Marital Quality, Marital Disruption, and Immune Function

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Marital disruption is associated with significant increases in a variety of psychologic and physical disorders. In order to examine psychologic and physiologic mediators, self-report data and blood samples were obtained from 38 married women and 38 separated/divorced women. Among married subjects, poorer marital quality was associated with greater depression and a poorer response on three qualitative measures of immune function. Women who had been separated 1 year or less had significantly poorer qualitative and quantitative immune function than their sociodemographically matched married counterparts. Among the separated/divorced cohort, shorter separation periods and greater attachment to the (ex)husband were associated with poorer immune function and greater depression. These data are consistent with epidemiologic evidence linking marital disruption with increased morbidity and mortality.

INTRODUCTION

Marital quality appears to be an important factor in psychologic well-being. Data from national surveys suggest that marital happiness contributes far more to global happiness than any other variable, including satisfaction with work and friendships (1). Persistent problems within marriages are reliably associated with increased distress, and unmarried people are happier on the average than those in troubled marriages (1, 2).

However, even the end of a troubled relationship may have significant consequences: marital disruption is one of the most stressful life events (3). Divorced and separated individuals have poorer mental and physical health than comparable married, widowed, or single adults (3–5). Separated and divorced adults are disproportionately represented in both inpatient and outpatient psychiatric populations (5, 6), with admission rates approximately six times as high as married individuals (3). This population also shows a higher incidence of clinical depression (7).

In addition to greater psychologic symptomatology, marital disruption is also strongly associated with increased health risks. Marital disruption is the single most powerful sociodemographic predictor of stress-related physical illness, with separated individuals having about 30% more acute illnesses and physician visits than married adults (8). Separated/divorced adults have the highest rates of acute medical problems, of chronic medical conditions that limit social activity, and of disability, even when age, race, and income

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are controlled (9); of particular relevance to the present study is the fact that separated/divorced individuals have higher rates of mortality from certain infectious diseases, including up to six times as many deaths from pneumonia (10).

Attachment theory (11) is the primary conceptual framework used in the divorce literature to explain postseparation increases in physical and psychologic symptomatology. Defining attachment as a bonding to the other [similar to Bowlby (12)], Weiss suggests that such bonds, once formed, are extremely difficult to break. Within this framework, the intensely ambivalent feelings toward the spouse are a function of the persistence of attachment despite the erosion of love; the inaccessibility of the spouse following marital disruption leads to "separation distress" characterized by increased symptomatology (13). Since such bonds are normally formed within the first 2 years of marriage (11), length of marriage is neither a good predictor of attachment nor a good predictor of adjustment following divorce (14). Although attachment and distress are both related to a variety of situational changes produced by marital disruption, attachment feelings appear to cause distress, rather than vice versa (15). Factors that are associated with less attachment include greater time since separation, the development of a new relationship (15), and being the initiator of the separation (15–18).

Available data indicate that psychologic adaptation following separation occurs over a several-year period. Weiss (11) suggests that the establishment of a more resilient and stable identity may take 2–4 years. In their longitudinal sample, Wallerstein and Kelly (19) found that it was 3.3 years after separation before the average woman's life assumed a sense of coherence and stability; however, it is noteworthy that 5 years after separation 42% of their female subjects had not fully adjusted to their divorce. Data from Cartwright (20) show depression-related alterations in REM sleep that persisted 2 years after divorce in a sample of women. We were interested in the possibility that there were distress-related alterations in immune function associated with marital disruption, especially in view of the prolonged elevations in distress found across studies.

Health-related epidemiologic studies on marital disruption have most often aggregated individuals without considering the time lapse since marital separation or possible psychologic mediators of underlying physiologic changes. This study addresses the psychologic and immunologic concomitants of marital quality and marital disruption. We chose to examine immune function because research on the interrelatedness of the immune and neuroendocrine systems provides evidence of pathways through which distress-producing events may modulate immune function and health (21–23).

In order to study the psychologic and immunologic concomitants of marital quality and marital disruption, we collected self-report data and blood samples from 38 married women and 38 separated/divorced women. A battery of six immunologic assays provided information on both qualitative or functional and quantitative aspects of cellular immunity.

We tested three hypotheses concerning marital quality and marital disruption in this cross-sectional study: 1) Among married subjects, higher marital satisfaction was expected to be associated with better mental health and immunologic functioning (24, 25). 2) Within the separated/divorced subject group, it was expected that attachment to the (ex)husband would be inversely related to psychologic and im-

munologic functioning. 3) It was expected that the short-term consequences of marital disruption would be increased distress and physical symptomatology, i.e., women who had been separated for 1 year or less would, as a group, have poorer immunologic and psychologic functioning than an age- and sociodemographically matched married comparison sample.

METHOD

Subjects

Data were collected from 38 separated/divorced women and 38 married women. Both married and separated/divorced subjects were recruited in several ways to provide a heterogeneous sample. We placed ads in a suburban newspaper distributed free of charge to households in Columbus. A pastor recruited eight subjects from his congregation (four married and four separated/divorced). We recruited a total of eight women from Parents Without Partners (PWP). These subjects were paid $10 for the blood draw and completion of questionnaires, with the exception of the subjects from Parents Without Partners, where the organizational bylaws require that the money be paid to the chapter treasury. We also recruited a quarter of the sample (10 married women and 8 separated/divorced women) from the psychology undergraduate subject pool by making announcements in the evening classes that had older students. For these subjects experimental participation was one method of fulfilling a course research requirement. The data were collected from groups of 2 to 20 subjects at a time, with concurrent data collection from married and separated/divorced individuals. During the latter phase of the study we had more separated/divorced women than married women; to be sure that we would have matched groups, we selectively recruited married women of the appropriate age and SES from responses to further newspaper ads. Thus, with the exception of the PWP group, the two groups of subjects were recruited from similar sources.

As the study progressed we attempted to balance the two groups on certain interrelated sociodemographic dimensions, including age, education, socioeconomic status of the (ex)husband, length of marriage, relative number of childless marriages, and number of children. Other studies have emphasized the importance of these variables as mediators of postdivorce adjustment (16, 19, 26, 27). The education of the (ex)wife and the SES of the (ex)husband have been important variables in past divorce research because they are both related to change (or lack thereof) in the financial circumstances of women after divorce. Women most frequently experience downward mobility on the economic ladder following a divorce, and more severe financial strains are associated with poorer divorce adjustment (26). In addition, women who have more education have less restricted occupational choices, and may suffer less economic hardship (14).

Subjects were screened by telephone prior to participation, and the same health-related questions were also included in their questionnaire packet. Potential subjects could not be using any prescription or nonprescription medication with possible immunologic consequences, nor could they have any acute or chronic health problems that might have an immunologic or endocrinologic component. Subjects who were pregnant or who had recently given birth or had recent surgeries were excluded, as were those who reported drinking more than ten alcoholic drinks per week.

The separated/divorced group was limited to women who had separated from their husbands within the previous 6 years. We used the date of the actual separation, rather than the divorce date for those who had completed formal court proceedings, because evidence suggests that distress is maximal within the first year after separation (27).

The divorce literature clearly indicates that marital disruption may be quite different for men and women for a variety of reasons (27), including a more prolonged period of adjustment for certain subgroups of women. Since we were not able to double our sample to adequately study both sexes, we chose to use only female subjects.

Self-Report Data

History and Demographic Data. Questions included length of marriage, timing of separation and divorce, and frequency and degree of satisfaction with dating relationships since the separation. Following Pettit and Bloom (18), initiator status was determined by the response to the question of who made the decision to separate, with possible responses of 1) it was completely my decision, 2) it was mostly my decision, 3) it was a mutual decision, 4) it was mostly my husband's decision, and 5) it was completely my

husband's decision. Subjects were classified as initiators if they said that the decision was completely or mostly theirs or a mutual one.

Health status data included medication usage and recent alcohol intake. Subjects were asked how many hours of sleep they had had in the previous 3 days, as well as the amount of any weight changes in the previous week. They were asked the number of days they had been unable to perform their normal daily activities in the previous 2 months due to acute illness, and the number of physician visits during the same period.

Distress/Depression. The 53-item Brief Symptom Inventory (BSI; 28) provided information on nine symptom indices and three global scales. The scales of particular interest for the present study were the depression scale and the global severity index (GSI), with the latter providing a summary distress measure. Subjects rated the degree of associated discomfort during the past week for each item from 0 (not at all) to 4 (extremely). The BSI raw scores for subjects were converted to T-scores values, using the normative tables for nonpsychiatric subject samples, so that the values can be compared to the normal population mean of 50 (SD = 10).

Marital Quality. The 32-item Dyadic Adjustment Scale (DAS; 29) was given to married subjects. The DAS is one of the most commonly used scales in marital research, and there are good data supporting its reliability and validity (30–32). Married subjects were asked to respond based on their relationship with their husband over the previous 6 months.

Attachment. The Attachment Scale was developed by Kitson (15) to operationalize attachment after separation and divorce. The items assess preoccupation with the (ex)spouse, and disbelief about the separation/divorce. Responses on the 4-point scale range from "not at all" to "very much," with higher scores indicating greater attachment. Although attachment and distress are both related to a variety of situational changes produced by marital disruption, attachment feelings appear to cause distress, rather than vice versa (13, 15). Research with the scale has provided evidence of its reliability and validity (13, 15, 30).

Loneliness. Loneliness has frequently been reported as a problem for separated/divorced individuals (17, 26, 33). In particular, loneliness may be a longer-term problem for adults after divorce (34). Loneliness is also of interest because of its theoretical ties to the absence of attachment figures (35) and its association with depressed cellular immunity in medical students (1, 11) and psychiatric inpatients (36). Therefore, we gave all subjects the four-item survey version of the UCLA Loneliness Scale (37, 38).

Life Changes. The Psychiatric Epidemiological Research Inventory Life Events Scale (PERI; 39) was used to assess the number of major life changes over the previous year. We were interested in the number of negative events, since health changes appear to be reliably associated only with negative events (40), and the number of such events is as good a predictor as the weighted sum (41). The PERI data were also included to help discriminate the contribution of attachment from more global distress related to life changes, as has been done in previous research (13).

Immunologic Assays. The three functional assays included blastogenesis with two different mitogens, concanavalin A (Con A) and phytohemagglutinin (PHA), as well as antibody titers to the latent herpesvirus Epstein–Barr virus (EBV), the infectious agent for infectious mononucleosis. Blastogenesis measures the proliferative response of lymphocytes, since cellular proliferation following mitogen exposure is thought to provide an in vitro model of the body's response to challenge by infectious agents such as bacteria or viruses. Bereaved individuals and depressed psychiatric patients have lower proliferative responses than controls (42, 43), and the responsiveness of lymphocytes is poorer in blood samples taken from medical students on examination days, compared to lower-stress baseline days (44).

We measured antibody to EBV because antibody titers to latent herpesviruses appear to provide an indirect measure of cellular immune system competency (45). For example, patients on immunosuppressive therapies like chemotherapy or patients with immunosuppressive diseases (e.g., AIDS) have characteristic elevated herpesvirus antibody titers; cessation of an immunosuppressive drug therapy is ultimately followed by a drop in antibody titers to latent herpesviruses. The increased herpesvirus antibody production in immunosuppressive conditions is thought to reflect the humoral immune system's response to an increased load of viral antigens. We have previously shown large and reliable stress-related changes in antibody titers to EBV and herpes simplex virus using a Type 1 antigen (HSV-1) in medical students (46) as well as decrements in HSV-1 antibody titers in elderly adults following a relaxation intervention (47).

Monoclonal antibodies were used to provide data

on certain quantitative aspects of immune function. Natural killer (NK) cell percentages were assessed because NK cells are thought to be an important antiviral and antitumor defense. Distress-related changes in NK cell percentages have been found previously in medical students (46). Reliable stress-related changes in a functional NK measure, NK cell lysis, have been shown with two different target cells (48–50).

Data on the relative percentages of helper and suppressor T lymphocytes were also collected. Helper T cells stimulate important immunologic activities, including the production of antibody by B lymphocytes, an important defense against bacterial infections. Suppressor T cells act to shut off the activity of helper cells when sufficient antibody has been produced. Low helper/suppressor cell ratios are associated with immunodeficient conditions (51). Alterations in the percentages of helper and suppressor cells have been associated with examination stress (44, 49).

NK and T Lymphocyte Subset Assay. The percentages of helper/inducer T cells, suppressor/cytotoxic T cells, and helper-to-suppressor cell ratios were determined using the monoclonal antibodies OKT-4 and OKT-8, respectively (Ortho), as previously described (49). The Leu-11b monoclonal antibody (Becton-Dickerson) was used to measure the percentage of NK cells.

Briefly, lymphocytes isolated on Hypaque-Ficoll gradients were washed with trypsin diluent, then resuspended in complete RPMI 1640 medium supplemented with 20% fetal bovine serum. Monocytes were removed by placing the cell suspensions in plastic tissue culture flasks and incubating at 37°C in a CO_2 incubator for 2 hr. The nonadherent cells were washed off and used to determine percentage of T-cell subsets. Lymphocytes (10^6) were incubated in 0.0l ml of Leu-11b, OKT-4, or OKT-8 monoclonal antibody for 30 min on ice. Cells were washed with cold RPMI 1640/PBS (1:1), resuspended in goat antimouse IgG conjugated to fluorescein isothiocyanate (Cappel Laboratories), and incubated for an additional 30 min on ice. The cells were washed and assayed, using an Ortho System 50 fluorescence activated cell sorter (FACS).

Blastogenesis. Mitogens were used at a final concentration of 2.5, 5.0, and 10.0 μg/ml for concanavalin (Con A) and 0.25, 0.5, 1.0 and 2.0 μg/ml for phytohemagglutinin (PHA). Each assay was performed in triplicate. Complete medium supplemented with 20% fetal bovine serum was used for baseline controls. One-tenth of a milliliter of mitogen was added to 1×10^5 lymphocytes (in 0.1 ml complete medium) in 96 well plates, and incubated at 37°C for 48 hr. Fifty microliters of tritiated thymidine (10 μCi/ml, specific activity 83 Ci/mM) were added to each well and the plates incubated at 37°C for 4 hr. Cells were harvested onto GF/A filters. Radioactivity was measured using a Beckman LS7000 scintillation counter. The data are presented as the counts per minute (cpm) in the stimulated samples minus the cpm of the unstimulated samples (Δ cpm). A logarithmic transformation was performed on the resulting values.

Immunofluorescence Assay. The indirect immunofluorescence (IF) assay was used to measure antibodies to EBV virus capsid antigen (VCA) (46). Antibody titers were assayed using smears of HR-1 cells. Cells were fixed in acetone at room temperature for 10 min, adsorbed with twofold dilutions of plasma prepared in phosphate-buffered saline (PBS) pH 7.4, for 30 min at 37°C. The cells were washed with PBS and readsorbed with goat antihuman IgG conjugated to fluorescein isothiocyanate (FITC) for 30 min at 37°C. The cells were washed with PBS, counterstained with Evans blue, mounted in Protex, and examined with a Zeiss UV microscope. Antibody titers were determined by the highest dilution of plasma still able to demonstrate IF positive cells. All slides were read blind coded.

Nutritional Assays

Albumin and transferrin, two nutritional assays with relatively shorter and longer half-lives, were included to provide objective information on the nutritional status of subjects. There are well-documented impairments in various aspects of immune function in undernourished individuals, and moderate to severe protein-caloric malnutrition is associated with increased frequency and severity of infection (52).

Protein assays provide better information on global nutritional status than those for carbohydrates and fats, since the former have varied nutritional building blocks, as well as very complex synthetic pathways. Different protein markers were used because of the differences in their half-lives; the half-life of albumin is 2–3 weeks, in comparison to 8 days for transferrin.

The procedure used to measure albumin is an adaptation of the bromcresol green dye-binding method of Rodkey (53), later modified by Doumas (54). This procedure is recognized as a particularly good procedure as compared to other dye-binding techniques

because of its specificity and freedom from interference.

Transferrin is an iron-transporting protein. Concentration in plasma is affected by dietary intake of iron. Nutritionally deficient but calorie-rich diets are generally lacking in iron, and, as a result, plasma iron levels tend to be low and transferrin levels high. It has been shown that estimation of transferrin levels may be used to assess the effectiveness of total parenteral nutrition (55).

A rate nephelometry procedure using a Beckman human immunoglobulin reagent kit and a Beckman immunochemistry analyzer system was used to analyze transferrin levels. Antibody to human transferrin was used in the assay, in which the peak rate signal caused by the antigen/antibody complex is proportional to the increase in light scatter that is read by the instrument (56).

RESULTS

Table 1 provides sociodemographic information on married and separated/divorced cohorts. The two groups do not differ reliably on age $F(1,75) = 1.30$, education $F(1,75) = 1.11$, or occupation, $F < 1$, the (ex)husband's education, $F(1,75) = 1.30$, or occupation, $F < 1$, number of years married, $F < 1$, or number of children, $F < 1$.

We do not have data on all immunologic assays for all subjects due to occasional technical problems, e.g., insufficient numbers of cells for assays, or technical difficulties with an assay. In addition, consistent with seroepidemiologic studies (57), 89% of our subjects were EBV seropositive, i.e., had previously been exposed to the virus and thereafter were latently infected. Thus, those subjects who were not previously infected did not have antibody data.

Marital Quality

The mean DAS score for the 38 married subjects was 110.98 (SD = 13.00). For comparison purposes, Spanier (29) reported that the mean score on the DAS in a normative married sample that included both men and women was 114.8 (SD = 14.8).

Marital quality was not significantly different for those subjects who had children (DAS mean = 109.92, SD = 14.27) and those who did not (mean = 112.67, $F < 1$. DAS scores did not correlate significantly with number of children, $r = -0.08$. There were not significant correlations between marital quality and a number of variables, including age ($r = -0.15$), subjects' education ($r = -0.08$), or years married (-0.15).

Multiple regression equations were used to evaluate the contribution of marital quality to psychologic and immunologic functioning. Using a hierarchical procedure, the subject's educational level and the husband's Hollingshead SES were entered on the first step, the number of negative life changes in the previous year was entered on the second step, and marital quality was entered on the third step. This analysis provides a fairly strict evaluation of the contribution of marital quality, since lower socioeconomic status and greater numbers of negative life changes have been associated with greater distress and poorer health. It also provides information on the extent to which this set of variables predicts certain immunologic and psychologic indices.

As can be seen in Table 2, poorer marital adjustment was a strong and significant predictor of BSI depression and GSI scores, as well as loneliness, even after taking out the significant contribution of recent negative life changes. Poorer marital quality was also strongly and positively related to EBV VCA antibody titers, or poorer cellular immune system control of virus latency. None of the variables significantly predicted the three quantitative assays, or

TABLE 1. Subjects' Sociodemographic Characteristics

	Married women	Separated/divorced women
Age	29.94 (6.53)	31.47 (6.85)
Education		
High school	6	9
Partial college	18	16
College graduate	9	9
Graduate professional training	5	4
Occupation		
Major and lesser professionals and business managers	7	5
Administrative personnel, minor professionals, clerical, sales	12	17
Skilled, semi-skilled, and unskilled	2	4
Housewife	7	2
College student	10	10
Years married	8.05 (6.39)	7.65 (6.78)
Number of children	1.49 (1.24)	1 30 (1.29)
Number of childless marriages	12/38	14/38
(Ex) Husband's Education		
Partial high school	1	2
High school	7	10
Partial college	6	8
College graduate	13	10
Graduate professional training	7	8
(Ex) Husband's Occupation		
Major and lesser professionals, and business managers	7	9
Administrative personnel, minor professionals, clerical, sales	17	17
Skilled, semi-skilled, and unskilled	9	11
College student	5	1

the helper-to-suppressor ratio (data not shown for these latter analyses).

Blastogenesis data, shown in Figure 1, were analyzed using repeated measures analyses of variance (ANOVA), with one within-subjects variable (change over mitogen concentrations) and one between-subjects variable (high versus low marital quality), in order to examine possible dose–response interactions between marital quality and the proliferative response of lymphocytes to different mitogen concentrations. Low marital quality was operationalized as scores below 100 ($n = 9$), based on research with the DAS that suggests that scores below 100 reliably reflect

TABLE 2. Marital Quality as a Predictor of Psychologic and Immunologic Data[a]

	BSI Depression (n = 38)							BSI GSI Scores (n = 38)					
	Simple r	Multiple r	r^2	Beta	F Entries	F Steps		Simple r	Multiple r	r^2	Beta	F Entries	F Steps
Step 1:							Step 1:						
Education	0.18	0.21	0.04	0.04	1.47		Education	0.32	0 32	0.10	0.26	2.80	
Spouse's SES	−0 05	0.21	0.04	0	0.13	0.74	Spouse's SES	−0.21	0.33	0.11	−0.02	0.03	2.03
Step 2:													
Negative life events	0.38	0.55	0.30	0.26	6.19[b]	4.58[b]	Negative life events	0.52	0.57	0 33	0.38	5.90[b]	3.16[c]
Step 3:							Step 3:						
DAS	−0.38	0.65	0.43	0.13	6.82[b]	5.74[b]	DAS	−0.39	0.62	0.39	−0.27	3.16[c]	4.94[b]
	UCLA Loneliness Scale (n = 38)							EBV VCA (n = 34)					
	Simple r	Multiple r	r^2	Beta	F Entries	F Steps		Simple r	Multiple r	r^2	Beta	F Entries	F Steps
Step 1:							Step 1:						
Education	0.02	0.02	0	0.13	0.69		Education	0.28	0.28	0.08	0.39	5.57[c]	
Spouse's SES	0.14	0.16	0.02	0.11	0.49	0.46	Spouse's SES	−0.03	0.31	0.09	0.07	0.17	1.68
Step 2:							Step 2:						
Negative life events	−0 04	0.16	0.03	−0.24	2.42	0.30	Negative life events	0.09	0.33	0.11	−.32	3.57[c]	2.22
Step 3:							Step 3:						
DAS	−0.54	0.61	0.36	−0.62	16.56[b]	4.48[b]	DAS	−0.40	0.59	0 34	−0.52	3.81[c]	10.34[c]

[a]For both education and husband's SES, higher values indicate a higher level of educational or occupational attainment.
[b]p <0.01.
[c]p <0.05.

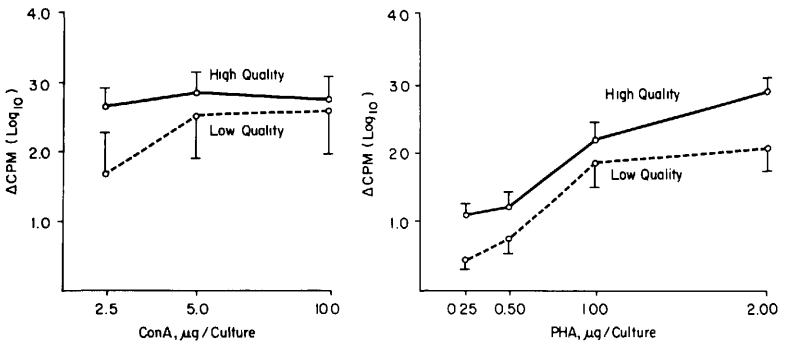

Fig. 1. Mean (± SEM) proliferative response of lymphocytes to stimulation by Con A and PHA, as a function of marital quality.

poorer marital adjustment (58). Correlations were computed between the values for the different mitogen concentrations and subjects' educational level, husband's SES, and number of negative life events. The only variable that produced reliable and significant correlations across concentrations was husband's SES with Con A, and thus it was the only covariate included in these analyses.

As shown in Figure 1, there was not a significant difference in the blastogenic response in lymphocytes obtained from high and low marital quality subgroups following Con A stimulation, $F < 1$. However, there was greater responsiveness across groups at higher concentrations of Con A, $F(2,56) = 9.31$, $p < 0.004$, and the interaction between group membership and change over concentrations was significant, $F(2,56) = 3.64$, $p < 0.004$.

Analysis of PHA data, also shown in Figure 1, showed a significant difference between high- and low-marital quality groups, $F(1,32) = 4.15$, $p < 0.05$, and a significant main effect for change across concentrations, $F(3,96) = 15.36$, $p < 0.0001$. There was not a significant interaction between these variables, $F < 1$.

Marital Disruption and Attachment

Scores on the attachment scale (15) were not significantly correlated with age ($r = -0.21$), years married ($r = -0.01$), education ($r = -0.02$), number of children ($r = -0.07$), occupation ($r = 0.18$), or the (ex)spouse's education ($r = 0.06$) or occupation ($r = 0.18$). However, consistent with previous research, greater attachment for separated/divorced women was significantly and inversely related to the amount of time women had been separated from their husbands, $r = -0.35$, $p < 0.01$, the frequency of dating since separation, $r = -.27$, $p < 0.01$, and rated satisfaction with their current social life, $r = -0.40$, $p < 0.01$. In addition, those women who reported having a currently satisfying relationship with a man reported significantly lower attachment, $F(1,37) = 9.79$, $p < 0.005$.

The length of marital separation ranged from 3 months to 6 years. Sixteen women

had been separated 1 year or less. The mean separation length was 1.72 years (SD = 1.43), and the median was 1.26 years. Seven subjects were separated but not divorced. Nine of the 38 subjects said they did not have primary responsibility for the separation, a percentage consistent with previous research (18).

It was possible that the PWP groups and those who attended church regularly might differ systematically as a function of greater social support. The four groups of subjects recruited from the newspaper ads, PWP, the church, and the evening psychology classes were compared on loneliness, the BSI depression, and GSI scales. There were no significant differences within the separated/divorced population on any of the three dimensions as a function of recruitment source, $F < 1$.

Length of time since separation was entered on the first step of the multiple regression equations, since it appears to be an extremely important factor in adjustment (e.g., 11, 19). Education and husband's SES were also entered on the first step, since education and husband's SES have been shown to be associated with postseparation adjustment, as previously described. The number of negative life events was entered on the second step of the equation, to help discriminate the contribution of attachment from more global distress related to life changes, as has been done in previous research (13). Subjects' scores on the attachment scale were entered on the third step. Thus, the analyses provide a fairly stringent test of the contribution of attachment to the total variance, while concurrently providing information on the contributions of time since separation, relevant sociodemographic variables, and negative life changes to total variance.

Consistent with our conceptual framework, time since separation and greater attachment to the (ex)spouse were inversely related to both psychologic and physiologic function, as shown in Tables 3 and 4. The BSI depression and GSI scales were both significantly and positively related to attachment, whereas the percentage of

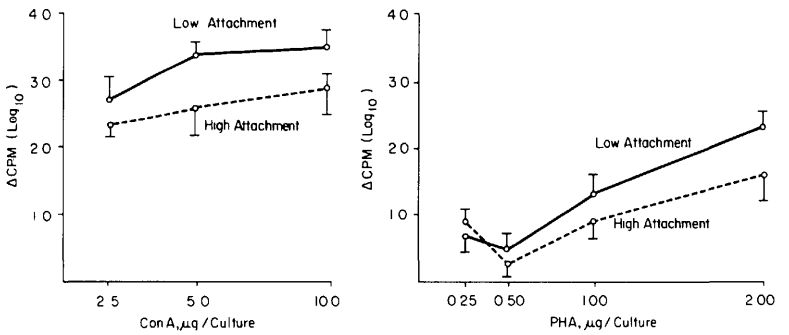

Fig. 2. Mean (± SEM) proliferative response of lymphocytes to stimulation by Con A and PHA, as a function of attachment.

TABLE 3. Length of Separation and Attachment as Predictors of Psychological Functioning

BSI Depression (n = 38)	Simple r	Multiple r	r^2	Beta	F Entries	F Steps
Step 1:						
Time separated	−0.16	0.16	0.03	0.03	0.05	
Education	0.01	0.16	0.03	0.02	0.01	
Spouse's SES	0.04	0.17	0.03	0.02	0.09	0.32
Step 2.						
Negative life events	0.40	0.43	0.19	0.27	3.61[a]	2.00
Step 3:						
Attachment	0.56	0.62	0.38	0.50	10.63[b]	4.17[b]
BSI GSI (n = 38)	**Simple r**	**Multiple r**	**r^2**	**Beta**	**F Entries**	**F Steps**
Step 1:						
Time separated	−0.01	0.01	0	0.21	2.61	
Education	−0.22	0.22	0.05	−0.18	2.00	
Spouse's SES	0.08	0 22	0.05	0.09	0.55	0.61
Step 2:						
Negative life events	0.34	0.44	0.20	0.21	2.90	2.12
Step 3:						
Attachment	0.64	0.73	0.53	0.65	24.40[b]	7.72[b]
UCLA Loneliness Scores (n = 38)	**Simple r**	**Multiple r**	**r^2**	**Beta**	**F Entries**	**F Steps**
Step 1:						
Time separated	0.06	0.06	0	0.18	1.26	
Education	0.06	0.08	0	0.06	0.13	
Spouses's SES	0.02	0.08	0.01	0.04	0.08	0.08
Step 2:						
Negative life events	0.34	0.36	0.13	0.27	2.84	1.36
Step 3:						
Attachment	0.31	0.45	0.21	0.31	3.21[a]	1.77

[a] $p < 0.05$.
[b] $p < 0.01$.

TABLE 4. Length of Separation and Attachment as Predictors of Immune Function

	EBV VCA Antibody Titers (n = 34)							NK Cells (n = 34)					
	Simple r	Multiple r	r^2	Beta	F Entries	F Steps		Simple r	Multiple r	r^2	Beta	F Entries	F Steps
Step 1:							Step 1:						
Time separated	−0.23	0.23	0.06	−0.44	6.14[a]		Time separated	0.32	0.31	0.10	0.37	3.55[a]	
Education	−0.19	0.50	0.25	−0.45	6.10[a]		Education	0.05	0.32	0.10	0.06	0.09	
Spouse's SES	−0.33	0.68	0.47	−0.50	8.35[b]	4.86[a]	Spouse's SES	0.14	0.40	0.16	0.22	1.03	1.42
Step 2:													
Negative life events	0.11	0.70	0.49	0.14	0.72	4.00[a]	Negative life events	−0 12	0.40	0.16	−0.07	0.13	1.03
Step 3·							Step 3:						
Attachment	0.17	0.70	0.49	0 01	0.01	3.37[a]	Attachment	−0.07	0.41	0.17	−0.10	0.19	0.83
	Helper T-Lymphocytes (n = 36)							Suppressor T-Lymphocytes (n = 36)					
	Simple r	Multiple r	r^2	Beta	F Entries	F Steps		Simple r	Multiple r	r^2	Beta	F Entries	F Steps
Step 1:							Step 1:						
Time separated	−0.11	0.11	0.01	−0.03	0.10		Time separated	0.64	0.64	0.41	0.74	20.14[b]	
Education	0.08	0.11	0.02	0.01	0.10		Education	−0.07	0.65	0.42	−0.17	1.05	
Spouse's SES	0.08	0.12	0.02	0.02	0.11	0.17	Spouse's SES	−0.02	0.69	0.48	−0.29	0.22	5.57[a]

Step 2:							Step 2:					
Negative life events	−0.22	0.25	0.06	−0.13	0.39	0.50	Negative life events	0.08	0.70	0.49	0.14	0.72	4.37[a]
Step 3:							Step 3:					
Attachment	−0 36	0.39	0.15	−0.33	3.29[a]	1.05	Attachment	0.11	0.72	0.52	0.19	1.40	3.94[a]

Helper/Suppressor Ratio (n = 36)

	Simple r	Multiple r	r^2	Beta	F Entries	F Steps
Step 1:						
Time separated	−0.10	0.10	0.01	−0.26	2.21	
Education	0.23	0.26	0.06	0 23	1.75	
Spouse's SES	0.08	0.26	0 06	0	0	0.80
Step 2:						
Negative life events	−0.21	0.32	0 10	−0.08	0.27	0.08
Step 3:						
Attachment	−0.31	0.46	0.21	−0.37	4.28[b]	1.63

[a] $p < 0.05$.
[b] $p < 0.01$.

helper T lymphocytes and the helper-suppressor ratio were inversely related to attachment. The percentage of suppressor T lymphocytes showed a strong positive correlation with length of separation, whereas the percentage of NK cells was inversely related to length of separation.

Attachment scores were divided at the median, 8.5, to form high- and low-attachment subgroups for blastogenesis analyses. There were significant differences related to attachment in the proliferative response of lymphocytes exposed to Con A. The difference between groups was significant, $F(1,26) = 4.47$, $p < 0.05$, as was the usual increase in responsiveness with different mitogen concentrations, $F(2,62) = 10.17$, $p < 0.0002$, whereas the interaction between these two variables was not significant, $F < 1$. Response of lymphocytes to PHA stimulation produced a nonsignificant difference between groups, $F < 1$, and a significant change over concentrations, $F(3,78) = 21.69$, $p < 0.0001$. The interaction between these two variables was significant, however, with greater differences at higher concentrations, $F(3,78) = 3.77$, $p < 0.01$. Correlations were computed between the values obtained at different mitogen concentrations and length of separation, education, husband's SES, and number of negative life events. Only length of separation showed a reliably significant relationship across PHA significant correlations, so it was the only covariate used in the analyses (Fig. 2).

Comparisons Between Recently Separated Women and Married Women

The mean BSI depression T-score (58.25, SD = 9.80) in the newly separated subjects was not significantly different from that of their married counterparts (54.47, SD = 5.59), $F(1,31) = 2.14$, $p < 0.15$. Similarly, there was not a significant difference on the GSI, $F < 1$. Data from the UCLA did not discriminate between the two groups, $F < 1$.

Comparisons of sociodemographic data did not show significant differences between the 16 women who had separated within the previous year and the 16 matched married women. They did not differ in age, number of children, or the Hollingshead education or occupational status of themselves or their spouse, with all $Fs < 1$. The two groups did not differ significantly in their distribution across stages of the menstrual cycle.

As predicted, there were reliable immunologic differences between the women who had been separated 1 year or less and their married counterparts, as shown in Table 5. The separated/divorced women

TABLE 5. Mean (± SDS) for the 16 Women Who Were Separated 1 Year or Less and 16 Matched Married Women

	Separated/ Divorced Women		Married Women	
EBV VCA[a]	520.50	(706.84)	147.12	(191.88)
Percentage of helper T lymphocytes[a]	26.43	(7.59)	32.91	(7.03)
Percentage of suppressor T lymphocytes	20.01	(6.70)	22.66	(7.76)
Helper–suppressor ratio	1.49	(0.66)	1.69	(1.47)
Percentage of NK cells[a]	7.50	(5.05)	12.79	(8.05)

[a] $p < 0.05$.

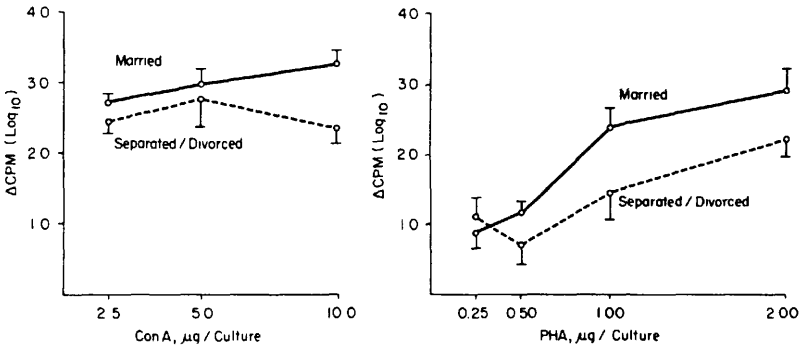

Fig. 3. Mean (± SEM) proliferative response of lymphocytes to stimulation by Con A and PHA for 16 women who were separated one year or less and 16 matched married women.

had significantly higher EBV VCA titers, $F(1,31) = 4.17$, $p < 0.05$, and significantly lower percentages of NK cells, $F(1,27) = 3.98$, $p < 0.05$, than the married women. Married women had significantly higher percentages of helper T lymphocytes than separated/divorced women, $F(1,31) = 4.08$, $p < 0.05$. There were not significant differences between the two groups in the percentage of suppressor T lymphocytes, $F(1,31) = 1.07$, or in the helper-suppressor ratio, $F(1,31) = 1.40$.

Blastogenesis data are shown in Figure 3. While the global response of lymphocytes to Con A stimulation did not significantly discriminate between the two groups, $F < 1$, there was a significant interaction between group membership and the three concentrations of Con A, $F(2,48) = 2.95$, $p < 0.05$, with greater differences at higher concentrations. In contrast, there was a significant difference between groups in their response to PHA, $F(1,22) = 3.89$, $p < 0.05$, and a significant change across concentrations, $F(3,66) = 15.20$, $p < 0.001$. The interaction between the two variables was not significant, $F(3,66) = 2.09$, $p < 0.10$.

All subjects were in the normal range on both nutritional assays. Albumin levels did not discriminate between the two groups, $F(1,31) = 1.10$, with a mean of 4.24 g/dl (SD = 0.39) in the newly separated group, compared to 4.38 g/dl (SD = 0.25) in the married cohort. The normal range for albumin is 3.8 to 5.1 g/dl. There was, however, a significant difference in transferrin between the two groups, $F(1,31) = 5.13$, $p < 0.05$, with the separated/divorced women having a mean of 347.38 mg/dl (SD = 59.96), compared to 303.30 mg/dl (SD = 37.43) in the married group. However, the normal range for transferrin is between 178 and 410 mg/dl, so both groups were still well within the normal range.

There was a marginally significant difference in weight change in the last week between the groups, $F(1,31) = 3.89$, $F < 0.06$. The difference did not parallel the immunologic differences; the mean loss was 0.82 pounds (SD = 1.85) in the married

group, compared to a mean gain of 0.43 (SD = 1.82) in the newly separated group.

The two groups did not differ in amount of sleep in the previous 3 days, $F < 1$. Both reported about 23 hr of sleep, or an average deficit of 1 hr. There were not significant differences between the newly separated subjects in the number of days they were ill during the previous 2 months, or in the number of physician visits for the treatment of acute illness, $Fs < 1$.

Overall Group Comparisons: Separated/Divorced vs. Married

We did not predict overall differences between the separated/divorced and the married cohorts, since our separated/divorced subjects, as a group, had been separated for some period of time. However, comparisons between the entire married and separated/divorced cohorts showed some significant differences on the psychologic variables, and on the functional assays, blastogenesis and EBV antibody titers, as well as in NK cell percentages.

There was a strong significant difference between married and separated/divorced subjects on depression, $F(1,75) = 12.11$, $p < 0.001$, but not for the GSI, $F(1,75) = 1.45$. The means for depression were 59.65 (SD = 9.02) in the separated divorced group and 53.11 (SD = 7.27) in the married group. Scores on the short form of the UCLA did not discriminate between the groups, $F(1,75) = 1.53$, with a mean of 7.75 (SD = 2.29) in the separated/divorced group, compared to 7.13 (SD = 2.06) among married women. For comparison purposes, in a telephone survey of working adults in a large city, the mean score for adults in the same age range as our subjects was 7.99 (SD = 1.96) (38).

The difference in antibody titers to EBV was significant, $F(1,68) = 4.01$, $p < 0.05$, with married subjects having significantly lower antibody titers (mean = 149.23, SD = 233.46) than the separated/divorced group (mean = 462.05, SD = 513.96). The separated/divorced subjects had significantly lower percentages of NK cells than married subjects. $F(1,65) = 8.96$, $p < 0.01$, with a mean of 7.31 (SD = 6.10) in the former and 11.93 (SD = 6.42) in the latter. There were not significant differences in the percentages of helper or suppressor T lymphocytes, or the helper-suppressor ratio, $Fs < 1$.

The separated/divorced and married subjects were also significantly different in their lymphocytes' response to PHA stimulation, $F(1,58) = 4.28$, $p < 0.05$, and in the interaction between group membership and change over concentrations, $F(3,74) = 7.00$, $p < 0.0003$. The main effect for change over concentrations was significant as well, $F(3,174) = 58.65$, $p < 0.0001$. For separated/divorced subjects the means for the four concentrations of PHA were 1.14 (SD = 1.24), 0.82 (SD = 1.11), 1.53 (SD = 1.25), and 2.16 (SD = 1.32). The comparable means for married subjects were 0.90 (SD = 1.17), 1.11 (SD = 1.15), 2.45 (SD = 0.76), and 3.05 (SD = 0.65).

There was neither a significant difference between these groups on response to Con A, nor a significant interaction between group membership and change over concentrations, $Fs < 1$.

The two groups did not differ significantly in amount of sleep in the last three days, $F < 1$. Weight change data paralleled the newly separated group, with an average loss of 0.86 lb (SD = 2.51) in the married subjects, compared to a mean gain of 0.14 lb (SD = 1.93) in the separated/divorced group, $F(1,75) = 4.08$, $p < 0.05$. Although there were not significant differences in albumin, $F < 1$, there was a

significant difference in transferrin, $F(1,64) = 5.39$, $p < 0.02$, with a mean of 335.22 (SD = 62.26) in the separated/divorced group, compared to 302.20 (SD = 49.51) for married subjects, with all values falling within normal limits. There were not differences in days ill or physician visits, $Fs < 1$.

The two groups did not show differences in smoking behavior, either on packs per week, $F < 1$, or in the relative proportion of smokers to nonsmokers; roughly 20% of each group were smokers. The two groups did differ significantly in alcohol use over the previous week, $F(1,75) = 7.73$, $p < 0.01$, with a mean of 1.92 drinks per week (SD = 2.44) in the separated/divorced group, compared to 0.70 in the married group (SD = 1.18). No subject reported more than ten drinks in the previous week, and only two subjects reported having had more than seven drinks. Subjects in the two groups did not differ significantly in their distribution across stages of the menstrual cycle.

DISCUSSION

Poorer marital quality in the married cohort was a significant predictor of depression and poorer response on the functional immunologic assays. These data are consistent with previous reports linking the quality of the marital relationship with mental and physical health (25), and they provide further evidence for the importance of satisfactory marital relationships.

Data from Levinson and Gottman (59, 60) provide evidence of one physiologic pathway through which chronically abrasive relationships might mediate immune function. They found that greater autonomic arousal in interacting married couples was strongly predictive of subsequent declines in marital satisfaction 3 years later. Moreover, they also reported that greater declines in marital satisfaction were strongly correlated with poorer health ratings at follow-up. If there is consistent physiologic arousal associated with the presence of a spouse in a disturbed relationship, then it is quite possible that there are concurrent persistant alterations in endocrine function that mediate immunologic changes (e.g., 61, 62)

We also found that more recent marital separation and greater attachment to the (ex)husband were significant predictors of both psychologic symptoms and certain aspects of immune function in separated/divorced women. In addition, as predicted, those women who had separated from their husbands within the previous year had poorer immune function than sociodemographically matched married women, with significantly poorer proliferation in response to two mitogens, significantly lower percentages of NK cells and helper cells, and significantly higher antibody titers to EBV VCA. These data are consistent with evidence from epidemiologic studies indicating that separated individuals have the greatest incidence of health impairments, followed in turn by divorced adults (9).

It has been suggested that nonmarried individuals may have riskier life-styles than married adults, e.g., they may drink, smoke, or use drugs more, thus exposing themselves to more chronic risks; nutrition and sleep might also differ by marital status (9). We chose a sample that did not abuse drugs or alcohol, so these factors do not differentiate between our married and separated/divorced subjects. Although we did not select our sample by nutrition or sleep criteria, we find no evidence of consistent differences of a magnitude that would account for the immunologic differences.

Thus, although it is certainly possible that risk-related life-style factors may influence health status, our data suggest that there may also be persistent immunologic alterations in certain individuals.

There are also data suggesting that marital disruption is associated with a significantly higher incidence of cancer (64). Speculatively, it is possible that the persistence of distress or dysphoria following separation and divorce in some more vulnerable individuals (34) could have adverse physiologic consequences that would increase cancer risk, including the lower percentages of NK cells in the separated/divorced group. In addition, persistent depression may have consequences at the molecular level in the speed and quality of DNA repair that could mediate increased cancer risk (65, 66).

It should be noted that although the immunologic changes are not large, these data do provide evidence of longer-term changes in immune function related to psychosocial stressors. Evidence consistent with more chronic stress-related changes in immunity has only been described in one other study (63). The actual health impact of these relatively small but presumably persistent changes in immune function are not known. Although it is possible that these changes may make some contribution to the greater incidence of infectious and malignant disease in separated/divorced adults that has been well-documented by others (9–11), the causal links have not been demonstrated.

There are problems with inferences about the direction of causality in cross-sectional studies such as this. For example, in the separated/divorced group of women it is possible that preexisting depressive symptoms were an underlying cause for the divorce (e.g., 3); moreover, such symptoms might have subsequently hampered the formation of alternative relationships, a factor associated with lower attachment. Similarly, those married women who are more depressed may view their marital relationship as less supportive, and/or their depressive symptoms might have adverse effects on the quality of the marital relationship (67). Although we cannot exclude these possibilities, evidence from other research supports alternative explanations.

Using longitudinal survey data, Menaghan (68) controlled for level of depression prior to marital termination and found that depression appeared more likely to be the result of marital disruption, and offered no support for the argument that preexisting depression was an important precipitant of changes in marital status. Similarly, a 1-year longitudinal study from Monroe et al. (69) showed that subsequent depressive symptoms were predicted by lower marital support in 473 women who were initially relatively asymptomatic and had nonconflicted marriages. Moreover, other work provides evidence that another form of separation distress is a potent mediator of immune and endocrine function in nonhuman primates (70).

Turning to the immunologic data, it appears that the three qualitative assays were more consistently related to the psychologic variables than were the three quantitative assays. In particular, EBV VCA antibody titers were significantly related to the psychologic variables in all four sets of analyses. Herpesvirus antibody titers appear to be quite sensitive to psychologic stressors (71).

Values from the mitogen assays, particularly PHA, were somewhat low; in our protocol we used a 48-hr incubation period in order to minimize variability. The mitogens we used presumably had low potency and, in combination with the 48-hr

incubation period, resulted in low counts. Once the data collection had begun, we were committed to using the same mitogens across all subjects so that meaningful comparisons could be made. Thus, the resultant values are lower than some of those reported elsewhere. However, although the values are low, the differences between groups are consistent and significant, reflecting differences in the proliferative responses of the groups.

Finally, the data from this study are relevant for the growing literature on social support and health. The data linking poorer marital quality with depression and poorer immune function suggest that the simple presence of a partner is not equivalent to a supportive relationship. Moreover, in separated/divorced women, greater attachment to a man who is no longer present is also linked to adverse psychologic and immunologic consequences; a new and satisfying relationship is associated with lower attachment. We have previously found that loneliness is associated with poorer immune function (36, 46, 48). Taken together, it appears that the quality of one's interpersonal relationships may have health-related consequences.

SUMMARY

Marital disruption is associated with significant increases in a number of psychologic and physical disorders. In order to examine psychologic and physiologic mediators, self-report data and blood samples were obtained from 38 married women and 38 separated/divorced women. Among the married subjects, poorer marital quality was associated with greater depression and a poorer response on the three qualitative immunologic assays, lymphocyte proliferation in response to two mitogens and antibody titers to EBV VCA. The 16 women who had been separated 1 year or less had significantly poorer immune function than a sociodemographically-matched married group, including lower percentages of NK and helper cells, poorer blastogenic responsiveness, and higher antibody titers to EBV VCA. Within the separated/divorced group shorter separation times and greater attachment to the (ex)husband were associated with poorer immune function and greater depression. These data are consistent with epidemiologic data linking marital disruption with increased morbidity and mortality.

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REFERENCES

1. Glenn ND, Weaver CN: The contribution of marital happiness to global happiness. J Marriage Fam 43:161–168, 1981
2. Pearlin LI, Lieberman MA: Social sources of emotional distress. In Simmons R (ed), Research in Community and Mental Health. Greenwich, CT, JAI Press, 1979

3. Bloom BL, Asher SJ, White SW: Marital disruption as a stressor: A review and analysis. Psychol Bull 85:867–894, 1978
4. Briscoe CS, Smith JB, Robins E, Marten S, Gaskin F: Divorce and psychiatric disease. Arch Gen Psychiatry 29:119–125, 1973
5. Bachrach LL: Marital Status and Mental Disorder: An Analytical Review. Washington D.C., U.S. Printing Office, 1975
6. Crago MA: Psychopathology in married couples. Psychol Bull 77:114–128, 1972
7. Blumenthal MD: Mental health among the divorced: A field study of divorced and never divorced persons. Arch Gen Psychiatry 16:603–608, 1967
8. Somers AR: Marital status, health, and use of health services. JAMA 241:1818–1822, 1979
9. Verbrugge LM: Marital status and health. J Marriage Fam 41:267–285, 1979
10. Lynch J: The Broken Heart. New York, Basic, 1977
11. Weiss RS: Marital Separation. New York, Basic, 1975
12. Bowlby J: Attachment and Loss: 1. Attachment. New York, Basic, 1975
13. Brown P, Felton BJ, Whiteman V, Manela R: Attachment and distress following marital separation. J Divorce 3:303–317, 1980
14. Spanier GB, Thompson LJ: Parting: The Aftermath of Separation and Divorce. Beverly Hills, CA, Sage, 1984
15. Kitson GC: Attachment to the spouse in divorce: A scale and its application. J Marriage Fam 44:379–393, 1982
16. Kitson GC, Raschke HJ: Divorce research: What we know: what we need to know. J Divorce 4:1–37, 1981
17. Kelly JB: Divorce: The adult perspective, In Wolman BB (ed), Handbook of Developmental Psychology. Englewood Cliffs, NJ, Prentice Hall, 1982
18. Pettit EF, Bloom BL: Whose decision was it: The effects of initiator status on adjustment to marital disruption. J Marriage Fam 46:587–595, 1984
19. Wallerstein JS, Kelly JB: Surviving the Breakup: How Children and Parents Cope With Divorce. New York, Basic, 1980
20. Cartwright RD: Rapid eye movement sleep characteristics during and after mood-disturbing events. Arch Gen Psychiatry 40:197–201, 1983
21. Ader R (ed): Psychoneuroimmunology. New York, Academic, 1981
22. Soloman GF: Emotional and personality factors in the onset and course of autoimmune disease, particularly rheumatoid arthritis. In Ader R (ed), Psychoneuroimmunology. New York, Academic, 1981
23. Kiecolt-Glaser JK, Glaser R: Behavioral influences on immune function: Evidence for the interplay between stress and health. In Field T, McCabe PM, Schneiderman N (eds), Stress and Coping. Hillsdale, NJ, Lawrence Erlbaum, in press, Vol II
24. Furstenberg FF, Spanier GB: Recycling the Family: Remarriage After Divorce. Beverly Hill, CA, Sage, 1984
25. Renne KS: Health and marital experience in an urban population. J Marriage Fam 23:338–350, 1971
26. Albrecht SL, Bahr HM, Goodman KL: Divorce and Remarriage. Problems, Adaptations, and Adjustments. Westport, CT, Greenwood, 1983
27. Bloom BL, Hodges WF, Kern MB, McFaddin SC: A preventive intervention program for the newly separated: Final evaluations. Am J Orthopsychiatry 55:9–26, 1985
28. *Derogatis LR, Spencer PM: The Brief Symptom Inventory (BSI), Administration, Scoring, and Procedures* Manual I. Baltimore, Clinical Psychometrics Research, 1982
29. Spanier GB: Measuring dyadic adjustment: New scales for assessing the quality of marriage and similar dyads. J Marriage Fam 38:15–28, 1976
30. Spanier GB, Thompson LJ: Relief and distress after marital separation. J Divorce 7:31–49, 1983
31. Kitson GC, Langlie JK: Couples who file for divorce but change their minds. Am J Orthopsychiatry 54:469–489, 1984
32. Spanier GB, Castro RF: In Levinger F, Moles OC (eds), Divorce and Separation: Context, Causes, and Consequences. New York, Basic, 1979

33. Bloom BL, Hodges WF, Caldwell RA: A preventive program for the newly separated: Initial evaluation. Am J Community Psychol 10:251–164, 1982
34. Wallerstein JS: Women after divorce: Preliminary report from a ten-year follow-up. Am J Orthopsychiatry 56:65–77, 1986
35. Weiss RS: Issues in the study of loneliness. In Peplau A, Perlman D (eds), Loneliness: A Sourcebook of Current Theory, Research and Therapy. New York, Wiley, 1982
36. Kiecolt-Glaser JK, Ricker D, George J, Messick G, Speicher CE, Garner W, Glaser R: Urinary cortisol levels, cellular immunocompetency, and loneliness in psychiatric inpatients. Psychosom Med 46:15–24, 1984
37. Russell D, Peplau LA, Cutrona CB: The revised UCLA Loneliness Scale: Concurrent and discriminant validity evidence. J. Person Soc Psychol 39:472–480, 1980
38. Russell D: The measurement of loneliness, in Peplau LA, Perman D (eds): Loneliness: A Sourcebook of Current Theory Research, and Therapy. New York, Wiley, 1982
39. Dohrenwend BS, Krasnoff L, Askenasy AR, Dohrenwend BP: Exemplification of a method for scaling life events: The PERI Life Events Scale. J Health Soc Behav 19:205–229, 1978
40. Sarason IG, Sarason BR, Potter EH, Antoni MH: Life events, social support, and illness. Psychosom Med 47:156–163, 1985
41. Blaney PH: Stress and depression in adults: A critical review. In Field T, McCabe P, Schneiderman N (eds), Stress and Coping. Hillsdale NJ, Lawrence Erlbaum, 1985
42. Schleifer SJ, Keller SE, Camerino M, Thornton JC, Stein M: Suppression of lymphocyte stimulation following bereavement. JAMA 250:374–377, 1983
43. Schleifer SJ, Keller SE, Meyerson AT, Raskin MJ, Davis KL, Stein M: Lymphocyte function in major depressive disorder. Arch Gen Psychiatry 41:484–486, 1984
44. Glaser R, Kiecolt-Glaser JK, Stout JC, Tarr KL, Speicher CE, Holliday JE: Stress-related impairments in cellular immunity. Psychiatr Res 16:233–239, 1985
45. Glaser R, Gottleib-Stematsky T: Human Herpesvirus Infections: Clinical Aspects. New York, Marcel Dekker, 1982
46. Glaser R, Kiecolt-Glaser JK, Speicher CE, Holliday JE: Stress, loneliness, and changes in herpesvirus latency. J Behav Med 8:249–260, 1985
47. Kiecolt-Glaser JK, Glaser R, Williger D, Stout J, Messick G, Sheppard S, Ricker D, Romisher SC, Briner W, Bonnell G, Donnerberg R: Psychosocial enhancement of immunocompetence in a geriatric population. Health Psychol 4:25–41, 1985
48. Kiecolt-Glaser JK, Garner W, Speicher CE, Penn G, Glaser R: Psychosocial modifiers of immunocompetence in medical students. Psychosom Med 46:7–14, 1984
49. Kiecolt-Glaser JK, Glaser R, Strain E, Stout J, Tarr K, Holliday J, Speicher C: Modulation of cellular immunity in medical students. J Behav Med 9:5–21, 1986
50. Glaser R, Rice J, Speicher CE, Stout JC, Kiecolt-Glaser JK: Stress depresses interferon production and natural killer cell activity in humans. Behav Neurosci, in press
51. Reinherz EL, Schlossmen SF: Current concepts in immunology: Regulation of the immune response—Inducer and suppressor T-lymphocyte subsets in human beings. N Engl J Med 303:370–373, 1980
52. Chandra RK, Newberne PM: Nutrition, Immunity and Infection: Mechanisms of Interactions. New York, Plenum, 1977
53. Rodkey FL: Direct spectrophotometric determination of albumin in human serum. Clin Chem 11:478–487, 1965
54. Doumas BT, Watson WA, Biggs HG: Albumin and the measurement of serum albumin with bromcresol green. Clin Chim Acta 31:87–96, 1971
55. Keyser JW: Human Plasma Proteins. New York, Wiley, 1979
56. Buffone GJ: Transferrin, ICS-14. Fullerton CA, Beckman Instruments, Inc, 1980
57. Henle W, Henle G: Epstein-Barr virus and infectious mononucleosis. In Glaser R, Gottlieb-Stematsky T (eds), Human Herpesvirus Infections: Clinical Aspects. New York, Marcel Dekker, 1982
58. Jacobson NS, McDonald DW, Follette WC, Berley RA: Attributional processes in distressed and nondistressed married couples. Cognit Ther Res 9:35–50, 1985

59. Levenson RW, Gottman JM: Marital interaction: physiological linkage and affective exchange. J Person Soc Psychol 3:587–597, 1983
60. Levenson RW, Gottman JM: Physiological and affective predictors of change in relationship satisfaction. J Person Soc Psychol 49:85–94, 1985
61. O'Dorisio MS, Wood CL, O'Dorisio TM: Vasoactive intestinal peptide and neuropeptide modulation of the immune response. J Immunol 135:792s–796s, 1985
62. Pert CB, Ruff MR, Weber RJ, Herkenham M: Neuropeptides and their receptors: A psychosomatic network. J Immunol 135:820s–826s, 1985
63. Schaeffer MA, McKinnon W, Baum A, Reynolds CP, Rikli P, Davidson LM, Fleming I: Immune status as a function of chronic stress at Three Mile Island. Psychosom Med 47:85, 1985
64. Ernster BL, Sacks S, Selvin S, Petrakis NL: Cancer incidence by marital status: US third national cancer survey. J Natl Cancer Inst 63:587–585, 1979
65. Kiecolt-Glaser JK, Stephens R, Lipitz P, Speicher CE, Glaser R: Distress and DNA repair in human lymphocytes. J Behav Med 8:311–320, 1985
66. Glaser R, Thorn B, Tarr K, Kiecolt-Glaser JK, D'Ambrosio S: Effects of stress on methyltransferase synthesis: An important DNA repair enzyme. Health Psychol 4:403–412, 1985
67. Heller K: The effects of social support: Prevention and treatment implications. In Goldstein AP, Kanfer FH (eds), Maximizing Treatment Gains: Transfer Enhancement in Psychotherapy. New York, Academic, 1979
68. Menaghan, EG: Depressive affect and subsequent divorce. J Fam Issues 6:295–306, 1985
69. Monroe SM, Bromet EJ, Connell MM, Steiner SC: Social support, life events, and depressive symptoms: A one-year prospective study. J Consult Clin Psychol, 54:424–431, 1986
70. Coe CL, Levine S: Psychoimmunology: An old idea whose time has come. In Perez T, Chido J, Harvey, JH (eds), Biological and Behavorioral Correlates of Psychopathology. Lubbock, Texas Tech University Publications, in press
71. Kiecolt-Glaser JK, Glaser R: Psychosocial stress and human herpesvirus infections. In Kurstak E, Lipowski ZJ, Morozov PV (eds), Viruses, Immunity, and Mental Disorders. New York, Plenum, in press.