

# SOCIAL RELATIONSHIPS AND THE PROGRESSION OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION: A REVIEW OF EVIDENCE AND POSSIBLE UNDERLYING MECHANISMS<sup>1,2</sup>

Gregory E. Miller, Ph.D. and Steve W. Cole, Ph.D.  
University of California, Los Angeles

## ABSTRACT

*We review studies examining the quality and quantity of social relationships as potential risk factors for differential progression of human immunodeficiency virus (HIV) infection. Several well-conducted prospective studies suggest that the health effects associated with the presence of supportive social relationships vary according to disease stage and mode of transmission. For gay or bisexual males in the early stages of infection, the presence of supportive social relationships appears to be a risk factor for accelerated disease progression. For individuals in the later stages of infection and those who acquire HIV via intravenous drug use or transfusion, supportive social relationships appear to be associated with health protective effects similar to those observed in other disease settings. We consider a variety of potential explanations for accelerated disease progression in gay men with extensive networks of personal relationships.*

(*Ann Behav Med* 1998, 20(3):181–189)

## INTRODUCTION

The presence of supportive social relationships is associated with improved physical health and psychological well-being. Prospective studies have documented higher rates of morbidity and mortality among individuals who having few or no supportive social relationships (1,2), and these effects extend to cause-specific disease outcomes including coronary heart disease, cerebrovascular disease, cancer, and major depression (3–6). The impact of social relationships on overall physical health is comparable in magnitude to the effects of other well-established risk factors such as cigarette smoking, a sedentary lifestyle, obesity, and high blood lipid levels (7). Despite these health-promoting properties, an emerging body of evidence also indicates that close relationships can have deleterious effects on mental and physical health under certain circumstances. These effects have been most extensively documented for mental health outcomes. Among patients who are recovering from major depression or schizophrenia, the presence of intrusive and emotionally overinvolved family members has proven to be one of the best predictors of relapse (8,9). Research

also suggests that the presence of negative or stressful social interactions is often a stronger predictor of well-being than is the presence of positive social interactions (10). Few studies have examined the impact of negative or stressful close relationships on physical health outcomes, but stressful close relationships have been associated with poorer recovery from myocardial infarction (11–13).

Several prospective studies have examined the role of social relationships in the context of infection with human immunodeficiency virus (HIV) Type 1. Some of these studies have documented the positive effects of social relationships on health expected on the basis of previous research. However, research has also consistently identified negative effects under certain circumstances. In this article, we review existing studies of social support and HIV progression and consider the circumstances under which close social relationships are associated with positive versus negative health outcomes and the mechanisms through which close relationships could heighten risk for accelerated disease progression.

## SOCIAL RELATIONSHIPS AND HIV PROGRESSION

A computerized literature search of the Medline and Psychological Abstracts databases identified ten studies examining the role of social relationships in the progress of HIV infection. Keywords used were social support, HIV/AIDS, CD4 T lymphocytes, disease progression, and immune function. These studies vary substantially in research design, patient population, methods used to assess social relationships, and the markers of disease progression that serve as outcomes. Table 1 summarizes each study on these dimensions.

The particular parameter of social relationships measured represents one of the critical differences among these studies. Objective measures of social relationship status, which assess the size of an individual's social network and the frequency of his/her contact with that network, can be distinguished from subjective measures, which assess the quality of one's personal relationships and the degree to which the individual perceives that emotional, informational, and tangible assistance is available from network members. Although objective and subjective measures are typically correlated, their relationship is moderately strong at best (e.g.  $r$  typically  $< .40$ ; see 14). Another important characteristic differentiating studies is the research design utilized.

## Cross-Sectional Studies

Three investigations employed cross-sectional research designs, correlating measures of disease progression with social relationship measures obtained on the same occasion. Persson and colleagues (15) studied 47 gay and bisexual men at various stages of HIV infection and found that self-reports of infrequent social activity were associated with lower CD4 T lymphocyte levels but

<sup>1</sup> Preparation of this manuscript was supported in part by a National Research Service Award from the National Institute of Mental Health (F31 MH11366) to Gregory E. Miller. Steve W. Cole was supported by funding from the UCLA AIDS Institute (Clinical Science Research Grant 542476-18010) and the Norman Cousins Program in Psychoneuroimmunology.

<sup>2</sup> We thank Edith Chen and Margaret E. Kemeny for their helpful comments on earlier versions of this manuscript.

Reprint Address: G.E. Miller, Ph.D., Department of Psychology, Carnegie Mellon University, Pittsburgh, PA 15213.

© 1998 by The Society of Behavioral Medicine.

TABLE 1  
Studies Examining the Role of Social Relationships in HIV Progression

Study	Sample at Study Entry	Duration of Study	Measures of Social Support	Confounders Controlled For	Outcome Measures	Summary of Key Findings
<b>Cross-Sectional Studies</b>						
Persson et al. (1994) (15)	47 gay, bisexual males at all stages of disease	N/A	OBJ: Social network size Frequency of contact with network members SUBJ: Quality of social network Adequacy of social activity	Age Time since seroconversion	CD4 levels AIDS symptoms	Lower CD4 levels were associated with infrequent social activity and with the perception that social activity was inadequate. Social network size and quality of network were unrelated to CD4 levels. None of the social support measures were related to symptomatology.
Goodkin et al. (1992) (17)	62 gay, bisexual males with Category B infection	N/A	SUBJ: Perceived social support	Alcohol use Drug use Nutrition	NKCA	Perceived social support was related to higher NKCA among subjects with low levels of life stress but unrelated among subjects with high levels of life stress.
Straits-Troster et al. (1994) (16)	88 heterosexual and gay males, none of whom were IV drug users, at all stages of disease	N/A	SUBJ: Loneliness	Disease stage Medication use	CD4 levels	Higher levels of loneliness were associated with lower CD4 levels.
<b>Prospective Natural History Studies</b>						
Blomkvist et al. (1994) (21)	33 hemophilic males with Category B infection	7 years	SUBJ: Extent to which future activities would involve others or be alone Adequacy and availability of emotional support	Initial CD4 levels Age	AIDS mortality	Subjects who reported at baseline that they would engage in most future activities with others had higher levels of HIV mortality over the follow-up period than subjects who planned to engage in future activities alone. Adequacy, availability of emotional support were unrelated to mortality.
Miller et al. (1997) (14)	205 gay, bisexual males with Category B infection	3 years	OBJ: Social network size Frequency of contact with network members SUBJ: Loneliness	Initial CD4 levels Drug use Alcohol use Medication use Sexual behavior Sleep, exercise habits Negative affect Symptom profile	CD4 decline AIDS morbidity AIDS	Lower levels of loneliness at baseline predicted more rapid declines in CD4 levels over the follow-up period but were not associated with morbidity or mortality. Social network variables were not related to any of the outcome measures.
Patterson et al. (1996) (18)	414 heterosexual, gay males at all stages of disease	5 years	OBJ: Social network size SUBJ: Emotional support Informational support	Initial CD4 levels Depression Symptom profile	Stage advance in CD4 decline Stage advance in symptom onset AIDS morbidity AIDS mortality	Among subjects who were asymptomatic at baseline, larger social network sizes were associated with faster progression to AIDS-defining symptoms. Among subjects who were symptomatic or had AIDS at baseline, however, larger network sizes and higher ratings of emotional support predicted longer survival times from baseline.

TABLE 1  
Continued

Study	Sample at Study Entry	Duration of Study	Measures of Social Support	Confounders Controlled For	Outcome Measures	Summary of Key Findings
Prospective Natural History Studies (continued)						
Patterson et al. (1996) (18) (continued)						None of the social relationship measures were associated with AIDS morbidity or with CD4 changes over the course of the follow-up period.
Perry et al. (1992) (22)	221 men and women, 75% gay or lesbian, 20% IV drug users, all with Category B infection	1 year	SUBJ: Perceived social support	Initial CD4 levels	CD4 levels CD8 levels CD4:CD8 ratio Symptom onset	No cross-sectional or prospective relations between perceived social support and outcomes measures.
Persson et al. (1994) (19)	75 gay, bisexual males with Category B infection	6 years	SUBJ: Social anchorage	Initial CD4 levels	CD4 levels	Subjects who felt greater affinity with members of their social network showed more rapid declines in CD4 numbers than subjects who felt less affinity.
Solano et al. (1993) (23)	100 men and women, 77% IV drug users, 10% gay or lesbian, all with Category B infection	1 year	OBJ: Social network size SUBJ: Loneliness Perceived social support	Initial CD4 levels	CD4 levels Symptom onset	Among subjects with fewer than 400 CD4 cells/mm <sup>3</sup> at study entry, lower perceived social support was associated with faster symptom onset but not with changes in CD4 levels. Loneliness and network size were unrelated to both of the outcome measures.
Theorell et al. (1995) (20)	37 hemophiliac males at all stages of disease	5 years	SUBJ: Availability of emotional support during crises	Initial CD4 levels	CD4 levels AIDS morbidity AIDS mortality	Individuals who believed social and emotional support would be available to them during crises had slower CD4 declines than individuals who did not. Support variables were not related to morbidity or mortality.

*Note:* A study was coded as cross-sectional if all data for a given subject were collected at one time point; otherwise it was coded as prospective natural history. Information not provided in the table was missing from the original report. Category B = Category B HIV infection (Clinical Latency Period); CD4 = Helper/inducer T lymphocytes; CD8 = Cytolytic T lymphocytes; N/A = Not applicable; NKCA = Natural killer cell activity; OBJ = Objective measures of social relationship status; SUBJ = Subjective measures of social relationship status.

not with differences in acquired immune deficiency syndrome (AIDS)-related symptomatology. These associations were independent of age and length of time since seroconversion. Straits-Troster and colleagues (16) found that loneliness was associated with lower CD4 T lymphocyte levels in a sample of 88 gay and heterosexual men at various stages of HIV progression. These findings were not explained by differences in medication use. Goodkin and colleagues (17) studied 62 asymptomatic gay and bisexual males and reported that high subjective social support was associated with higher natural killer cell cytotoxicity among subjects with low levels of life stress but not among those with higher levels of life stress. The relationship between social support and natural killer cell cytotoxicity was independent of alcohol and drug use and nutrition. It should be noted that natural killer cell cytotoxicity is not a recognized indicator of HIV progression, and

Goodkin et al. did not find similar results for indicators such as CD4 T lymphocyte levels.

In summary, the evidence from cross-sectional studies suggests that HIV-infected individuals who report subjectively satisfying social relationships and report frequent social contact may have higher CD4 T lymphocyte levels than their lonely, socially inactive peers (15,16). However, it is not possible to draw causal conclusions from these studies. Although cross-sectional designs are useful in generating hypotheses for subsequent prospective research, they are vulnerable to confounding and reverse-directionality errors. The latter is a particularly serious issue in the context of HIV infection because disease progression itself may alter social behavior (e.g. those too ill to leave home or too fatigued to interact with others will naturally suffer from reduced social contact). Prospective natural history studies provide a stronger basis for

causal inferences by using differences in baseline social relationship status to predict changes in disease status over time while controlling for any potential differences in disease status at the time that social relationships are assessed.

### Prospective Natural History Studies

Seven of the ten studies utilized prospective natural history designs. These investigations typically assessed social relationships and disease status at a baseline measurement and then followed subjects for a number of years, collecting information about disease progression on one or more follow-up occasions.

Miller and colleagues (14) found that among 205 asymptomatic gay and bisexual men, lower levels of baseline loneliness predicted more rapid declines in CD4 level over a three-year follow-up. This association was independent of baseline CD4 values, high-risk sexual behavior, alcohol and drug use, exercise and sleep habits, medication utilization, and depressed mood. No differences in time to AIDS onset or time to AIDS-specific mortality emerged as a function of loneliness, and measures of social network size and contact were unrelated to HIV progression.

Patterson and colleagues (18) studied 414 heterosexual and gay men and reported that the association between social relationships and HIV progression varied according to disease stage and according to the endpoint examined. Among participants who were asymptomatic at baseline, larger social network sizes were associated with faster progression to HIV-related symptoms over follow-up periods ranging from one to five years. In contrast, among those participants who were symptomatic or had AIDS at baseline, larger network sizes and higher ratings of emotional support predicted longer survival times from study entry. Despite these significant differences in clinical outcomes, none of the social relationship measures were associated with changes in CD4 T lymphocyte levels. All of Patterson et al.'s findings remained statistically significant after adjustment for participants' CD4 T lymphocyte levels and HIV-related symptomatology at baseline.

In an interim report from an ongoing prospective study of 75 asymptomatic gay and bisexual men, Persson and colleagues (19) found that individuals who perceived themselves as having a strong affinity with members of their social network showed more rapid declines in CD4 T lymphocytes during a five- to six-year follow-up than did those who perceived themselves as having a weak affinity. These effects were independent of baseline CD4 T lymphocyte levels.

Theorell and colleagues (20) studied 37 hemophiliacs who varied in disease stage at study entry. Subjects who reported at baseline that social and emotional support would not be available to them during crisis situations had more rapid declines in CD4 T lymphocytes over a five-year follow-up than did those who believed that such support would be available. These findings were not accounted for by differences in CD4 levels at study entry. No differences in AIDS-related morbidity or mortality emerged as a function of perceived support.

Blomkvist and colleagues (21) followed 33 asymptomatic hemophiliacs for seven years and found that individuals who predicted at baseline that they would engage in the majority of their future leisure activities with others had higher HIV mortality rates than individuals who predicted they would engage in the majority of such activities by themselves. The groups did not differ in CD4 T lymphocyte levels or age at study entry. Participants' ratings of the availability and adequacy of social support were unrelated to HIV mortality; only predictions of future time spent with others predicted HIV mortality.

Perry and colleagues (22) recruited a sample of 221 males and females who were infected with HIV, 75% of whom were gay, lesbian, or bisexual and the remainder of whom were intravenous drug users. All participants were asymptomatic at the time of study entry. Perry and colleagues found no relationship between perceived social support at baseline and serologic measures of disease progression (CD4 T lymphocyte levels, CD8 T lymphocyte levels, CD4:CD8 ratio) of males collected six and twelve months later.

Solano and colleagues (23) followed a sample of 100 asymptomatic males and females for a one-year period. This sample was comprised of intravenous drug users (77%), gay men and bisexual individuals (10%), and heterosexuals (13%). Among subjects who entered the study with CD4 T lymphocyte levels lower than 400 per mm<sup>3</sup>, lower perceived social support at baseline predicted greater HIV symptomatology at one year but was unrelated to changes in CD4 levels. Among subjects who entered the study with CD4 levels greater than 400 per mm<sup>3</sup>, social support was unrelated to measures of disease progression. Baseline loneliness and network size also were unrelated to measures of disease progression.

### Summary of Prospective Natural History Studies

On superficial examination, the findings from the seven prospective natural history studies of social relationships and HIV appear contradictory. Three studies found that the presence of satisfying social relationships was associated with accelerated progression of HIV/AIDS, as indexed by more rapid declines in CD4 T lymphocyte numbers (14,19) and elevated HIV-specific mortality (21). Two found that the perception of available social support available was associated with slower disease progression, as measured by slower CD4 T lymphocyte declines (20) and symptom onset (23). One study found mixed results, reporting that among asymptomatic individuals, the presence of social relationships was associated with faster progression to AIDS-defining symptoms, whereas among participants who were symptomatic or had AIDS, the presence of social relationships and emotional support predicted decreases in HIV mortality (18). The final study found no relationship between perceptions of social support and CD4 T lymphocyte changes over one year of follow-up (22).

A closer examination of these findings reveals that two factors—the stage of infection and the likely mode of transmission—differentiate studies that find negative versus positive relationships between social characteristics and HIV progression. Studies that identified negative effects of social relationships on disease status sampled primarily individuals experiencing Category B infection, the asymptomatic or “clinical latency” phase of disease that follows seroconversion but can last for extended periods of time (14,18,19,21). Of the studies that identified positive effects of social relationships on health, one utilized subjects who were at later stages of the disease (18), and one used subjects at all stages of infection but did not examine separately early- and late-stage subjects (20). Only one study that found positive effects utilized exclusively subjects with Category B infection (23), but participants in this study were followed up for only one year, providing little opportunity to observe marked changes in immunologic or clinical markers of disease status.

With regard to source of initial HIV infection, three of the four studies that identified negative effects of social relationships utilized samples of gay and bisexual men or samples that were predominately composed of gay and bisexual males but had a small percentage of heterosexual males (14,18,19). One study with hemophiliacs also found negative effects (21). Neither of the

studies that included intravenous drug users found that social relationships were a risk factor for more rapid disease progression: one of them (23) found that social support was associated with less HIV symptomatology at a one-year follow-up period, and the other found perceived social support to be uncorrelated with immunologic measures of disease progression (22).

Subjective versus objective measures of social relationships did not differentiate between studies that identified negative versus positive health effects. Three of the four studies that identified negative health effects did so utilizing subjective measures of social relationship status. These measures assessed feelings of loneliness (14), affinity with their social network (19), and estimates of how many future activities would involve other people (21). One study that identified negative effects of social relationships utilized an objective measure, social network size (18). Two of three studies that found positive health effects used subjective measures assessing perceived availability of social support (20,23); the third study found that both a subjective measure (the availability of emotional support) and an objective measure (network size) predicted better health outcomes (18).

Thus, existing prospective studies of social relationships and HIV progression suggest that the presence of supportive social relationships is associated with negative health outcomes in samples comprised of gay or bisexual males who are in earlier stages of the infection when their social relationship status is assessed (14,18,19) and the presence of supportive social relationships is associated with positive health outcomes among individuals at more advanced stages of the infection (symptomatic or AIDS-diagnosed) when their social relationship status is assessed (18,20,23). Positive effects of social relationships seem to cut across populations, having been observed in samples comprised of hemophiliacs (20), heterosexual and gay males (18), and intravenous drug users, gay and bisexual males, and lesbians (23). These findings are consistent with the cross-sectional studies reviewed earlier, which examined participants who were at both early and late stages of HIV infection and found that social activity covaried with high CD4 T lymphocyte levels (15,16).

#### **MECHANISMS LINKING SUPPORTIVE SOCIAL RELATIONSHIPS TO ACCELERATED HIV PROGRESSION**

Several reviews have examined the mechanisms through which social relationships might exert a positive impact on physical health (7,24). Two broad hypotheses have been advanced. Behavioral hypotheses emphasize the role that social relationships play in fostering healthy behaviors such as exercise, health service utilization, adherence to medication and other treatment regimens, and abstinence from alcohol, drug, and cigarette use (24). Stress-buffering hypotheses emphasize the protective effects that social relationships have on emotional and physiological responses to stressful experiences (24). Several laboratory studies have shown that the presence of supportive others can blunt autonomic nervous system and hypothalamic-pituitary-adrenal axis responses to acute mental stress (25,26). Both types of mechanisms could conceivably influence HIV disease progression, because HIV disease represents a powerful personal stressor as well as a significant occupational, financial, medical, legal, and treatment-compliance challenge.

Much less research has been done to clarify the mechanisms by which social relationships might negatively affect physical health. In the remainder of this article, we consider some of the behavioral and social factors that may explain the negative

association between social relationships and disease progression in HIV-seropositive gay and bisexual men. This list is by no means exhaustive, but it is intended to provide examples of biobehavioral processes that have proven important in understanding the natural course of HIV infection and then consider their applicability to the issue of social relationships and HIV progression.

#### **High-Risk Sexual Behavior**

Individuals who possess large networks of supportive social relationships may engage in risky sexual behavior at a higher frequency than more socially isolated individuals. Those with extensive networks of close personal relationships would thus be at increased risk for both infection with multiple HIV strains and for coinfection with pathogens that give rise to sexually transmitted diseases. Both infection with multiple strains of HIV and coinfection with non-HIV microbial pathogens appear to accelerate CD4 decline and AIDS morbidity and mortality (27,28). Although this hypothesis could potentially explain an association between social relationship variables and HIV progression in gay men, it would not explain why social relationship status is independent of disease progression in intravenous drug users (22,23). It is possible that social relationship parameters and high-risk sexual behaviors are more directly related in gay men than in intravenous drug users. At least one study (14) has measured and controlled for rates of anal-receptive intercourse without a condom (the sexual behavior most strongly related to HIV transmission) and still identified a negative effect of social relationships. However, given the difficulties in reliably identifying and measuring high-risk sexual behaviors, associations between risky sexual behavior and social network parameters remain a potentially powerful explanation for the negative effects observed in gay men.

#### **Socially Facilitated Health-Compromising Behavior**

Individual social relationships and membership in social groups could facilitate the performance of health-compromising behaviors that impair immune response to HIV or render the individual vulnerable to coinfection with other pathogens. Health-compromising behaviors known to alter immune system function include sleep deprivation (29); alcohol, drug, and tobacco consumption (30,31); and non-adherence to medication regimens. However, available research indicates that health-compromising behaviors are more prevalent among socially isolated, unsupported individuals than among socially embedded persons (32). The extent to which social relationships are associated with health-compromising behaviors in HIV-infected populations has not been systematically examined. However, in one of the prospective studies reviewed above (14), both objective and subjective measures of social relationships were unrelated to health behavior practices (including drug, alcohol, and tobacco use), and negative effects of social relationship status on HIV progression emerged despite controls for these health-compromising behaviors.

#### **Cumulative Exposure to AIDS-Related Bereavement**

HIV-infected gay men who possess extensive networks of meaningful personal relationships may experience more rapid HIV progression because of greater personal exposure to the continuing tragedies of the AIDS epidemic. HIV/AIDS has dramatically increased the prevalence of bereavement in the gay community. Martin and Dean (33) found that 27% of their sample of gay men in New York City had lost a partner or close friend to AIDS by 1985. The average number of losses was six (34). A number of studies have found that AIDS-related bereavement of a close friend or

partner is prospectively associated with altered immune function and CD4 T lymphocyte declines (35–37). Bereavement is associated with elevated risk of morbidity and mortality in other conditions as well (38–40). It is possible that gay men with extensive networks of close personal relationships may experience the negative health effects associated with bereavement more frequently than those who lack supportive close relationships.

One advantage of this hypothesis is its capacity to explain how social relationships might impact HIV progression differently in the three primary populations studied—gay and bisexual males, intravenous drug users, and hemophiliacs. The social networks of HIV-seropositive gay men are likely to include substantial numbers of other HIV-seropositive gay men, and greater involvement with this network would expose such individuals to higher rates of AIDS-related bereavement. In contrast, intravenous drug users and hemophiliacs may not possess such large numbers of close friends and romantic partners who are HIV-seropositive. As a result, the negative effects of social relationships on disease progression might be less pronounced in these groups.

Only one published study has evaluated this hypothesis. As part of their prospective study on loneliness and HIV progression, Miller et al. (14) assessed the number of close friends and primary romantic partners each participant had lost to AIDS over the course of the three-year follow-up period. Bereavement was not associated with either baseline CD4 levels or changes in CD4 levels during the follow-up period. Mediation analyses indicated that bereavement rates did not account for the finding that lower levels of baseline loneliness predicted more rapid declines in CD4 level over the follow-up period.

### Physiologic Burden of Chronic Caregiving

Another possibility is that gay men who possess large networks of supportive relationships more often find themselves providing care for an HIV-infected individual (e.g. a close friend or romantic partner). Individuals caring for the chronically ill experience substantial psychological stress as well as decrements in immunologic function, including slower wound healing (41) and blunted antibody responses to influenza vaccination (42). Such deficits could conceivably impair resistance to HIV or opportunistic pathogens.

Like the bereavement exposure hypothesis, this account offers a potential explanation for why the negative effects of social relationships might be most pronounced in the gay and bisexual community, where the high concentration of HIV-infected individuals would increase the probability that one will assume caregiving responsibilities for a seriously ill close friend or romantic partner. Negative effects of social relationships might not be so pronounced in the hemophiliac and intravenous drug user communities because fewer close friends or partners may be stricken with AIDS and require substantial care. Unlike the bereavement exposure hypothesis, however, all of the evidence suggesting that immunologic deficits accompany caregiving has been conducted with healthy individuals. It is thus unclear whether any resulting alterations in immune function would have relevance for the progression of HIV infection.

### Effects of Disease Progression on Social Behavior

Psychological and behavioral concomitants of disease progression may alter social behavior and thus induce a correlation between social involvement and disease status. Research has shown that HIV-seropositive gay men who are approaching AIDS diagnosis or death actively narrow their social networks in order to

focus on their most significant relationships (43). Such a dynamic might lead to the paradoxical finding that both smaller social network size and higher satisfaction with social relationships are associated with HIV progression. This prediction is born out to some extent in the prospective studies of Miller et al. (14) and Persson et al. (19), but it remains counter to the findings of Patterson et al. (18). Although this account can explain the negative association between social relationships and disease progression in late-stage HIV infection, it does not parsimoniously explain either the negative association observed in early stages of the infection (14,18,19) or the positive association observed in late stages (18,20). Moreover, it is not clear if this account should produce prospective predictions of disease progression (rather than cross-sectional correlations) or how it would explain differential findings for gay men versus intravenous drug users and hemophiliacs. No research has examined whether similar social relationship dynamics occur in HIV infection among intravenous drug users and hemophiliacs.

HIV infection may also induce less voluntary modes of social withdrawal or social selectivity. Advanced HIV infection can produce profound neuropsychiatric impairments that manifest themselves as changes in affect and cognition and loss or weakening of social relationships (44,45). Although such a dynamic could explain the negative association between social relationships and disease progression during late-stage HIV infection (when neuropsychiatric impairment becomes most prevalent), it would not explain the negative relationships observed during early-stage infection or the differential results for gay men versus intravenous drug users and hemophiliacs.

### Personality and Temperament

Differences in social behavior are related to, and in some cases even define, major dimensions of personality and temperament (e.g. Introversion–Extroversion, Socially Inhibited Temperament, Agreeableness–Hostility) (46–48). Some of these personality characteristics have also been linked to differences in autonomic nervous system and hypothalamic-pituitary-adrenal axis activity that may be relevant to disease resistance (47,48). Unfortunately, measures of temperament and its physiologic correlates have not been collected in most studies of HIV progression, so it is difficult to determine whether these characteristics can account for the observed association between social relationships and the progression of HIV infection. It is also not clear how such hypotheses would account for the differential findings in early- versus late-stage disease or in gay men versus intravenous drug users and hemophiliacs.

### LIMITATIONS AND QUALIFICATIONS

Although the available data suggest that social relationships may have negative implications for the health of individuals infected with HIV, this conclusion is best viewed as tentative until corroborative evidence is available. Only seven prospective studies have been conducted in this area, and in three of them, the association between social relationships and HIV progression was not the sole focus of the investigation. Additionally, most studies have followed too few patients for too short of a period of time to detect prospective associations between social relationships and HIV disease progression. Other important limitations of this literature are the considerable variability in how social relationships have been conceptualized and measured across studies and the variability in how HIV progression has been operationalized (i.e. both as biological markers of disease progression such as CD4

levels and clinical endpoints such as time to AIDS onset and mortality).

### DIRECTIONS FOR FUTURE RESEARCH

An important next step will be for investigators to replicate the central pattern of results emerging from existing research—that large social networks and/or intimate personal relationships may have negative implications for the health of individuals who are at the early stages of HIV infection, particularly if they are gay or bisexual, and more positive implications for the health of individuals during later stages of the disease. Several technical features can improve the rigor of future studies and ensure the validity of findings that emerge. Researchers should study moderately sized samples (e.g. at least 100–250 individuals) of HIV-seropositive individuals beginning in the early stages of infection (49). These individuals should be followed for extended periods of time (e.g. four years or more) to allow clinically meaningful changes in disease status to unfold. Finally, efforts should be made to measure both biologic mediators of disease progression (e.g. CD4 T lymphocyte numbers, viral load) and clinically relevant endpoints, such as AIDS onset and HIV-specific mortality.

Researchers could gain a more complete understanding of how social relationships operate in the context of HIV infection by including a comprehensive assessment of social relationship measures in each study. A discussion of the conceptual and methodological issues involved in such an assessment is beyond the scope of this review, but we refer the interested reader to other discussions of this issue (50). At the minimum, future studies in this area should include objective measures of social relationship status, which assess the size of an individual's social network and the frequency of his/her contact with that network, and subjective measures, which assess the quality of one's personal relationships and the degree to which the individual perceives that emotional, informational, and tangible assistance is available from network members. At least one objective measure of social relationship status has been validated with HIV-seropositive gay and bisexual men (51), and it has been shown to predict declines in CD4 T lymphocyte levels over time (14). We are not aware of subjective measures that have undergone extensive validation studies with HIV-seropositive samples, but the Social Support Questionnaire (52) has been validated in other medically ill populations and has shown some predictive validity in the context of HIV infection (23). Supplementing these more traditional measures with interview techniques, observational measures of social interaction, and daily diary studies may also prove useful, as these methods would yield important information about the role that social relationships play in the everyday existence of HIV-seropositive individuals and perhaps suggest additional pathways through which social relations could relate to disease progression.

It also will be important for investigators to measure more directly the various behavioral and biological mechanisms through which supportive social relationships might increase risk for negative health outcomes. Additional prospective natural history studies which assess putative behavioral and biological mediators at multiple timepoints are needed. Another promising context for conducting research on biological mediators is simian immunodeficiency virus (SIV) infection. Capatano and colleagues have conducted two studies of social factors in SIV infection and find that disruption of early life rearing conditions is predictive of shorter latencies to leukopenia and lymphopenia following primary SIV infection (53), and lower rates of affiliative social behavior and higher rates of agonistic social behavior are associ-

ated with poorer SIV-specific immunoglobulin G responses and elevated SIV-specific mortality one year postinfection (54). These data, coupled with the highly social nature of primates, suggest that SIV primate models may provide a unique opportunity to examine the biological mechanisms underlying social factors' effects on immunodeficiency-inducing retroviral infections. An additional advantage of utilizing non-human primate models is that investigators can experimentally manipulate psychosocial variables (e.g. rearing conditions, social isolation, social interaction) that ethically and practically are impossible to manipulate in humans.

### CONCLUSIONS

Studies now suggest that characteristics of the social environment may be associated with differential progression of HIV infection. Although large and subjectively satisfying social networks are associated with better health outcomes during the later stages of disease, they appear to be associated with accelerated disease progression for gay men and bisexuals in the early stages of disease. The basis for these negative effects is not clear, although differences in sexual behavior, socially facilitated health-compromising behavior, exposure to bereavement, caregiving stress, and physiological correlates of social behavior and personality could conceivably play a role. Although we have attempted to present the strengths and weaknesses of each of these explanations from a conceptual point of view, very few data exist to either support or refute any specific hypothesis.

These data may have important implications for psychosocial research in other disease settings. Because of their capacity to foster health-protective behavior and buffer the individual from psychosocial stress, social relationships have primarily been viewed as having a positive influence on physical and mental health. Stressful aspects of social relationships have been hypothesized to heighten vulnerability to disease or interfere with recovery from it (11), but little research has emerged to support these assertions. The studies reviewed here are among the first to demonstrate that the presence of supportive social relationships may have negative implications for physical health. The differential effects of social relationships across populations and disease stages may provide insight into factors that govern when social relationships exert protective versus deleterious effects on health. Further research will provide deeper insights into the mechanisms by which this occurs.

### REFERENCES

- (1) Berkman LF, Syme SL: Social networks, host resistance, and mortality: A nine-year follow-up of Alameda County residents. *American Journal of Epidemiology*. 1979, 109:186–204.
- (2) Breslow L, Enstrom JE: Persistence of health habits and their relationship to mortality. *Preventive Medicine*. 1980, 9:469–483.
- (3) House JS, Robbins C, Metzner HL: The association of social relationships and activities with mortality: Prospective evidence from the Tecumseh Community Health Study. *American Journal of Epidemiology*. 1982, 116:123–140.
- (4) Kessler RC, McLeod JD: Social support and mental health in community samples. In Cohen S, Syme SL (eds), *Social Support and Health*. New York: Academic Press, 1994, 219–240.
- (5) Schoenbach VJ, Kaplan BH, Fredman L, Kleinbaum DG: Social ties and mortality in Evans County, Georgia. *American Journal of Epidemiology*. 1986, 123:577–591.
- (6) Vogt TM, Mullooly JP, Ernst D, Popoe CR, Hollis JF: Social networks as predictors of ischemic heart disease, cancer, stroke, and hypertension: Incidence, survival, and mortality. *Journal of Clinical Epidemiology*. 1989, 45:659–666.

- (7) House JS, Landis KR, Umberson D: Social relationships and health. *Science*. 1992, 241:540-545.
- (8) Hooley JM: Expressed emotion: A review of the critical literature. *Clinical Psychology Review*. 1985, 5:119-139.
- (9) Kavanagh DJ: Recent developments in expressed emotion and schizophrenia. *British Journal of Psychiatry*. 1992, 160:601-620.
- (10) Rook KS: The negative side of social interaction: Impact on psychological well-being. *Journal of Personality and Social Psychology*. 1984, 46:1097-1108.
- (11) Burg MM, Seeman TE: Families and health: The negative side of social ties. *Annals of Behavioral Medicine*. 1994, 6:109-115.
- (12) Taylor CB, Bandura A, Ewart CK, Miller NH, DeBusk RH: Exercise testing to enhance wives' confidence in their husbands' cardiac capability soon after clinically uncomplicated acute myocardial infarction. *American Journal of Cardiology*. 1985, 55:635-638.
- (13) Wishnie HA, Hackett TP, Cassem NH: Psychological hazards of convalescence following myocardial infarction. *Journal of the American Medical Association*. 1971, 215:1292-1296.
- (14) Miller GE, Kemeny ME, Taylor SE, Cole SW, Visscher B: Social relationships and immune processes in HIV seropositive gay and bisexual men. *Annals of Behavioral Medicine*. 1997, 19:139-151.
- (15) Persson L, Gullberg B, Hanson BS, Moestrup T, Ostergreen PO: HIV infection: Social network, social support, and CD4 lymphocyte values in infected homosexual men in Malmo, Sweden. *Journal of Epidemiology and Community Health*. 1994, 48:580-585.
- (16) Straits-Troster KA, Patterson TL, Semple SJ, et al: The relationship between loneliness, interpersonal competence, and immunologic status in HIV-infected men. *Psychology and Health*. 1994, 9:205-219.
- (17) Goodkin K, Blaney NT, Feaster D, et al: Active coping style is associated with natural killer cell cytotoxicity in asymptomatic HIV-1 seropositive homosexual men. *Journal of Psychosomatic Research*. 1992, 6:635-650.
- (18) Patterson TL, Shaw WS, Semple SJ, et al: Relationship of psychosocial factors to HIV disease progression. *Annals of Behavioral Medicine*. 1996, 18:30-39.
- (19) Persson L, Gullberg B, Hanson BS, Moestrup T, Ostergreen PO: Influences of social network and social support on the development of the CD4-lymphocyte level—A prospective population study of HIV-infected homo- and bi-sexual men in Malmo, Sweden. Second International Conference on Psychosocial Aspects of AIDS. Brighton, UK: 1994.
- (20) Theorell T, Blomkvist V, Jonsson H, et al: Social support and the development of immune function in human immunodeficiency virus infection. *Psychosomatic Medicine*. 1995, 57:32-36.
- (21) Blomkvist V, Theorell T, Jonsson H, et al: Psychosocial self-prognosis in relation to mortality and morbidity in hemophiliacs with HIV infection. *Psychotherapy and Psychosomatics*. 1994, 62:185-192.
- (22) Perry S, Fishman B, Jacobsberg L, Frances A: Relationships over one year between lymphocyte subsets and psychosocial variables among adults with infection by human immunodeficiency virus. *Archives of General Psychiatry*. 1992, 49:396-401.
- (23) Solano L, Costa M, Salvati S, et al: Psychosocial factors and clinical evolution in HIV-1 infection: A longitudinal study. *Journal of Psychosomatic Research*. 1993, 37:39-51.
- (24) Cohen S: Psychosocial models of the role of social support in the etiology of physical disease. *Health Psychology*. 1988, 7:269-297.
- (25) Kamarck TW, Annunziato B, Amateau LW: Affiliation moderates the effects of social threat on stress-related cardiovascular responses: Boundary conditions for a laboratory model of social support. *Psychosomatic Medicine*. 1995, 57:183-194.
- (26) Kirschbaum C, Klauer T, Sigrun-Heide F, Hellhammer DH: Sex-specific effects of social support on cortisol and subjective responses to acute psychological stress. *Psychosomatic Medicine*. 1995, 57:23-31.
- (27) Phair J, Jacobson L, Detels R, et al: Acquired immune deficiency syndrome within 5 years of infection with human immunodeficiency virus Type-1: The Multicenter AIDS Cohort Study. *Journal of Acquired Immune Deficiency Syndromes*. 1992, 5:490-496.
- (28) Saah AJ, Hoover DR, He Y, et al: Factors influencing survival after AIDS: Report from the Multicenter AIDS Cohort Study. *Journal of Acquired Immune Deficiency Syndromes*. 1994, 7:287-295.
- (29) Irwin M, Smith TL, Gillin C: Electroencephalographic sleep and natural killer cell cytotoxicity in depressed patients and control subjects. *Psychosomatic Medicine*. 1992, 54:10-21.
- (30) Cohen S, Tyrrell DAJ, Russell DAH, Jarvis MJ, Smith AP: Smoking, alcohol consumption, and susceptibility to the common cold. *American Journal of Public Health*. 1993, 83:1277-1283.
- (31) Kiecolt-Glaser JK, Glaser R: Methodological issues in behavioral immunology research with humans. *Brain, Behavior and Immunity*. 1988, 2:67-78.
- (32) Umberson D: Family status and health behaviors: Social control as a dimension of social integration. *Journal of Health and Social Behavior*. 1987, 28:306-319.
- (33) Martin JL, Dean L: Risk factors for AIDS-related bereavement in a cohort of homosexual men in New York City. In Cooper B, Helgason T (eds), *Epidemiology and the Prevention of Mental Disorders*. London: Routledge, 1989, 112-133.
- (34) Dean L, Hall WE, Martin JL: Chronic and intermittent AIDS-related bereavement in a panel of homosexual men in New York City. *Journal of Palliative Care*. 1988, 4:54-57.
- (35) Kemeny ME, Dean L: Effects of AIDS-related bereavement on HIV progression among gay men in New York City. *AIDS Education and Prevention*. 1995, 7:36-47.
- (36) Kemeny ME, Weiner H, Duran R, et al: Immune system changes after the death of a partner in HIV positive gay men. *Psychosomatic Medicine*. 1995, 57:547-554.
- (37) Kessler RC, Foster C, Joseph J, et al: Stressful life events and symptom onset in HIV infection. *American Journal of Psychiatry*. 1991, 148:733-738.
- (38) Clayton PJ: Mortality and morbidity in the first year of widowhood. *Archives of General Psychiatry*. 1974, 30:747-750.
- (39) Kaprio J, Koskenvuo M, Rita H: Mortality after bereavement: A prospective study of 95,647 widowed persons. *American Journal of Public Health*. 1987, 71:802-809.
- (40) Stroebe W, Stroebe MS: *Bereavement and Health: The Psychological and Physical Consequences of Partner Loss*. New York: Cambridge University Press, 1987.
- (41) Kiecolt-Glaser JK, Glaser R, Gravenstein S, Malarkey WB, Sheridan J: Chronic stress alters the immune response to influenza virus vaccine in older adults. *Proceedings of the National Academy of Science USA*. 1996, 93:3043-3047.
- (42) Kiecolt-Glaser JK, Marucha PT, Malarkey WB, Mercado AM, Glaser R: Slowing of wound healing by psychological stress. *Lancet*. 1995, 346:1194-1196.
- (43) Carstensen LL, Fredrickson BF: Aging, illness and social preferences. Manuscript submitted for publication, 1997.
- (44) Heaton RK, Velin RA, McCutchan JA, et al: Neuropsychological impairment in human immunodeficiency virus infection: Implications for employment. *Psychosomatic Medicine*. 1994, 56:8-17.
- (45) Price RW, Brew B, Sidtis J, et al: The brain and AIDS: Central nervous system HIV-1 infection and AIDS dementia complex. *Science*. 1988, 239:586-592.
- (46) Costa PT, McCrae RR: Four ways five factors are basic. *Personality and Individual Differences*. 1992, 13:653-655.
- (47) Kagan J: The concept of behavioral inhibition to the unfamiliar. In Reznick JS (ed), *Perspectives on Behavioral Inhibition*. Chicago: University of Chicago Press, 1989, 1-23.
- (48) Smith TW: Hostility and health: Current status of a psychosomatic hypothesis. *Health Psychology*. 1992, 11:139-150.



- (49) Cole SW, Kemeny ME: Psychobiology of HIV infection. *Critical Reviews in Neurobiology*. 1997, 11:289–321.
- (50) Sarason BR, Sarason IG: Assessment of social support. In Shumaker S, Czajkowski SM (eds), *Social Support and Cardiovascular Disease*. New York: Plenum Press, 1994, 41–63.
- (51) Schwarzer R, Dunkel-Schetter C, Kemeny ME: The multidimensional nature of received social support in gay men at risk of HIV infection and AIDS. *American Journal of Community Psychology*. 1994, 22:319–339.
- (52) Schaefer C, Coyne JC, Lazarus R: The health-related functions of social support. *Journal of Behavioral Medicine*. 1981, 4:381–406.
- (53) Captanio JP, Lerche NW: Psychosocial factors and disease progression in simian AIDS: A preliminary report. *AIDS*. 1991, 5:1103–1106.
- (54) Captanio JP, Mendoza SP, Lerche NW: Affiliation and agonism influence pituitary–adrenal activity and SIV disease progression in adult male rhesus macaques. Psychoneuroimmunology Research Society Meeting. Los Angeles: 1996.