

2008

### Psychological Stress and Immune Function

Allison Rubin

Follow this and additional works at: [https://touroscholar.touro.edu/quill\\_and\\_scope](https://touroscholar.touro.edu/quill_and_scope)



Part of the [Arts and Humanities Commons](#), and the [Medicine and Health Sciences Commons](#)

---

#### Recommended Citation

Rubin, A. (2008). Psychological Stress and Immune Function. *Quill & Scope*, 1 (1). Retrieved from

This Review is brought to you for free and open access by the Students at Touro Scholar. It has been accepted for inclusion in Quill & Scope by an authorized editor of Touro Scholar. . For more information, please contact [touro.scholar@touro.edu](mailto:touro.scholar@touro.edu).

## ***Psychological Stress and Immune Function***

Allison Rubin

The medical community has always acknowledged that psychological stress can affect physical well-being, even though the mechanism was not always known. Now we know that this phenomenon is mediated by the body's response to external stress, which originates in the central nervous system (CNS). The limbic system of the CNS is involved in adaptation, the process by which humans adapt physically and emotionally to a new environment, and organizing neuroendocrine and emotional responses to stressful stimuli. "The limbic system evaluates the stressful signals and compares them with stored information collected from past experience. Within the system the septo-hippocampal cholinergic structure is heavily engaged in adaptation processes to stressful conditions" (Khansari, Murgo, & Faith, 170). Therefore, the extent to which the body responds physiologically to stress is in part due to the way the individual is capable of coping with stress. A person who does not handle stress appropriately may have stronger/longer responses, which can trigger the HPA axis to produce cortisol and the SNS to release norepinephrine. Cortisol and norepinephrine ultimately cause repression of the immune system (O'Connor, O'Halloran, & Shanahan, 2000; Webster, Tonelli, & Sternberg, 2002).

Several studies have illustrated the effects of stress on immune functioning. Glaser et al. (1998) found a decreased antibody response to vaccination among caregivers of Alzheimer's disease patients. Additionally, Workman and La Via (1987) found that medical students taking national board examinations had significantly lower T-lymphocyte proliferation than less stressed individuals.

The relationship between a stressful life and decreased immune functioning is especially important for the already immunosuppressed HIV population. In human HIV, studies have shown that psychological stress is associated with decreased helper T cell and B cell counts (Motivala et al., 2003). Petitto et al. (2000) found that increased cortisol levels were associated with lower amounts of CD8+ and NK cells in medication-free HIV+ men. In addition, Goodkin et al. (1992) discusses how homosexual men with a more passive coping style and more life stressors have lower numbers of helper T lymphocytes than men with an active coping style and less life stressors.

Not only can psychological stress cause further suppression of the immune system but it can also contribute to reactivation of HIV during latent stages of infection. HIV is characterized by a period of latency that can last several years. However, some HIV+ individuals develop health problems (opportunistic infections, secondary cancers, HIV related mental deficits, etc.) rapidly. It is thought that certain "co-factors" are involved in determining the rate of immune dysfunction for an individual. Co-factors are defined as the number of exposures to HIV, genetic predisposition to retroviral infection, infection with other viruses that may activate HIV, and age (Gorman & Kertzner, 1990). Currently, psychological and social factors are not completely accepted as co-factors in HIV progression. However, there are many studies that implicate the effects of stress hormones on the proliferation of HIV. For example, the ability of HIV to infect human monocytes and lymphocytes was enhanced by the addition of hydrocortisone (Gorman & Kertzner, 1990). Additionally, cortisol can combine with gp-120, the envelope protein of HIV-1 that is discarded during infection, to induce apoptosis in normal lymphocytes (Nair et al., 2000). Evans et al. (1997) found that higher severe life stress increased the odds of developing HIV

disease progression nearly four fold and is associated with an increased rate of early disease progression.

Additionally, the HIV population is susceptible to unique life stresses that have been shown to contribute to immunosuppression. For example, the Highly Active Antiretroviral Therapy (HAART) has strict guidelines for food intake, the number of doses required a day, and dosing times. While having a significant impact on reducing HIV progression, these guidelines also produce chronic stressors such as coping with side effects, the economic strain of paying for treatment, and major shifts in life schedules and tasks (Safren et al., 2002). Although some may argue that these stressors have limited effects because HAART slows disease progression, Safren et al. (2002) suggest that HAART can negatively impact quality of life and cause patients to have low adherence to the regimen. This can have a drastic effect on HAART's success because even low levels of nonadherence have been related to faster disease progression (Chesney et al., 2000).

Another significant stress is the social stigma related to HIV. "Social rejections, disapproval, and discrimination related to HIV may heighten a person's sense of shame regarding their illness and serve to lessen their motivation to maintain optimal health" (Venable et al., 1994, 474). The social stigma associated with HIV is propagated by the fact that many people are misinformed and uneducated about disease transmission. One in four Americans are afraid of interactions with HIV+ individuals and one in three Americans say they would actively avoid contact with HIV+ people (Venable et al., 2006). Schmitz and Crystal (2000) suggest that stigmatization leads to decreased social support because of rejection by family members and discrimination based on HIV status. This is important because decreased social support is associated with accelerated HIV progression (Lesserman et al., 1999). In addition, Venable et al. (2006) found that stigmatization is linked to greater subjective reports of HIV related symptoms but not viral load. They also discovered that the social stigma surrounding HIV is correlated with depressive symptoms. Depression has been correlated with immunosuppression in HIV+ males. For example, Burack et al. (1993) found a significant relationship between depression and a reduction of helper T cells in HIV+ men. Furthermore, the fear of being stigmatized may prevent people from being tested for HIV permitting them to spread the disease to others.

HIV+ individuals can also suffer from Posttraumatic Stress Disorder (PTSD) after learning about their diagnosis. Ironson et al. (1997) found that post traumatic stress symptoms (after Hurricane Andrew) were related to decreased amounts of helper T cells, cytotoxic T cells, and natural killer cell cytotoxicity. Although the relationship between PTSD and immune function is still unclear, PTSD is associated with decreased adherence to HAART therapy and consequently increased viral load (Delahanty, Bogart, & Figler, 2004). Taking medication may remind HIV+ individuals with PTSD of the traumatic diagnosis and bring unwanted attention from peers. The social stigma surrounding HIV may also contribute to PTSD after diagnosis.

HIV+ individuals also experience extreme psychological distress following the death of close friends with HIV. Kessler et al. (1991) determined that HIV seropositive men reported more deaths from AIDS in their social networks than seronegative men. Not only are HIV+ people grieving for the loss of their friends, but they are also watching their peers die of the same disease that could eventually cause their own demise. Goodkin et al. (1996) found that decreased natural killer cell cytotoxicity and lymphocyte proliferation was associated with bereavement in HIV+ homosexual men.

HIV infected individuals are at a high risk of depression because of the enormous amount of stresses in their lives. Nearly 38% of HIV patients have anxiety disorders (Basu, Chwastiak, &

Bruce, 2005). Depression can negatively impact the immune system and have dire consequences for HIV+ people. It is associated with increased mortality (including nonsuicidal mortality), increased incidence of heart attacks, and higher odds of death from cancer (Gorman & Kertzner, 1990). Appropriate treatment for depression is necessary in HIV+ individuals because depressive symptoms can mask somatic symptoms of HIV. Depression also contributes to relapse into drug abuse, which is a prominent problem among HIV+ patients.

HIV+ individuals face an enormous amount of stress everyday either relating to the disease itself or the stigma surrounding HIV. Although the relationship between these variables and disease progression is still not well understood, there have been a number of studies that have shown the effectiveness of interventions on the well-being of HIV+ patients.

The interventions generally focus on behavioral changes and increased social support. This is the case because, as examined by Wolf et al. (1991), active behavioral coping is associated with greater perceived social support and improved mood while avoidance coping is associated with lower social support and mood disturbance. Mulder et al. (1995) used cognitive behavioral group therapy and experiential group therapy to decrease psychological distress, depressive symptoms, and psychiatric symptoms among HIV+ homosexual men. The program lasted for 15 weeks and decreases in distress were related to increases in CD4+ cell counts. Similarly, HIV+ individuals that participated in a structured 8 week Mindfulness-Based Stress Reduction (MBSR) Program showed increased natural killer cell activity. This program emphasized the importance of self-observation, moment-to-moment awareness, and concentration. It used awareness exercises, meditation, and yoga to teach the importance of self-awareness and its application (Robinson, Mathews, & Witek-Janusek, 2003). Additionally, enhanced social support from clinicians and the community and modification of individual risk behaviors enhanced the quality of life among HIV+ individuals (Liu et al., 2006).

Depression is also an important area for intervention as it is prevalent among the HIV+ community and may contribute to disease progression. Therefore effectively coping with depression is crucial. Cruess et al. (2005) found that the resolution of depression among HIV+ women was associated with increased natural killer cell activity. In order to effectively cope with depression an individual may seek social support, the guidance of a psychologist, or even the effects of antidepressants. However, HIV+ individuals must be careful not to use medications that increase norepinephrine levels that may impair lymphocyte function (Gorman & Kertzner, 1990).

While the previous interventions focus directly on managing stressful life events and depressive symptoms, other studies examine the effects of secondary lifestyle choices on HIV disease progression. For example, Tuck et al. (2001) found that spirituality was positively related to quality of life, social support, effective coping strategies, and negatively related to perceived stress, uncertainty, psychological distress and emotional-focused coping. Also, massage therapy and exercise have been correlated with enhanced immune functioning and slower disease progression among HIV+ individuals (Ironson et al., 1996; Mustafa et al., 1999).

HIV disease progression is a multivariate phenomenon encompassing the damaging effects the virus has on the immune system and its regulatory processes, and the effects of HIV specific psychological factors on immune functioning. Therefore, a widespread body of research is needed in order to better understand the complicated relationships between the external environment, the brain, and the immune system. It is possible that once the link between life stresses and HIV disease reactivation is understood that specific medications and interventions

may be developed to help maintain the period of latency experienced early on. Psychological interventions and alternative therapies could become an integral part of HIV treatment.

There is an abundance of research that shows psychological stress has profound consequences for patients with any disease. Therefore, it seems likely that stress could contribute to pathology, or make one more prone to disease. This is an important possibility and should be considered when treating both sick and healthy patients. Future physicians and physicians alike should not overlook the role stress plays in disease progression or the effectiveness of psychological interventions and alternative therapies on both the emotional and physical well being of their patients.

## References

- Basu, S., Chwastiak, L. A., & Bruce, R. D. (2005). Clinical management of depression and anxiety in HIV-infected adults. *AIDS*, *19*, 2057-67.
- Burack, J. H., Barret, D. C., Stall, R. D., Chesney, M. A., Ekstrand, M. L., & Coates, T. J. (1993). Depressive symptoms and CD4 lymphocyte decline among HIV-infected men. *The Journal of the American Medical Association*, *270*, 2568-73.
- Chesney, M. A., Ickovics, J. R., Chambers, D. B., Gifford, A. L., Deidig, J., Zwickl, B., & Wu, A. W. (2000). Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: The AACTG adherence instruments. *AIDS Care*, *12*, 255-66.
- Cruess, D. G., Douglas, S. D., Pettito, J. M., Have, T. T., Gettes, D., Dube, B., Cary, M., & Evans, D. L. (2005). Association of resolution of major depression with increased natural killer cell activity among HIV-seropositive women. *American Journal of Psychiatry*, *162*, 2125-30.
- Delahanty, D. L., Bogart, L. M., & Figler, J. L. (2004). Posttraumatic stress disorder symptoms, salivary cortisol, medication adherence, and CD4 levels in HIV-positive individuals. *AIDS Care*, *16*, 247-60.
- Evans, D. L., Leserman, J., Perkins, D. O., Stern, R. A., Murphy, C., Zheng, B., Gettes, D., Longmate, J. A., Silva, S. G., van der Horst, C. M., Hall, C. D., Folds, J. D., Golden, R. N., & Pettito, J. M. (1997). Severe life stress as a predictor of early disease progression in HIV infection. *American Journal of Psychiatry*, *154*, 630-4.
- Glaser, R., Kiecolt Glaser, J. K., Malarkey, W. B., & Sheridan, J. F. (1998). The influence of psychological stress on the immune response to vaccines. *Annals of the New York Academy of Sciences*, *840*, 649-55.
- Goodkin, K., Blaney, N. T., Feaster, D., Fletcher, M. A., Baum, M. K., Mantero-Atienza, E., Klimas, N. G., Millon, C., Szapocznik, J., & Eisdorfer, C. (1992). Active coping style is associated with natural killer cell cytotoxicity in asymptomatic HIV-1 seropositive homosexual men. *Journal of Psychosomatic Research*, *36*, 635-50.
- Goodkin, K., Feaster, D. J., Tuttle, R., Blaney, N. T., Kumar, M., Baum, M. K., Shapshak, P., & Fletcher, M. A. (1996). Bereavement is associated with time-dependent decrements in cellular immune function in asymptomatic HIV type-1 seropositive homosexual men. *Clinical and Diagnostic Laboratory Immunology*, *3*, 109-18.
- Gorman, J. M. & Kertzner, R. (1990). Psychoneuroimmunology and HIV infection. *Journal of Neuropsychiatry and Clinical Neurosciences*, *2*, 241-52.
- Ironson, G., Field, T., Scafidi, F., Hashimoto, M., Kumar, M., Kumar, A., Price, A., Concalves, A., Burman, I., Tetenman, C., Patarca, R., & Fletcher, M. A. (1996). Massage therapy is associated with enhancement of the immune system's cytotoxic capacity. *International Journal of Neuroscience*, *84*, 205-17.
- Ironson, G., Wynings, C., Schneiderman, N., Baum, A., Rodriguez, M., Greenwood, D., Benight, C., Antoni, M., LaPerriere, A., Huang, H.S., Klimas, N., & Fletcher, M. A. (1997). Posttraumatic stress symptoms, intrusive thoughts, loss, and immune function after hurricane Andrew. *Psychosomatic Medicine*, *59*, 128-41.

- Kessler, R. C., Foster, C., Joseph, J., Ostrow, D., Wortman, C., Phair, J., & Chmiel, J. (1991). Stressful life events and symptom onset in HIV infection. *American Journal of Psychiatry*, 148, 733-8.
- Khansari, D. N., Murgo, A. J., & Faith, R. E. (1990). Effects of stress on the immune system. *Immunology Today*, 11, 170-5.
- Lesserman, J., Jackson, E. D., Petitto, J. M., Golden, R. N., Silva, S. G., Perkins, D. O., Cai, J., Folds, J. D., & Evans, D. L. (1999). Progression to AIDS: The effects of stress, depressive symptoms, and social support. *Psychosomatic Medicine*, 61, 397-406.
- Liu, C., Johnson, L., Silvestre, A., Visscher, B., & Jacobson, L. P. (2006). Predictors for lower quality of life in the HAART era among HIV-infected men. *Journal of Acquired Immune Deficiency Syndrome*, 42, 470-77.
- Motivala, S. J., Hurwitz, B. E., Llabre, M. M., Klimas, N. G., Fletcher, M. A., Antoni, M. H., LeBlanc, W. G., & Schneiderman, N. (2003). Psychological distress is associated with decreased memory helper T-cell and B-cell counts in pre-AIDS HIV seropositive men and women but only in those with low viral load. *Psychosomatic Medicine*, 65, 627-35.
- Mulder, C. L., Antoni, M. H., Emmelkamp, P. M. G., Veugelers, P. J., Sandfort, T. G. M., va de Vijver, F. A. J. R., & de Vries, M. G. (1995). Psychosocial group intervention and the rate of decline of immunological parameters in asymptomatic HIV-infected homosexual men. *Psychother Psychosom*, 63, 185-92.
- Mustafa, T., Sy, F. S., Macera, C. A., Thompson, S. J., Jackson, K. L., Selassie, A., & Dean, L. L. (1999). Association between exercise and HIV disease progression in a cohort of homosexual men. *Annals of Epidemiology*, 9, 127-31.
- Nair, M. P. N., Mahajan, S., Hou, J., Sweet, A. M., & Schwartz, S. A. (2000). The stress hormone, cortisol, synergizes with HIV-1 gp-120 to induce apoptosis of normal human peripheral blood mononuclear cells. *Cell and Molecular Biology*, 46, 1227-38.
- O'Connor, T. M., O'Halloran, D. J., & Shanahan, F. (2000). The stress response and the hypothalamic-pituitary-adrenal axis: From molecule to melancholia. *Quarterly Journal of Medicine*, 93, 323-33.
- Petitto, J. M., Lesserman, J., Perkins, D. O., Stern, R. A., Silva, S. G., Gettes, D., Zheng, B., Folds, J. D., Golden, R. N., & Evans, D. L. (2000). High versus low basal cortisol secretion in asymptomatic, medication-free HIV infected men: Differential effects of severe life stress on parameters of immune status. *Behavioral Medicine*, 25, 143-51.
- Robinson, F. P., Mathews, H. L., & Witek-Janusek, L. (2003). Psycho-endocrine-immune response to mindfulness-based stress reduction in individuals with HIV: A quasiexperimental study. *The Journal of Alternative and Complementary Medicine*, 9, 683-94.
- Safren, S. A., Rdomsky, A. S., Otto, M. W., & Salomon, E. (2002). Predictors of psychological well-being in a diverse sample of HIV-positive patients receiving HAART. *Psychosomatics*, 43, 478-85.
- Schmitz, M. F., & Crystal, S. (2000). Social relations, coping, and psychological distress among persons with HIV/AIDS. *Journal of Applied Psychology*, 30, 665-85.
- Tuck, I., McCain, N. L., & Elswick, R. K. (2001). Spirituality and psychosocial factors in persons living with HIV. *Journal of Advanced Nursing*, 33, 776-83.
- Vanable, P. A., Carey, M. P., Blair, D. C., & Littlewood, R. A. (2006). Impact of HIV related stigma on health behaviors and psychological adjustment among HIV-positive men and women. *AIDS and Behavior*, 10, 473-82.
- Vedhara, K., & Irwin, M. (2005). *Human Psychoneuroimmunology*. New York: Oxford University Press.
- Webster, J. I., Tonelli, L., & Sternberg, E. M. (2002). Neuroendocrine regulation of immunity. *Annual Review of Immunology*, 20, 125-63.
- Wolf, T., Balson, P., Morse, E., Simon, P., Gaumer, R., Dralle, P., & Williams, M.

- (1991). Relationship of coping style to affective state and perceived social support in asymptomatic and symptomatic HIV-infected persons: Implications for clinical management. *Journal of Clinical Psychiatry*, 52, 171-173.
- Workman, A., & La Via, M. F. (1987). T-lymphocyte proliferation: Effects of stress and stress response style on medical students taking national board examinations. *Clinical Immunology and Immunopathology*, 43, 308-13.