Psychoneuroimmunology and HIV Disease Progression

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By J. Stephen Mcdaniel, MD [2] and David R. Gillenwater, MD [3]

Among psychiatrists who treat patients with HIV/AIDS, the question of how psychosocial distress affects the progression of HIV disease is likely to arise. Even for healthy individuals, we are only beginning to clarify the complex pathways by which thoughts and emotions impact immune function. Due to the bidirectionality of the communications of the brain and the immune system, this is a complicated scenario. The fact that HIV alters the function of the immune system during the course of its progression creates greater confounds to the understanding of these systems. We will address the rationale that progression from HIV infection to AIDS may be modulated by psychosocial factors, discuss possible reasons for conflicting findings and posit some clinically relevant recommendations drawn from research findings.

Psychosocial Variables: Modulators of HIV Disease Progression?

The progression of HIV disease is highly variable among individuals. Factors known to play a role in determining the rate of progression include the viral strain, genetic characteristics of the host immune system, co-infections with other pathogenic organisms (Zorilla et al., 1996) and health maintenance habits (e.g., diet, exercise, medical treatment). However, these factors do not fully explain the extreme degree of variability noted in the course of HIV disease (Cole and Kemeny, 1997).

Given that certain immune parameters are modulated by physiologic mediators of the stress response (i.e., catecholamines and glucocorticoid hormones), it would seem logical to investigate the role of stress and other psychosocial factors in the progression of HIV infection. In fact, changes in immune function and disease susceptibility have been well documented in healthy individuals during times of psychic distress (Ader et al., 1995; Miller et al., 1997), and studies over the past 15 years have shown significant correlations between psychosocial variables and HIV progression. However, there have also been a number of studies showing no such correlation.

Stressful Life Experiences. Studies examining stressful life events and HIV have shown interesting but conflicting results. For example, Rabkin et al. (1991) studied 124 HIV-positive men and found no association between clinician-rated anxiety and CD4+ lymphocyte counts at study entry and at six-month follow-up. However, Evans et al. (1995), performing a similar cross-sectional study of HIV-positive men, did show a significant correlation between increased frequency of negative life events over the six months prior to interview and decreased CD8+ cytotoxic T-cells. Evans et al. (1997) continued with a two-year prospective study and found that not only were severe life stressors predictive of greater declines in some lymphocyte populations (natural killer [NK] cells and CD8+ cytotoxic lymphocytes), but also that such stressors increased the rate of HIV progression to AIDS. The researchers emphasized that their results were noted only in those experiencing severe life stress, not stresses associated with everyday living. For every severe life stress reported, they found the risk of HIV disease progression to AIDS doubled. In their most recent work, these investigators followed 82 HIV-positive gay men at six-month intervals for up to 5.5 years. They found that more cumulative life stress and less cumulative social support doubled or tripled the probability of progressing to AIDS (Leserman et al., 1999).

Depression. Studies examining the effect of depression on HIV progression have had variable results. For example, Rabkin et al. (1991) found no correlation in their cross-sectional study between depression and CD4+ lymphocyte count or stage of HIV illness; however, a relationship was found...
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Factors Contributing to the Differences Observed in Studies to Date

In attempting to compare the studies cited above, confounding elements include both the heterogeneity of the study populations and methodological differences among investigators. The majority of studies have been conducted among groups consisting primarily of Caucasian, well-educated, homosexual men living in metropolitan locations. However, even within this subgroup, there are variables that might skew study data (e.g., age group, unknown time since HIV infection, access to antiretroviral treatment and so forth). A variety of methodological difficulties deserve mention. HIV/AIDS is an illness with an extraordinarily long latency period, so following patients even for several years may yield no substantive change in disease status. Putative immunologic changes brought about by psychosocial factors tend to be small, necessitating larger samples to reveal significant findings (Cole et al., 1997). Many psychiatric...
disorders tend to be recurring, time-limited entities, and our measurement techniques for these typically yield only a cross-sectional glimpse of mental health at a given time. These factors could preclude significant findings in a disease like HIV/AIDS, which has a lengthy asymptomatic phase (Zorilla et al., 1996).

Currently, several known laboratory findings correlate with HIV progression, but their predictive value is questionable. The most common marker, the CD4+ lymphocyte, is predictive of increased risk for opportunistic infections once it drops below a critical level. Another promising marker is the plasma viral load. However, with the advent of newer antiretroviral therapies, CD4+ lymphocyte levels can rise markedly and viral load can become undetectable for years. **Clinical Recommendations and Applications: Lengthier Studies are Needed**

Many studies give us hope that psychosocial interventions can not only improve our patients' quality of life, but also improve their physical health. For example, a study of 10 HIV-positive men by Taylor (1995), showed that behavioral stress management over a 20-week period significantly slowed the rate of CD4+ lymphocyte decline. These results are tempered by conflicting findings such as those of Mulder et al. (1995). Working with 26 asymptomatic, HIV-positive men in either cognitive-behavioral group therapy or experiential group therapy, these researchers found no significant differences in CD4+ lymphocyte changes between group members and controls over a 24-month period. Lengthier studies of larger populations are clearly needed to elucidate further findings and to translate them from laboratory data into real-world scenarios.

Exercise training has been studied among several HIV-positive cohorts, revealing numerous psychological benefits including decreases in anxiety and depression and increases in active, positive coping styles. In a review of pertinent literature, LaPerriere et al. (1997) concluded that a typical regimen of aerobic exercise can result in increases in CD4+ lymphocyte counts in all HIV-positive patients, except those with AIDS. However, even among AIDS patients, the CD4+ lymphocyte counts remained stable over an 18-month study (whereas control patients' levels continued to decline).

The impact of HIV on neural tissue remains questionable. There is evidence, at least in the case of depression, that HIV-positive individuals respond to antidepressant therapy at rates similar to seronegative controls. The side-effect profiles of these medications also seem to differ minimally based on HIV status (Rabkin et al., 1994).

A significant finding about HIV and depression in the meta-analysis by Zorilla and colleagues (1996) was that depression was associated with increased reporting of HIV physical symptoms, regardless of objective markers of physical disease. Depressed HIV-positive individuals may have a more painful experience of HIV illness, regardless of objective physical signs and markers. Also, alleviating depression in some cases may facilitate compliance with medication regimens and medical follow-up, improve self-care, and decrease self-destructive behavior-all variables associated with diminished morbidity and mortality (Stober et al., 1997).

Overall, evidence remains inconclusive regarding the role of psychosocial factors in HIV disease progression, as well as the long-term effectiveness of interventions directed at such factors. However, it is certain that psychiatric disorders and social stressors occur frequently during the course of HIV disease. While it is unclear whether specific psychiatric and psychosocial interventions will extend life or improve physical health among HIV/AIDS patients, we do know definitively that treatment can alleviate psychiatric disorders, relieve distress, and improve quality of life and such critical variables as treatment adherence.

With more HIV-positive individuals being seen in general psychiatric practice, one should not underestimate the positive effects of comprehensive psychiatric care.

**References:**

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