced to create new particles of viral RNA for packaging of new virus, until the T-cell eventually dies. The destruction of T-helper cells below 200 per cubic milliliter, results in what is estimated to be 70% immune damage. The destruction of the immune system to this point results in the diagnosis of AIDS. The destruction of T-helper cells also leaves the person infected vulnerable to opportunistic infections, which can ultimately lead to death.

Recent research has shown that HIV was present in the African continent as early as the 1940's. Research has also shown that HIV could be a genetic relative to SIV or simian immunodeficiency virus. SIV could have been transmitted to humans through the ingestion of meat from simians, or exposure to their blood in during hunting.

The AIDS epidemic is now in its third decade of existence. In the past 18 years, AIDS has distinguished itself as a worldwide epidemic or pandemic. The UNAIDS Report (1999) estimates that there are 33.6 million people currently living with HIV or AIDS worldwide.

Thirty-two million of the total number of HIV/AIDS cases are adults, 14.8 million are women and 1.2 million are children. To date there have been 16.3 million deaths
worldwide due to AIDS. In 1999 alone, 5.6 million persons were newly infected and 2.6 million persons died from AIDS.

In this country, The Centers for Disease Control (CDC) reports that 1.5 million Americans are currently infected with HIV. Further, over half a million persons are now diagnosed with AIDS (CDC, 1999). To date, over 300,000 Americans have died of AIDS. AIDS is now a leading cause of death for men and women ages 20-45. As AIDS has permeated every corner of the globe, so too is it affecting every state in this country. However, AIDS is disproportionately represented in large metropolitan areas as well as in minority groups. African-Americans have a death rate 10 times greater than whites (CDC, 1999).

The prognosis for persons diagnosed with HIV has changed substantially within the past few years. A combination of drugs has been shown to keep the human immunodeficiency virus from at very low levels in the blood. This is hoped to keep the virus from progressing and depleting the immune system, specifically T4 helper cells. The CDC has recently reported a 20% drop in mortality in deaths from AIDS between 1997 and 1998 (CDC, 1999). The drop in mortality rates from AIDS is attributable to the new combination of drug treatments available. However, given the viruses ability to mutate coupled with a high rate of replication, caution must be exercised when reviewing these statistics (Baker, 1997). Clearly, HIV can be kept from replicating in persons newly diagnosed. However, in persons with full blown AIDS a second problem must be addressed; how to rebuild the immune system. Persons who meet the CDC definition of AIDS have under 200 T-cells which equates roughly to 70% immune damage.
Given the gravity of the current AIDS pandemic and the grim estimates for the future of this disease: it is surprising that there is very little data available regarding the psychological aspects of HIV and AIDS, including prevention and treatment. In 1992 the authors of "AIDS in the World" reported that a Medline search showed that only 10% of all research published since the beginning of the pandemic focuses on psychology's impact on all facets of the pandemic (Mann, Tarantola & Netter, 1992). The fact that HIV is primarily a behavior driven illness establishes the need for psychology's contribution to prevention and treatment research. The lack of research on HIV and AIDS has been recognized by the American Psychological Association (APA). A special committee of APA recommended that psychologists take a more active role in the prevention and treatment of HIV/AIDS. The committee estimated that research in the area of behavioral modification could cut the number of new HIV infections in half (Michaelson, 1993). Kelly, Murphy, Sikkema and Kalichman (1993) noted that as behavior change is the only method for prevention of new HIV infections, psychology should take a leading role in prevention efforts. However, psychology’s response has not been proportionate to the severity of this health crisis. In particular, outcome studies and collaborations between community based organizations could drastically change the face of the pandemic. Given the lack of a successful preventative vaccine, psychology's contribution to the AIDS pandemic could be substantial.

Even less research is being conducted on the psychological effects of a diagnosis of HIV or AIDS. As Kelly & Murphy (1992) point out, it will prove to be essential to identify the different coping needs of the varied groups of persons effected by HIV/AIDS; so as to develop specific interventions to help persons infected with HIV
cope and potentially ameliorate disease progression. Developing gender and culturally specific psychological interventions is needed to address the pressing needs of persons with HIV/AIDS. However, research is also needed to understand more clearly the psychological sequelae of HIV infection prior to developing interventions. As has been shown with other illness understanding the psychological effects of a medical diagnosis can assist in bettering patient compliance and alerting the primary physician to potential problems with substance abuse or suicidal ideation.

Researchers suggest that psychologists should focus on the development of strategies to promote adherence to the potentially complicated HIV/AIDS drug regimens (Kelly, Otto-Salaj, Sikkema, Pinkerton & Bloom, 1998; Rabkin & Ferrando, 1997). The authors also suggest that understanding how people cope with HIV/AIDS is vital. Psychologists could intervene not only when persons are newly diagnosed but also when new drug therapies bring them back to relatively good health after periods of serious illness. Closely tied to the issue of adherence is the need to focus on psychological treatment of continued risk behavior. If persons with HIV/AIDS who are on drug therapies have unprotected sex with a drug naive HIV/AIDS infected person; they risk infecting their partner with their own strain of virus, which carries its own mutations and possible resistance to drugs. Lastly, Kelly et al. (1998) state the need for behavioral research in prevention and care policy areas.

Clearly, psychology's contribution to prevent new infections of HIV as well as ameliorating the prognosis of persons diagnosed with HIV or AIDS could be substantial. Psychology continues to search for venues where it can show that its treatments are efficacious and the HIV/AIDS pandemic offers the opportunity of such an examination
on a global scale. The face of HIV/AIDS has changed dramatically. Along with these changes is the opportunity for psychology to contribute to the well being of those diagnosed with HIV/AIDS (Kelly et al, 1998) and the pandemic overall.

As Ferrando (1998) states "it is incumbent on those of us in the behavioral sciences to continue efforts toward keeping pace and integrating more fully with accelerating medical advances." Research and training are inextricably tied. Without basic research, training of emerging psychologists will be unaffected and the net amount of research will remain static. It is reasonable to believe that a lack of training at the graduate school level is impacting the amount of research being conducted on HIV/AIDS. Campos, Brasfield and Kelly (1987) conducted a survey of APA accredited graduate programs regarding HIV and AIDS training in 1987. The survey showed that 75% of the responding graduate programs’ curricula did not cover HIV/AIDS. Further, the authors found that other key areas where HIV/AIDS information could be provided were also deficient. For example, 51% of the responding programs did not offer any courses on human sexuality.

Pingitore and Morrison (1993) reassessed AIDS-related academic and clinical activities in 1989. The authors concluded that psychology programs were engaged in many AIDS-related activities. Furthermore, the authors stated that psychology departments were successful in establishing cooperative relationships with hospitals for AIDS-related training activities. It should be noted however that this study's findings are not directly comparable with the study conducted by Campos, Brasfield and Kelly (1989). Pingitore and Morrissjon used a different survey form than the Campos et al (1989) study. Also, the information gathered was divergent enough from the original
study to warrant an additional investigation. More importantly, Pingitore and Morrison’s study assessed change only two years after the Campos et al. study (1989), which is a very narrow window.

In 1997, APA surveyed graduate teaching faculty who offer HIV-related courses in various areas of psychology (Anderson, J., Campos, P. & Hamid, G., 1998). As with the previous study (Campos et al., 1989), only a small percentage (14%) of courses had HIV/AIDS as their primary focus. HIV/AIDS information was provided by approximately 54% of the respondents as part of other courses such as clinical or counseling psychology, health psychology, social psychology and human sexuality.

Similar findings have been reported in other clinical fields. Diaz & Kelly (1991) surveyed social work programs using the same instrument used by Campos et al. (1989). The authors reported that 65% of the responding programs provided HIV/AIDS training as part of another course or colloquia. Likewise, Hunt (1996) assessed counseling education programs. Fifty-one percent reported using colloquia to provide HIV/AIDS information. What should be noted is that previous research has focused on clinical and counseling graduate programs. Experimental graduate programs also are responsible for conducting research that encompasses the area of HIV and AIDS.

Research has consistently demonstrated that training on HIV/AIDS is an issue that needs to be addressed (Campos et al., 1987; Pingitore & Morris; Diaz et. el. 1991; Hunt, 1996). Escoto (in press) conducted a replication of the Campos et. al. study and found that reassessment results indicate that in general, HIV/AIDS training is now present in approximately one half of all programs surveyed and that AIDS prevention course coverage has increased. While 31% of the programs surveyed offered no training
regarding HIV/AIDS, this is a substantial improvement over the 75% of graduate programs that offered no training regarding HIV/AIDS in 1987. There are several other training issues to address. While, there are a greater number of students currently involved in HIV/AIDS research, the number of faculty involved in HIV/AIDS-related research and clinical activities has not increased. The dearth of faculty members involved in training opportunities is of continued concern. Active recruitment of faculty interested in HIV/AIDS research and teaching is necessary for continued training and service enhancement for HIV/AIDS treatment and/or HIV prevention (1991; Diaz & Kelly, 1991; Hunt, 1996; Anderson et al., 1998).

Chronic illnesses by definition are “long term illnesses which typically cannot be cured but rather managed” (Taylor, 1999). Acute and chronic disease both have a temporary adjustment phase where normal functioning is affected. However, chronic diseases sometimes also require making other adjustments either personally, vocationally and socially to cope with disease course (Taylor, 1999). As chronic illnesses impact patient functioning and require adjustment to the “patient” role, psychopathology can result. Research has shown that there is a 15% to 33% comorbidity rate between medical and psychological diagnoses (Baum, Gatchel & Krantz, 1997).

In general, very little research has focused on psychological assessment in the HIV and AIDS population. Of the research that has been conducted on the psychological manifestations of HIV/AIDS, the majority has focused on organic neurological problems. Some studies have reported delusions and hallucinations (Alciati, 2001) and mania (El-Mallakh, 1991). Other studies have found neuropathy, dementia, and other cognitive deficits in persons with HIV and AIDS. The organic problems reported in this population
could be explained by atrophy seen in the brains of persons with HIV and AIDS (Maj, 1990).

A potential explanation for the lack of research on the psychological effects of HIV could be the classification of HIV and AIDS as similar to other chronic illnesses. It has been proposed that since cancer and HIV are both chronic illnesses, it could be expected that the same types of psychopathologies could be found in both populations. Specifically, depression, dysthymia and anxiety could be anticipated in both cancer and HIV patients (Michels & Marzuk, 1993). While it may be argued that this hypothesis is reasonable, there are obvious differences in the social stigma and perceptions associated with both diseases.

Maj (1990) described an acute stress reaction that occurs with initial diagnosis of HIV but that also coincides with changes in the individual’s clinical state. Further, depression, other mood disorders and adjustment disorder are reported by Maj as the most common diagnoses in persons with HIV and AIDS. These findings have been corroborated by other studies. For example, depression, anxiety and adjustment disorder with depressed mood were reported as frequent diagnoses by Kim and Rickman (1988). Another study identified depression as the most prevalent psychiatric disorder in hospitalized HIV and AIDS patients (Seth, Granville-Grossman, Goldmeier & Lynch, 1991). These published reports are predominately literature reviews with data collected from patient files. Clearly, generalizations from case study data are problematic.

However, there have been empirical studies which have also reported mood disorder as the most consistent diagnosis in HIV positive patients (McDaniel, Fowlie, Summerville, Farber and Cohen-Cole, 1995; Krikorian, Kay and Liang, 1995).
Of studies designed to evaluate the psychological effects of HIV, the majority have focused on brief instruments such as the Hamilton Depression and Anxiety scales and the Structured Clinical Interview for Diagnosis (SCID). A study conducted on HIV positive men in the military reported higher lifetime rates of major depression and alcohol use (Brown, Rundell, McManis, Kendall, Zachary & Temoshok, 1992). Of the 442 men in the study, 39% were diagnosed with an Axis I disorder. Twenty-two percent were diagnosed with sexual dysfunctions. Twenty-one percent were diagnosed with an Axis II disorder. The figures reported by Brown et al. (1992) are much higher than the levels of depression and anxiety reported by other studies (Maj, 1990; Kim et. al., 1998; Seth et. al. 1991). Perkins, Davidson, Leserman, Liao & Evans (1993) reported similar findings. Thirty-three percent of the sample of HIV positive participants were diagnosed with a personality disorder versus only 15% in the control group. However, the actual rates of specific personality disorders reported differ significantly from those reported by Brown et al. (1992).

Dew, Becker, Sanches, and Caldararo (1997) conducted a longitudinal study on psychopathology in HIV and AIDS patients. The authors concluded that despite no lifetime rates prior to baseline assessment, men with HIV were at greater risk for psychological disorders during the follow-up period. In a review article by Fishman and Lyketsos (1997), major depression and mania prevalence rates were reported to be elevated.

In contrast, other studies have shown no significant psychopathology in persons with HIV and AIDS. An Australian study found no psychological differences between an HIV-positive sample and a control group. More important, no differences were detected
between groups on age, educational level or state/trait anxiety or depression scores. Severity of anxiety and depression was related to the magnitude of symptomatology but not associated with degree of immunodeficiency. Interestingly, neither the symptoms reported, their duration, severity or frequency was significantly different between person with HIV, AIDS or ARC (AIDS Related Complex). These findings were replicated by Perry, Jacobsberg, Card, Ashman, Frances, & Fishman (1993). The authors concluded that HIV infection does not increase psychiatric morbidity. Elevated scores on the Hamilton Rating Scale for Depression, BDI (Beck Depression Inventory) and Spielberger State-Trait Anxiety Inventory were not predicted by HIV status but by socio-economic status. Similarly, Hays, Turner and Coates (1993) found that it was the degree of physical symptoms experienced from being HIV positive that predicted depression scores in a group of 508 gay men.

Chart reviews have also corroborated previous data (Sacks, Burton, Dermatis, Looser-Ott, Salome; et.al., 1995). These researchers concluded that the majority of HIV-related admissions were persons who were experiencing extreme psychological reactions to the risk of HIV infection. The second largest category of HIV-related admissions came from organic disorders. Further, HIV-related admissions had similar length of stay and levels of psychopathology at discharge compared to other non-HIV related admissions.

Michael King states in his book "AIDS, HIV and Mental Health" that the results on psychopathology are inconclusive (King, 1993). More research is required to substantiate the presence of, or the lack of psychopathology in persons with HIV or AIDS. More specifically, prospective studies and review articles would further serve to elucidate the presence of psychopathology in this population.
A prospective study was conducted using an HIV-negative control group and 112 HIV patients. Results did not show any significant increases in DSM-III-R diagnoses of depression or anxiety over a four-year period in the HIV positive men (Rabkin, Goetz, Remien, Williams, Todak & Gorman, 1997). The authors also reported that psychopathology did not predict mortality. However, there were differences between the HIV-positive and HIV-negative samples in overall depression and anxiety. The HIV-positive sample showed slightly higher anxiety and depressive symptoms throughout the study. Combs and Livingston (2001) examined psychopathology subtypes as measured by the Beck Depression Inventory, Life Orientation Scale, Rosenberg Self-Esteem Test and The Internal Control Index. Fifty-three HIV-positive men were placed into one of three groups based on a cluster analysis of their scores on the psychological assessments. Only 24% of the sample could be classified as "severely dysfunctional." Seventy-five percent of the sample (n = 40) fell into the average performing and highly adaptive subtypes. What should be noted is that 22% of the sample appeared to cope exceptionally well with their HIV diagnosis.

A review article reported that HIV status and stage of illness are not predictive of mood or anxiety disorders (Rabkin, 1996). Psychiatric disturbance was, however, related to a history of depression and membership in a "high risk group." Overall one-month prevalence rates for major depression were reported to be between 5% and 8%. While this figure is double that of the "normal" population it could be considered relatively low compared to others with life-threatening illness. Rabkin (1996) also reported in this review of the literature that the SCID was the most commonly used tool to identify psychopathology in persons with HIV or AIDS. Of the studies that have used pencil and
paper psychological assessments, the vast majority have used brief instruments such as the Beck or Hamilton Depression Scale.

Neither the MMPI nor the MMPI-2 were designed to be used in medical populations. However, the MMPI has much data supporting its usefulness in medical populations. Specifically the MMPI-2 screens patients for serious psychopathology, substance abuse problems, underlying personality, psychogenic versus organic pain, and indications of psychological response to medical treatment as well as the psychological effects of a medical diagnosis (Graham, 1990). For example, research has been conducted on breast cancer patients (Kirkcaldy & Kobylińska, 1989), chronic pain (Naliboff, Cohen & Yellen, 1983; Robinson, Greene & Geisser, 1994; Bombardier, Divine, Jordan, Brooks & Blair et.al, 1994) and chronic fatigue syndrome (Miller-Iger, 1992). The MMPI-2 has proven itself to be useful in identifying psychological states which could exacerbate treatment outcome.

Very few studies have been conducted in the HIV/AIDS populations using the MMPI or MMPI-2. In 1993, a Russian study reported the MMPI profiles for 24 HIV infected adults. Results showed that there was anxiety, tension and skepticism in this population (Reshetnikov et. al., 1991). The majority of other studies conducted using the MMPI-2 have been published in Dissertation Abstracts.

Escoto, Jacquin and Flowers (2002, under review) found that the majority of participants in their sample showed T-scores above 65 on at least one of the clinical scales of the MMPI-2. The average profile for male and female participants showed a code type of 7-8. Most participants (91.4% of males and 85.7% of females) showed elevations on these scales, suggesting that this code type may be used to describe this
Specifically, individuals with this code type are experiencing a significant amount of turbulence. They have psychological problems, including depression and anxiety. They may tend to ruminate about problems and have difficulties coping (Graham, 1990).

These results contradict previous reports that medical patients are no more likely than non-patient populations to show psychopathology (Graham, 1990; Rustad, 1985). However, the findings support several previous studies, such as those using the MMPI and MMPI-2 with chronically ill populations, which have found depression rates from 33% to 50% (Chang, Nesbit, Youngren & Robison, 1987; Kurman, Hursey & Mathew, 1992; Dworkin, 1990, Ahlls, 1986). Similarly, the results are consistent with previous research showing significant levels of depression and anxiety among HIV and AIDS patients (Kim & Rickman, 1988; Krikorian et al., 1995; Maj, 1990; McDaniel et al., 1995: Seth et al., 1991).

Previous research has reported psychological disorder prevalence rates of up to 33% in HIV and AIDS patient samples. Among the sample studied by Escoto et al. (under review), 98% had at least one elevation on clinical scales. Forty-two to 51% of the participants scored above the clinical norms on the "neurotic triad", specifically Scale 1 (Hysteria), Scale 2 (Depression) and Scale 3 (Hypochondriasis). Elevations on these three clinical scales are common in persons diagnosed with chronic illness.

Scores on the clinical scales of the MMPI-2 were significantly correlated with length of time of diagnosis, t-cell count, the number of opportunistic infections experienced and the number of medications taken. These findings support the inferences
of Hays et al. (1992), who concluded that psychopathology is a product of symptomatology versus the diagnosis itself.

A notable finding is the high Internal Locus of Control scores on the Multidimensional Health Locus of Control (MHLC-A) in comparison to persons with other chronic illness. The HIV and AIDS sample studied had a mean Internal Locus of Control score more similar to patients with diabetes (Wallston, Stein, & Smith, 1994). Internal locus of control has been shown to be related to increased levels of involvement in health care from the patient (Strickland, 1987). The sample studied also showed lower scores on the Powerful Others and Chance subscales of the MHLCA than those documented by Fontaine, McKenna and Cheskin (1997).

For persons with AIDS, other interventions must be investigated that could improve the prognosis of persons with substantial immune damage. One potential point of intervention lies in the area of psychoneuroimmunology (PNI). PNI points to the ability of psychological interventions to directly effect immunity. The severity and symptomatology seen at various stages of AIDS is highly variable. Some of the variability seen in the course of illness including AIDS may attributable to psychological variables (Cohen & Herbert, 1996).

**Psychoneuroimmunology**

Psychoneuroimmunology (PNI) can be defined as the study of the interaction between the central nervous system and the immune system. PNI serves as an overarching theory that could explain the mechanisms by which psychological states could impact immunity and ultimately health. It was previously believed that the immune system was an independent closed system with the key function of
distinguishing between the self and the non-self or antigens. However, research has continuously shown that psychological states do impact immunity.

The emerging science of psychoneuroimmunology is based on the premise that there is bi-directional communication between the central nervous system and the immune system. Likewise the field of neuroimmunoendocrinology postulates the same type of communication pattern between the central nervous system, immune system and the endocrine system. Both of these new sciences are still not widely accepted by the scientific community. This is due to the lack of understanding currently of what relevance the proposed communication links have ultimately on overall health and how this information can be used to better the overall treatment of patients.

Theories that a positive mental state was important for good physical health have been present for much of recorded history. Likewise, the importance of the placebo effect or the betterment of health due to a belief or some other cognitive process implicated, the connection of the central nervous and immune systems. Some of the first scientific support for this theory came in 1926 when Metal'nikov and Chorine showed that an immune response could be classically conditioned in guinea pigs (Ader, Felten & Cohen, 2001). Classical conditioning of the immune system was accomplished more systematically and was better statistically analyzed by Ader and Cohen in 1975 (Ader et al., 2001). Each of these studies showed that both immuno-enhancement as well as immuno-suppression could be classically conditioned.

While the evidence of our ability to condition the immune system of animals is compelling, the immune systems of humans and animals are not directly comparable. In 1992 however, further support for the immune-central nervous system interaction came
from a classical conditioning study conducted with humans (Ader, et al., 2001). This study confirmed that immuno-enhancement of the immune system could be accomplished via classical conditioning even in humans. Specifically, Buske’s research team paired a sweet sherbet with epinephrine and conditioned an increase in natural killer cell activity.

The Hebb model of strengthening of a synapse with a motor neuron that was just active and that may have previously had a weak connection may explain how classical conditioning works in the central nervous system. Other evidence has shown that the central nucleus of the amygdala is a key system for stimulus-response learning or classical conditioning (Carlson, 1994). Classical conditioning is considered a form of learning which occurs in the brain. Thus this provides good support for the interaction of the central nervous system and the immune system which were previously conceived as separate systems. Much remains to be learned about the exact psychobiological mechanisms of learning and memory but it promises to elucidate our understanding of how classical conditioning of the immune system could operate.

Other evidence that supports the interaction of the central nervous and immune systems is that of the ablation of various brain structures using stereotaxical procedures being related to changes in immune function. The evidence from ablation studies point to the importance of the hypothalamus in immuno-regulation. In particular, it appears that destruction of the pre-optic/anterior hypothalamus is related to a decrease in proliferative responses of t-cell, decreased NK cell activity and decreased antibody production (Ader, et al., 2001). What is compelling about this finding is that destruction of this area of the brain appears to affect both arms of the immune system, the cellular and
humoral immune systems. However, here again this evidence comes from studies of animals and should be considered in that light. Also, the results of ablation studies are difficult to interpret due to the small size of the hypothalamic nuclei which make them difficult to lesion.

Corroborating evidence that implicates the role of the anterior hypothalamus has come from the finding that lesioning of the dorsal hippocampus and amygdaloid complex result in similar immune system impairments seen with hypothalamic lesions (Ader, et al., 2001). As these brain structures have extensive connections into the hypothalamus and can also regulate both endocrine and autonomic outflow. What remains to be seen is which of these brain structures plays the key role in immuno-regulation or whether it is a combination of the effects of these structures which effect the immune system.

Other brain structures have been shown to be important to immune function. When the caudal reticular formation and the rostral raphe nuclei of the brainstem were lesioned, this resulted in an inhibition of the delayed type hypersensitivity response of the immune system as well as thymic involution (Ader, et al., 2001). It should be noted that these brain structure also project to the hypothalamus.

The cerebral cortex may play an important role in the modulation of the immune system. Specifically, the lesioning of large portions of the left hemisphere resulted in a decrease in t-cell numbers and response as well as decreases in NK cell activity. There appeared to be no affect to the humoral arm of the immune system as shown by no change in B cell or macrophage activity. It has been postulated that as the cerebral cortex is believed to be involved in the interpretation of and response to psychosocial factors such as stress, that the cerebral cortex may be a crucial link between these phenomena
and the CNS outflow which then would affect immune function. The frontal, cingulate and temporal areas of the cortex have been shown to have connections to the hypothalamus, limbic system, brain stem as well as some autonomic pre-ganglionic neurons. Other evidence that supports the cortex as a potential modulator of the immune system comes from a study that shows that drugs which modulate the immune system may act via the central nervous system (Renoux, G., 1988)

Clearly, this evidence converges on the hypothalamus as a key structure in immuno-regulation. Further support is provided by a study on the firing rates of the ventromedial nucleus of the hypothalamus after immunization. Increased neuronal firing rates in the anterior hypothalamic region of the brain at the time of peak antibody response which also corresponds to the primary immune response (Ader, et. al., 2001).

A wealth of information has been compiled by Russian researchers on electrophysiological reactions during the immune systems response to an antigen. Here again the most important sites of electrophysiological activity was the hypothalamus, hippocampus and the reticular formation (Felten & Felten, 1988). The importance of the hypothalamus in immuno-regulation points toward the mediation of the immune system via the endocrine system. This has been corroborated by the finding that hormones have receptors in and on leukocytes. It has been long well understood that a steroid hormone (ACTH) plays a key role in the physiological reaction to stress. More recently peptide hormones have been implicated in immuno-regulation. Endorphins, Enkephalins, Thyrotropin, Growth Hormone, Arginine Vasopressin and Oxytocin, Substance P, Vasoactive intestinal Peptide, and Human Chorionic Gonadotropin I are all able to influence the function of most of the major types of cells involved in the immune
system. The converse is true, key components of the immune system affect the endocrine system. Alpha-interferon, IL-1, Thymosin-alpha and beta, as well as IL-2 have been shown to directly impact the function of the endocrine system by triggering release of various hormones via the pituitary and hypothalamus as well as increasing adrenal activity which in turn results in increased glucocorticoid levels (Bla
clock, 1989). This information has led to the postulation of an hypothalamic-pituitary-adrenal axis.

Evidence for another mode of communication between the central nervous system and the immune system comes from the many studies which have found that bone marrow, thymus, spleen and lymph nodes are all innervated by the CNS (Felten, 1986; 1987). Felten goes on to postulate that this innervation as well as the finding that there is bi-directional communication between the immune system and the nervous system via the endocrine and immune system products (interleukins) suggest: " these two great memory and communication systems are poised to respond to internal and external challenges for the protection and preservation of the organism are inter-dependent" (Felten & Felten, 1988).

The bulk of the data support the link between the central nervous and immune system. The probable locus of control within the brain of the immune system has been identified as the hypothalamus. Further, we now understand how the brain influences the immune system via the endocrine system. However, like other areas of psychobiology the exact nature and sequence of this interaction remains a mystery until our technology allow us to more clearly see what is happening at the molecular level in the brain. Further, it will be necessary for the area of psychoneuroimmunology to show that
alteration of the immune system by the nervous system ultimately impacts the overall health of the organism. Also, the usefulness of this information remains to be proven.

Understanding how to up-regulate the brain structures which can stimulate the immune system could present a new point of intervention for persons diagnosed with secondary immune dysfunction. This new point of intervention is necessary as our knowledge of how to regulate the immune system itself is minuscule.

Another key area that has supplied a wealth of data, albeit conflicting is in the area of stress' effect on disease progression via the immune system (Ader, et al., 2001). Many different types of stressors have been examined as modulators of immune function. For example, acute stressors or stress associated with a single event have provided some of the most conflicting data in this area of research (O'Leary, 1990). Studies conducted with Apollo astronauts during splashdown showed an increase in higher lymphocyte counts but no change in proliferative response of the humoral (antibody) or cell-mediated (t-cell) arms of the immune system (Ader et al., 2001). These findings must be viewed with some skepticism as the physical stress of this unique situation clearly serves as a confounding variable in this study. Also, the generalizability of this study's findings are limited in that such a small percentage of persons actually are provided the opportunity to experience space flight. Studies on sleep deprivation have shown decreased phagocytic capabilities of leukocytes as well as decreased proliferative responses to mitogens and increased production of interferons (Palmblad et al., 1979). However here too the physical stress of the situation may confound the findings of this study.
More important, the relevance of increase absolute counts of immune markers is questionable. As no norms per se are established for immune markers increases may be artifacts of inter-individual differences. Kiecolt-Glaser & Glaser (1992) cite the finding that the time of day of a blood draw can account for as much as 85% of the variance between individuals.

In contrast, the study of medical students undergoing the stress of examinations has shown that stress does impact immunity. Among the immunologic changes seen during examinations from baseline data was an increase in the antibody titers to Herpes Simplex-1, Epstein Barr Virus and Cytomeglovirus. This is generally interpreted as the immune systems inability to keep in check viruses which normally are kept under control by the cell-mediated arm of the immune system. Also, the percentages of T-helper to T-suppressor cells as well as proliferative response to mitogens was reduced (Kiecolt-Glaser, Garner, Penn & Glaser, 1984). However, here again caution must be taken in interpreting the results of these findings. The use of "healthy" subjects makes shifts in immunity of little clinical significance. Also, it is a well documented finding that stress can effect diet and sleep patterns and this may be the cause of the immune alterations seen (Kiecolt-Glaser et al., 1986). What may account for the differences in these results is that acute stressors are likely to be associated with activation of the sympathetic nervous system as well as the adrenocortical stress system each of which may effect the immune system differently.

There is very little data available concerning the effects of long term or chronic stress in humans. In animals the effects of stress on immunity have been shown to change over time (Monijan & Collector, 1977). Of the few studies that have studied
chronic stressors the results appear to converge on the immuno-suppressive effects of chronic stress. A study of residents of the area surrounding the Three Mile Island nuclear power plant after the infamous accident in 1979 which left radioactive gas and water trapped inside the containment building for some time after the accident. The residents remained worried over future health consequences of the accident and the possibility that the plant may reopen. These residents were found to have higher antibody titers to Herpes Simplex and Cytomeglovirus compared to demographically matched control subjects. Increased numbers of Neutrophils (Large Granular Leukocytes) and fewer B cells, T-suppressor and cytotoxic and Natural Killer cells were also found (Ader et al., 2001)

Likewise, the chronic stress of unemployment has been associated with increased mortality and morbidity rates. Women in Sweden who had lost their job nine months before the study began showed reduced proliferative response to mitogens. While it could be assumed that these findings are the result of poor diet, inadequate housing or other effects of lack of pay, this is not the case as the subjects were receiving 90% of their previous pay from the state unemployment benefits.

Stress accompanying social disruption can also be considered a chronic stressor. In particular being a caregiver for a person with a chronic illness has been examined in relation to immune functioning. Kiecolt-Glaser & Glaser (1987) examined persons caring for relatives diagnosed with Alzheimer's disease. Compared to a control group, caregivers had higher antibody titers to Epstein Barr virus and lower percentages of T-lymphocytes and helper t-cells to t-suppressor cells. The subjects did report significant
changes in sleeping habits, however this was not related to any of the immune outcomes found by the study.

The loss of a spouse or close relative has been examined for its effect on the immune system. Madison & Viola (1968) found that there is increased mortality and morbidity associated with being widowed in the year following the death of the spouse. This could be due to the decreased lymphocyte response to mitogens found by Bartrop, Lazarus, Luckhurst, Kiloch & Penny (1977). But this study showed no differences in absolute number of immune markers. Likewise, men who had wives that were diagnosed with terminal breast cancer have been studied (Schleifer, Keller, Camerino, Torntton & Stein, 1983). The researchers found that 2 months into bereavement, no differences in absolute numbers of immune markers could be detected. However, NK cell activity was reduced by 50%.

Men and women have been studied after marital separation. Both men and women's immune system appears to be adversely affected by the separation with a spouse (Kiecolt-Glaser et al., 1988). Divorced or separated men and women showed decreased responsiveness to mitogens and increased antibody titers to Herpes Simplex 1 and Epstein Barr virus. Similarly, Kiecolt-Glaser & Glaser (1984) showed that social-deprivation or loneliness affected immunity. Medical students scoring above the median on the UCLA Loneliness Scale showed significantly reduced NK cell activity and higher antibody titers to Herpes Simplex than students scoring below the median. Also psychiatric inpatients who reported more loneliness showed similar immune dysfunction (Kiecolt-Glaser et al., 1984).
Most interesting, is the overwhelming consensus, with a few exceptions that social disruption and or loneliness is associated consistently with immuno-suppression. Further support for these findings comes from research that has shown that immuno-enhancement and betterment of prognosis can be achieved via psychological support such as support groups (Andersen, 1992). These findings are compelling evidence of our need for support from others to mediate stress.

Stress has been shown to be associated with illness behaviors and the increased susceptibility and reactivation of infectious diseases. Retrospective and prospective studies have demonstrated that stress is related to the onset of upper respiratory infections, specifically colds and the flu. It should be noted however that a correlation is not causation and further research is needed with controlled experiments from which causation can be inferred. Similarly, there is evidence to suggest that reactivation of latent viruses such as Herpes Simplex and Epstein Barr can be triggered by stress. In particular, emotional distress appears to be related to higher antibody titers to latent viruses. In this arena as well, more research is necessary to clarify the nature of this association. Specifically, prospective studies using more representative samples could elucidate many of the questions still remaining. Bacterial infections have also been shown to be effected by stress. (Cohen & Williamson, 1991).

Research with persons with Cancer, HIV/AIDS, Autoimmune Diseases and Genital Herpes has shown that psychosocial influences do impact the course of many disease processes. Following psychological interventions NK cell activity was significantly enhanced. This is particularly important as NK cells have been implicated in phagocytizing or destroying of malignancies and small metastases. Also, Herpes
Simplex antibody titers were also statistically significantly reduced (Kiecolt-Glaser & Glaser, 1985). More important is the finding that stress management interventions with medical students resulted in better NK cell activity as well as increased percentages of helper t-cell to t-suppressor ratios compared to controls (Kiecolt-Glaser et al., 1986). Overall there is strong evidence that relaxation training and stress management with subsequent use are related to immuno-enhancement.

Meta-Analysis which provides a mode of encapsulating research in a specific area was used by Herbert & Cohen (1993) on stress and immunity. The authors concluded after a review of the bulk of the literature on stress and immunity that stress is associated with reliable decreases in the proliferative response to mitogens, specifically PHA and Con A as well as NK cell activity. It is noted however, that the statistical effect size of these findings are considered to be low to moderate. Despite this, credence is given to these findings in that the magnitude of the effect size or variance accounted for by stress on immune measures is consistent across parameters.

The meta-analysis also showed that stress is associated consistently to a higher number of white blood cells or leukocytes and lower numbers of B-cells, the producers of antibodies. Similarly, stress is related overall to a lower percent of lymphocytes specifically T-helper to t-suppressor. This results in a suppressed immune response due to a lower number of T-helper cells which orchestrate the cell-mediated immune response.

In relation to immunoglobulins or antibodies made by activated B-cells, stress is correlated with decreases in total serum IgM and IgA. Most important and related to this
finding is that large increases in antibody titers to Epstein Barr virus as well as Herpes Simplex-1 are associated in a statistically powerful way with stress.

However, the exact mechanism by which this is made possible remains unclear. While research supports the role of stress as a modulator of immune function, stress itself may be modulated by other factors such as personality, coping style and social support.

Personality factors have also been linked to immune function. Research has led to a hypothesized immuno-suppression prone personality pattern. Traits such as repressive coping style, lack of assertiveness, low levels of social support and social compliance have been postulated by Temoshok (1992) to be a Type-C or cancer prone personality. Similar findings have been reported by Solomon and Pennebaker (Solomon, 1981; Pennebaker, Keilcot-Glaser & Glaser, 1988). The personality trait or coping style which has been most often documented to effect the immune system is the repressive coping style. A repressive coping style has been shown to be linked with lower absolute numbers of immune markers as well as lower overall functioning (Lamner, Schwartz & Leigh, 1988; Weinberger & Schwartz, 1979; Temeshok, 1992). The mechanism by which this occurs is via the endocrine system which regulates the bodies functions as well as the immune system (Ader, et al.,2001). Temoshok describes repressive coping style as persons who have difficulty expressing negative emotions such as anger sadness or fear, are emotionally detached, self-sacrificing and are overly accommodating to the needs of others. Inhibited and stressed power motivation as well as a repressive coping style have been implicated as potential causes of immuno-suppression have also been reported by McClelland & Jemmott, 1980; Jamner, Schwartz & Leigh, 1988. Temoshok (1992) discusses the scientific evidence which shows that psychological interventions can alter
or improve a patient's coping style. In particular, therapies such as behavioral modification, which require active participation by the patient are well suited to altering coping style.

Two meta-analysis reports have shown that clinical depression is associated with changes in the cellular arm of the immune system. Specifically changes in the proliferative response of lymphocytes to mitogens lower natural killer cell activity and in absolute numbers of several white blood cell populations. Both meta-analyses, found a distinctively linear relationship found between intensity of depression and immunity (Herbert & Cohen, 1993; Zorrilla et al. 2001).

Depression is associated with poorer prognosis in patients with chronic illness through changes in health behaviors coupled with immuno-suppression. Lack of social support has been shown to be a predictor of depression. However, social support is not a unitary construct. Treatment of depression using social support may improve health outcome. Further, as social support also decreases the levels of stress experienced, incorporating social support into HIV/AIDS care warrants investigation (Escoto, in progress).

Kiecolt-Glaser, McGuire, Robles and Glaser (2002) have postulated that negative emotions can impact health either directly through IL-6 (an inflammatory response cytokine) or by causing delays in wound healing. These authors conclude after a review of the literature that "distress-related immune dysregulation may be one core mechanism behind the health risks associated with negative emotions." Research has been focusing on the effect of proinflammatory cytokines, which have been shown to impact cardiovascular disease, infectious disease and wound healing which could serve to
elucidate the mechanism by which stress and depression impact the immune system. (Kiecolt-Glaser, McGuire, Robles & Glaser 2002)

Many challenges remain for the field of psychoneuroimmunology. Among them, do the immune changes found with stress and other psychological phenomena result ultimately in better or worse health outcome over the long term? It is one thing to say that the immune system is suppressed. But it is quite another to say that the immunosuppression seen will ultimately result in poorer health. Also, the specific characteristics of stress that are associated to immune system changes need to be better understood. Specifically, we need to be able to understand which immune effects are associated with specific stressor characteristics. Stressor characteristics should include the controllability and predictability of the stressor as well as the uniqueness of the stressor to the individual. One way to address this issue is longitudinal studies. Longitudinal studies will help clarify the process of change between psychosocial and immunity (Ratliff-Crain, J., Temoshok, L., Kiecolt-Glaser, J. & Tamarkin, L., 1989).

While the body of research that supports PNI is now substantial, many challenges still remain. Many studies have shown that absolute number of immune markers can be increased or decreased via psychological and neurological manipulations, it has yet to be shown that an increase/decrease in absolute numbers translates to better or worse health overall. The inherent idiosyncrasies in each individual's range of immune markers make ideal" immune profiles problematic. Second, it is unethical to suppress the immune system of humans for experimentation.

While this has led to an abundance of research with animals, PNI will ultimately have to be shown to be successful in humans. Of the studies that have been conducted on
humans, most have focused on persons with auto-immune diseases such as lupus, rheumatoid arthritis and persons with HIV or AIDS. Lastly, research has also focused on geriatric populations who are naturally immuno-suppressed or have immunoscience. Most important is the translation of the substantial amount of PNI research into therapeutic intervention. PNI has shown that psychotherapeutic intervention can change the emotional state, mental state, coping mechanism and subsequently the immune system in persons diagnosed with cancer or HIV/AIDS (Fawzy, Kemeny, Fawzy, Elahoff, Morton, Cousins & Fahey, 1990; Antoni, 1991). Similarly, in the geriatric population research has shown that interventions such as relaxation training could improve the immuno-competence of persons ages 60-80 (Kielcot-Glaser, Glaser, Williger, Stout, Messick, Sheppard, Ricker, Romisher, Briner, Bonnell & Donnnerberg, 1985). It is a well documented fact that with age comes a deregulation of the immune system. In particular the immuno-suppression that occurs in old age appears to primarily effect lymphocytes (white blood cells). A subpopulation of lymphocytes or Natural Killer Cells have been shown most amenable to increase or decrease in number and function. Similarly, Absolute Neutrophil count has also shown to be very sensitive to change in the geriatric population as well as in other populations (Solomon & Benton, 1994). What has not been shown is that improved immuno-competence or immuno-suppression as indicated by an increase or decrease of absolute numbers of immune markers actually translates into better overall health for this or any other population including in animal models.
HIV/AIDS and Psychoneuroimmunology

Kiecolt-Glaser & Glaser (1995) posit that given the substantial evidence which supports that immune function is impacted by psychological states such as depression and stress; that individuals whose immune system is already impaired by an immunosuppressive disease like AIDS would be more likely to produce changes in health. As it would be unethical to intentionally suppress a human being's immune system, AIDS presents persons who are immuno-suppressed. Research in the area of psychoneuroimmunology and persons with HIV and AIDS promises to add to the wealth of data that support the science of PNI.

More important, is the impact PNI could have on bettering the prognosis of persons with HIV/AIDS. Particularly, if psychosocial variables which can account of a clinically significant amount of variance can be identified. These same psychosocial variables could serve as a point of intervention for clinical health psychology. Much has changed in the medical treatment of persons with HIV and AIDS. Drug combinations have been shown to be able to keep levels of viral RNA in the blood at low levels for extended periods of time. However, what remains to be shown is how long these new drug combinations will be efficacious (Mellors, 1998). Persons with AIDS, (defined by the CDC as a t-cell count below 200), need to be treated not only for suppression of HIV but also rebuilding of the immune system. This issue falls directly into the realm of PNI. Kiecolt-Glaser & Glaser (1995) conclude that sufficient data is available to conclude that modulation of the immune system by psychological states and interventions can lead to changes in health.
The variability in course of illness has also lead to investigations of psychosocial variables as potential causes. Ironson, Solomon, Cruess, Barroso & Stivers (1995) reviewed the studies which looked at the psychosocial factors related to survival time in person with AIDS and HIV progression. The authors conclude that four psychosocial categories were related to HIV/AIDS, (1) following healthy self care, (2) maintaining connectedness, (3) having a sense of meaning or purpose in life and (3) maintaining perspective. The psychological mechanism by which this could occur are identified as distress and behavioural disengagement. Physiological mechanisms are listed as sympathetic nervous system activation, neuroendocrinological and immunological. In a more recent review of studies assessing psychosocial aspects of long term survival with AIDS, Solomon, Ironson & Balbin (In Press) found the same four psychosocial strategies were related to HIV/AIDS progression.

Balbin, Ironson & Solomon (in press) have gone on to narrow the variables associated with HIV progression and AIDS. These authors have identified life event stress, sustained depression, denial/avoidance coping, and negative expectancies as correlating to faster disease progression. Further, protective psychosocial factors are identified including active, coping, finding new meaning and stress management.

Cole & Kemeny (1997) cite in their review 30 studies that have looked at the link between psychosocial variables and HIV. The authors report that evidence supports the correlation between reaction to stressors, inhibited psychosocial characteristics and immune HIV progression. Cole & Kemeny (1991) go on to discuss other variables which have had mixed results in research in their effect on HIV. Among the variables whose
results have been inconclusive are number of negative life events social support, depression and generalized attitudes or expectations.

Cole & Kemeny (in press) have more recently reviewed 50 studies which have examined the relationship between psychosocial variables and either disease progression and/or immunological function. The authors conclude that psychological reactions to stressors, passive coping, negative expectancies, self-blame, social inhibition and chronic depression have emerged as consistently related to various measures of disease progression or mortality. Cole & Kemeny go on to conclude that "a majority of well-conducted natural history and experimental studies contain data supporting the hypothesis that psychosocial factors can influence disease progression."

A recent longitudinal study focusing on heterosexual African-Americans found that subjects with lower but consistent levels of depression and anxiety predicted death. In contrast, those subjects that initially reported higher levels of depression and anxiety at baseline, but showed a consistent decrease in depression and anxiety survived for a longer duration of time (Lee & Rotheram-Borus, 2001).

Critical reviews of the literature on the psychoneuroimmunology of HIV and AIDS have provided suggestions for future studies (Ironson et al., 1995; Cole & Kemeny, 1997; Cole & Kemeny, in press). It has been recommended that future studies on HIV/AIDS have large sample sizes, better measures of disease progression and a long follow up duration to increase statistical power. Also, controlling for confounding influences (e.g. disease progression at study entry, demographics, health promoting behaviors and antiviral treatment and adherence) is suggested.
Statement of the Problem

Substantial gains have been made in the treatment of HIV and AIDS. However, the number of cases of new infections continues to be of concern. HIV and AIDS have a variable course in progression. This coupled with the increasing numbers of persons living with HIV and AIDS diagnoses, make it imperative that research focus on any potential moderation of immune status. The field of psychoneuroimmunology proposes the mechanism by which the course of disease progression could be attributed to psychosocial variables through the immune system.

Present Study

The present study looks at the relationship between established psychosocial variables that have been shown by previous research to impact disease progression in persons with HIV and survival time in persons with AIDS. Specifically, this study examined stress, depression, and negative expectancies.

However, the proposed study used hierarchical regression to examine the model proposed by psychoneuroimmunology (see Figure 1) or that the psychological states listed above impact immune function and ultimately result in differences in health outcome measures in persons with HIV and AIDS.

The goals of the present study are:

1) To understand the relative contribution of psychosocial variables on immunity and subsequently on clinical markers of HIV and AIDS progression. It is hypothesized that there will be a clear link between psychosocial, immunological and clinical markers in persons with HIV/AIDS.
2) The model will also look at the moderating effect of social support between psychological and immunological variables. This hypothesis will be tested using hierarchical regression to assess the directionality of the relationship between the psychosocial variables of study and hard end points such as survival, clinical events and measures of quality of life.

Research that tests the proposed model between psychology, the immune system and health are lacking in PNI data. The use of hierarchical regression will begin to address this issue.
Method

Participants

The present study utilized data from the medical records of men (n = 134) and women (n = 9) with HIV and AIDS. All of the patients included in the study had HIV or AIDS diagnoses confirmed by ELISA tests and or T-Cell count. However, complete medical and psychological data was only available for 92 subjects (males = 84) (females = 7). The mean age of male patients was 36.9 years (SD = 12.0) and for females 42.4 years (SD = 13.5). Other demographic information was not provided to maintain patient confidentiality.

Materials

The Beck Depression Inventory (BDI) is comprised of 21-items rated on a 4 point scale ranging from 0 to 3 which indicates level of severity. The BDI has been shown to be a reliable and valid instrument and is used frequently in research and clinical practice.

The Million Behavioral Health Inventory (MBHI) (Millon, Green & Meagher, Jr., 1982) is comprised of 150 true-false questions designed to assess personality styles, psychological characteristics which have been shown to exacerbate medical conditions. Four scales of the MBHI will be used to assess the remaining psychosocial factors being investigated. Specifically, the MBHI Chronic Tension and Recent Stress scales will be used to assess patient's level of stress. Also the scales which assess explanatory style Premorbid Pessimisssm and Future Despair will be examined.

Also, assessed by the MBHI are three predictors of psychosomatic disorders and three predictors of potential responses to medical diagnosis and/or treatment. All of the above scales have established reliability and validity.
The Social Provisions Scale (SPS) is a 25 item self-report instrument that measures perceived social support. Each item has 4 responses anchored from strongly disagree to strongly agree. The SPS has 6 subscales including Attachment, Social Integration, Reassurance of Worth, Reliable Alliance, Guidance and Opportunity for Nurturance. The 6 subscales have been verified through confirmatory factor analysis. Test-retest reliability and Cronbach's alpha have been reported as .59 and .76 to .84 respectively. Two composite scores were created by the physician's office for the SPS. One score was created to tap into "tangible support" or the provision of goods and services by others and "total support" to assess overall social support. Neither of these composite scores have been tested for reliability or validity.

Two questions from an un-normed Quality of Life Inventory used by the physician's office were used as outcome measure. One question asked the patients to rate their health today on a scale from 0 to 100 and the second question asked for a rating of their view of life now on a scale from 1 to 7. Lastly, patients were identified as living or deceased by attending medical staff.

Design and Procedure

This study used archival data from the Orange County Centers for Special Immunology, a private physician's office in Southern California. Informed consent was obtained by that clinic at baseline. Psychological testing was conducted in one session in a private office. Subjects were administered a psychosocial assessment battery via computer within 6 months of beginning treatment. Scoring of assessments were performed by a computer program written by the medical facility where testing took place.
Chart reviews were conducted to assess which patients completed all of the instruments being used in the study. All patients with completed files were included as participants in the study. Medical files were evaluated for each patient for, number of clinical events such as opportunistic infections as well whether the patient had expired or not. Immunological data was also gathered from patient charts. Mean counts for viral load and T4-cell count as well T4-cell percent were assessed from data gathered from patient charts. Limited demographic information was assessed to assure confidentiality and only patient numbers were used to identify participants in the study. All data was input and evaluated using SPSS to assess the models being tested and to provide descriptive statistics regarding the sample.
Results

Age was not correlated with any of the psychosocial, immunological or outcome variables. A Kruskall-Wallis test was used to identify any gender differences between scores on any of the variables being tested due to a lack of normality and differences in sample size. No significant gender differences were found on any of the psychosocial, immunological or outcome variables. Therefore the statistical analyses presented will collapse males and females into one group. Table 1 presents the mean scores and standard deviation of all the variables assessed for males and females.

Table 1

Means and Standard Deviations for all Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI</td>
<td>11.3</td>
<td>10.7</td>
</tr>
<tr>
<td>Chronic Tension</td>
<td>13.5</td>
<td>8.4</td>
</tr>
<tr>
<td>Recent Stress</td>
<td>10.0</td>
<td>8.8</td>
</tr>
<tr>
<td>Premorbid Pessimism</td>
<td>12.8</td>
<td>10.7</td>
</tr>
<tr>
<td>Future Despair</td>
<td>13.1</td>
<td>11.8</td>
</tr>
<tr>
<td>Total Social Support</td>
<td>79.3</td>
<td>18.1</td>
</tr>
<tr>
<td>T4-Cell Count</td>
<td>388.9</td>
<td>272.6</td>
</tr>
<tr>
<td>T4-Cell Percent</td>
<td>20.2</td>
<td>11.7</td>
</tr>
<tr>
<td>Viral Load</td>
<td>74090.1</td>
<td>144247.3</td>
</tr>
<tr>
<td>Health Today</td>
<td>76.8</td>
<td>14.0</td>
</tr>
<tr>
<td>Life Now</td>
<td>3.0</td>
<td>.97</td>
</tr>
<tr>
<td>Opportunistic Infections</td>
<td>2.1</td>
<td>1.6</td>
</tr>
</tbody>
</table>

The data was screened for outliers, multivariate normality and linearity using histograms in SPSS. Histograms revealed that variables being examined showed a significant degree of skew. Due to the archival nature of the study, sample size was
drastically reduced. Therefore, hierarchical regression was utilized instead of Structural Equation Modeling.

Four separate psychological inventories were used in the study, each with separate scoring. In preparation for statistical testing all scores were converted to z scores to assure comparability. The basic assumptions of the model were then assessed. The regression model required collapsing psychosocial variables into one construct. Therefore, the 2 scales of stress from the MBHI (chronic tension and recent stress) and 2 scales for explanatory style from the MBHI (premorbid pessimism and future despair) were collapsed into single categories. The collapsing of scores was supported by the high correlation of each scale score $r = .840, p = .000$ and $r = .923, p = .000$ respectively. The BDI, Stress and Explanatory Style (MBHI) scores were then assessed prior to their combination as one psychosocial construct. Table 2 shows the correlation matrix for the Psychosocial variables.

### Table 2

Correlation Matrix, Psychosocial Variables

<table>
<thead>
<tr>
<th></th>
<th>BDI</th>
<th>Stress</th>
<th>Expstyle</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress</td>
<td>.19 (p = .07)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Expstyle</td>
<td>.53 (p = .000)</td>
<td>.63 (p = .000)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

The standardized z scores for each measure were summed to create a composite called “psychosoc.”
Similarly, T-Cell count, T-Cell percent and viral load were to be combined for statistical testing. Table 3 shows the correlation matrix for all of the immune markers.

Table 3
Correlation Matrix, Immunological Variables

<table>
<thead>
<tr>
<th></th>
<th>T-Cell</th>
<th>T-Cell%</th>
<th>Viralload</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-Cell</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-Cell%</td>
<td>.81 (p = .000)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Viralload</td>
<td>.34 (p = .002)</td>
<td>.46 (p = .000)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Viral load was correlated negatively with the T-Cell and T-Cell %. Therefore, viralload was reverse coded. The summed standardized scores were then collapsed into a variable called “immune.” “Psychosoc” and “immune” were then correlated. There were no statistically significant relationships between psychosocial variables and immunological variables (r = .073, p = .53).

Hierarchical regression was used to assess the relationship between psychosocial variables (block1), social support (block 2) and the interaction of psychosocial and social support (block 3) on the immune variables. Psychosocial variables did not significantly predict immune scores ($R^2 = .007$, df = 71, $F = 5.08$, p = .478). Likewise, psychosocial variables and social support did not predict changed in immunity ($R^2 = .011$, df = 70, $F = .376$, p = .509, $R^2$ change = .004, p = .568). Psychosocial variables, social support and the interaction term did not account for a statistically significant degree of change in immune markers ($R^2 = .011$, df = 69, $F = .256$, p = .857, $R^2$ change = .000, p = .652).
A final test of the mediational relationship between all variables was then assessed using the composite psychosocial variable, the composite immunological variable and whether the patient had expired or not as a single outcome variable. As done previously, correlations assessed to show that the three variables being assessed were related in a statistically meaningful way. Table 4 shows the correlation matrix for all of the variables entered into the final model.

Table 4
Correlation Matrix, Psychosocial, Immunological and Outcome

<table>
<thead>
<tr>
<th></th>
<th>psychosoc</th>
<th>immune</th>
<th>expired</th>
</tr>
</thead>
<tbody>
<tr>
<td>psychosoc</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>immune</td>
<td>-.07 (p = .531)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>expired</td>
<td>-.05 (p = .635)</td>
<td>.58 (p = .000)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Based on these results another hierarchical regression was conducted using expired as the outcome measure, with immunity (block 1), psychosocial measure (block 2). The order of each variable was selected due to the significant relationship between immunity and the expired measure. When predicting the expired variable, hierarchical regression showed no statistically significant findings (immune $R^2 = .03$, df 74, $F = 2.24$, $p = .139$; immune and psychosocial $R^2 = .04$, df 73, $F = 1.51$, $p = .228$, $R^2$ change .010, $p = .379$).

To confirm the results of the hierarchical linear regression, correlations were conducted, removing the effects of the immunological variables (t-cell and viral load)
constant. None of the psychosocial variables accounted for a statistically significant amount of variance in survival in patients with HIV or AIDS.
Discussion and Conclusion

PNI is a relatively new field of study. However, in a short amount of time research supporting the theoretical and mechanical links between the psyche, nervous system and the immune system are substantial. Departments of PNI are being established in some of the most prominent universities worldwide. Research has elucidated the exact physiological and chemical process responsible for immuno-regulation. The list of psychosocial variables known to impact the immune system continues to grow.

However, to date few other studies have been published which examine the mediational relationship between psychological states, immunity and outcome measures in any population. Therefore the model tested in the present study was based on the assumption that the immune system serves as a mediator between psychosocial variables and health outcome. This hypothesis was disproved. According to the present data, immunity alone appears to be the sole contributor to health outcome in persons with HIV and AIDS. This is counterintuitive based on previous research. The biopsychosocial model proposes that biology, psychology and sociology work together to produce health or illness. Just as exposure to a pathogen does not automatically produce infection, so too does destruction of the immune system automatically lead to illness and death. However, this data does not bear this out. Further data analyses showed that none of the psychosocial measures accounted for a statistically significant amount of variance in survival of patients with HIV or AIDS even after for controlling for the effects of T-Cell and viral load.
In order to reduce the risk of a Type I Error, only one model was tested using a composite score of both type of stressors measured and for both types of explanatory styles measured. Of particular interest, is that social support did not moderate the effects of psychosocial variables such as depression, stress and negative explanatory style on immune markers in persons with HIV and AIDS, in this study. However, the social support measure used for this study was a composite score of all subscales of the social support scale created by the physician's office. The "total support" score used in the analysis is not validated and has no reported reliability. Future research should include all of the subscales of the SPS to assess which type of social support, if any, is a mediator for psychosocial variables on immunity or is a covariate with immunity and psychosocial variables.

Age has been shown to be accompanied with a decrease in immune function. This is particular concern to persons with HIV and AIDS, who already are experiencing immuno-suppression from the disease process. However, age in the sample studied was not related to any of the variables examined including psychosocial, immunological or outcome variables. A possible explanation for this finding is the limited nature of the sample. However, the use of anti-viral medications, prophylaxis and other complimentary therapies may contribute to lack of an age effect.

Limitations

Several limitations need to be considered when examining these results. First, the sample was predominately gay men of European decent receiving medical care from a private physicians office. Clearly future studies must include other ethnic groups.
Similarly, women were underrepresented in this study. While females are a minority of the total number of cases of HIV and AIDS in this country, women are in a "high risk" group for contraction of HIV. Efforts should be made to assess these results in female patients with HIV and AIDS despite the difficulty in accessing this group of patients.

Due to the archival nature of the data, no controls were in place to account for disease status at baseline. All patients were included in the analysis, regardless of t-cell count. Also, only enumerative assays were used to assess immune function. While this is somewhat justifiable, based on the key target of HIV being T4-cells. The number of circulating T4-cells does not account for T4-cells in various organs such as the thymus or lymph nodes. More important, T4-cell count and percentage do not assess the function of the existing T4-cells to do their job. Proliferation tests (ConA) should be included to account for the functionality of the immune system in persons with HIV and AIDS.

Recent research has pointed to the inflammatory response of the immune system as directly affecting immune status. Future research should assess IL-6, a chemical messenger of the immune system, as well as endocrinological measures such as cortisol, a known factor in immuno-suppression as a result of stress.

Also, to protect the confidentiality of the patients, limited demographic data was available which could have been included in the analysis. For example, the duration of disease and the history of medication use. Protease inhibitors have changed the prognosis for persons with HIV and AIDS. However, some persons are protease inhibitor naive. Similarly, compliance with medical regimens and complimentary therapy regimens including supplements and exercise should be accounted for in future studies.
Implications

The implications of this research question the predictions of PNI for patients with HIV or AIDS. Immunology alone impacted outcome measures in persons with secondary immune diseases. However, these results should be replicated to assess whether psycho-social variables impact the health outcome in persons with secondary immune diseases through changes in the immune system. Also, as the immune system is already impacted in persons with HIV or AIDS, this may limit the ability of psychosocial variables to impact immunity and ultimately survival. The biopsychosocial model proposes that biology, psychology and social factors together impact health. Further research should include social support factors as another covariate with immunity (bio), psychological states in their combined impact on health outcome. Also future research should focus on the mediating effect of coping style on psychosocial, immunological and social support on health outcome.

Escoto and Rotenberg (2002, under review) have proposed that the presence of psychosocial factors are not in themselves immuno-suppressive. Instead, if depression, anxiety (a by product of stress) are accompanied with "search activity" or the continued assessment of new ways to cope either behaviorally or internally may be immuno-enhancing. While the "renunciation of search" or what appears to be freezing behavior may be immuno-suppressive coupled with the presence of stress or depression.
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Appendix A

Data List

Patient #:

Patient Age:

Ethnicity:

Gender:

T-Cell Count:

Mean T-Cell Percent:

Mean Viral Load:

Mean Beta2 Microglobulin:

Time to Death (months):

Time to AIDS dx (months):

# of Clinical Events:

Scale A MBHI:

Scale B MBHI:

Scale C MBHI:

Scale D MBHI:

Beck Depression:
Appendix B

Letter of Cooperation

Paul Cimoch, M.D.
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Dr. Cimoch

As per our conversation, I am submitting a copy of the proposal for my dissertation as well as a copy of the data required for the study. Upon defense of the proposal, the data collection phase of this project will begin. I have been in contact with Wendy who is prepared to locate and bring to OCCSI files with completed psychological assessments. Wendy has offered to meet with me at OCCSI on the weekend to collect patient data in a manner that keeps patient confidentiality. Only patient numbers will be used in data analysis.

Your assistance as well as that by your staff will be of great assistance to me in the completion of my dissertation as well as contribute to the understanding of the role of psychosocial variables in disease progression in persons with HIV and AIDS. I look forward to meeting with you and your staff to address any concerns or questions you may have.

Respectfully

Carlos A. Escoto