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Disclosure of Trauma and Immune Response to a Hepatitis B Vaccination Program

Keith J. Petrie and Roger J. Booth
University of Auckland Medical School

James W. Pennebaker and Kathryn P. Davison
Southern Methodist University

Mark G. Thomas
University of Auckland Medical School

This study investigated whether emotional expression of traumatic experiences influenced the immune response to a hepatitis B vaccination program. Forty medical students who tested negative for hepatitis B antibodies were randomly assigned to write about personal traumatic events or control topics during 4 consecutive daily sessions. The day after completion of the writing, participants were given their first hepatitis B vaccination, with booster injections at 1 and 4 months after the writing. Blood was collected before each vaccination and at a 6-month follow-up. Compared with the control group, participants in the emotional expression group showed significantly higher antibody levels against hepatitis B at the 4 and 6-month follow-up periods. Other immune changes evident immediately after writing were significantly lower numbers of circulating *T* helper lymphocytes and basophils in the treatment group. The finding that a writing intervention influences immune response provides further support for a link between emotional disclosure and health.

A number of researchers have speculated about a link between the inhibition of strong emotions and the development of physical disease (Gross, 1989; Pennebaker, 1989; Schwartz, 1990). Suppression of emotional thoughts has been shown to be related to an increased autonomic system arousal including skin conductance levels (Gross & Levenson, 1993) and to produce unexpected cognitive effects such as an increased preoccupation with the suppressed material (Wegner, Shortt, Blake, & Page, 1990). It has been proposed that the psychological process of suppressing emotions over an extended period of time compromises immune competence and leads to poor physical health (Pennebaker, 1989; Temoshok, 1987). Recent research investigating this model has found an association between the expression of emotions from traumatic experiences and health outcomes. Many of these studies have used a writing experimental paradigm where participants are randomly assigned to write, typically once a day for 3 or 4 consecutive days, either about traumatic experiences or trivial topics. Follow-up data is then gathered in the form of subsequent symptom reports, health center visits, or immunological changes.

Various studies have reported that participants assigned to write about traumatic or stressful experiences show a reduction in health center visits for illness (Pennebaker & Beall, 1986; Pennebaker, Colder, & Sharp, 1990; Pennebaker, Kiecolt-Glaser, & Glaser, 1988) and a decrease in work absentee rates (Francis & Pennebaker, 1992). Other studies have reported health improvements only among participants who have written particularly traumatic essays (Greenberg & Stone, 1992). In studies that have noted positive health benefits, this effect seems strongest within the first 8 weeks after writing, and there is some evidence that certain types of narrative, such as the use of more negative emotion words, may produce a better positive effect (Pennebaker, 1993). Typically, there seems to be an increase in negative emotion immediately after each session of personal traumatic writing but improvements in participants' feelings about the traumatic incidents and themselves over the course of the four writing sessions (Murray & Segal, 1994).

Research examining immunological changes after writing has revealed significant differences 6 weeks after the intervention in the blastogenic response to Concanavalin A (ConA) between emotional expression and control writing groups (Pennebaker, Kiecolt-Glaser, & Glaser, 1988). Although ConA blastogenic responses measure the proliferative capacity of *T* lymphocytes in the blood, it is not clear whether small changes are indicative of any physiologically significant or health-related effects. Other workers have focused on the immune response to Epstein–Barr virus (EBV). Most adults carry a latent, persistent infection with this virus which can be reactivated by stressful events. In an investigation designed to explore the effects of emotional disclosure on EBV reactivation, Esterling, Antoni, Fletcher, Margulies, and Scheiderman (1994) found that partic-

Keith J. Petrie, Department of Psychiatry and Behavioral Science, University of Auckland Medical School, Auckland, New Zealand; Roger J. Booth and Mark G. Thomas, Department of Molecular Medicine, University of Auckland Medical School, Auckland, New Zealand; James W. Pennebaker and Kathryn P. Davison, Department of Psychology, Southern Methodist University.

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Correspondence concerning this article should be addressed to Keith J. Petrie, Department of Psychiatry and Behavioral Science, University of Auckland Medical School, Private Bag 92019, Auckland, New Zealand. Electronic mail may be sent via Internet to kj.petrie@auckland.ac.nz.

ipants assigned to express their emotions about stressful events verbally or through writing had lower titers of antibodies against EBV compared with participants in a control condition. Although both these studies suggest that the expression of emotions related to stressful or traumatic events can influence immune parameters, it has not yet been demonstrated that such immune changes have significant health consequences. As a way of addressing this issue, we focused the present study on the question of whether emotional disclosure could influence the immune response to a hepatitis B vaccination program.

Hepatitis B is a serious viral infection of the liver and represents a major public health problem in many parts of the world. The hepatitis B virus may cause acute hepatitis, chronic active hepatitis, cirrhosis, and primary hepatocellular carcinoma. The virus has been ranked as second only to tobacco as a human carcinogen (Rustgi, 1987). Transmission is by contact with contaminated blood or body fluids and, because treatment of the disease is effective only in a minority of cases, vaccination programs for individuals at risk of exposure to the virus have become increasingly important (Peter, 1992). When a series of three vaccinations is given over a period of several months, an antibody response occurs in at least 90% of healthy adults. There is evidence from recent studies on medical students that psychological factors, such as stress, can influence the response to hepatitis B vaccination. Glaser et al. (1992) found higher seroconversion rates after hepatitis B vaccination were significantly related to lower levels of anxiety and perceived stress, and this finding has been replicated in a Dutch study (Jabaaij, Grosheide, Heijtink, Duivenvoorden, Ballieux, & Vingerhoets, 1993). One implication of this work is that the outcome of hepatitis B vaccination may also be enhanced through the use of psychological interventions. In this study, we investigated whether expressing emotions through writing about stressful or emotional topics would influence the immunological response to a hepatitis B vaccination program.

Method

Participants

Forty third-year medical students from Auckland University, Auckland, New Zealand, who returned negative hepatitis B antibody tests on routine screening using a solid-phase enzyme-linked immunosorbent assay (ELISA) volunteered for the study. The sample comprised 19 women and 21 men, with an average age of 21.5 years (SD = 2.4). The sample comprised 29 Caucasians, 3 Pacific Islanders and 7 participants were from other races. The study ran from March to September and finished 2 months before the participants' examination period. All participants completed the study and received NZ$50 (50 New Zealand dollars) at that time.

Procedure

With informed consent and ethical committee approval, participants were randomly assigned to write about either emotional or control topics. All participants wrote in a small, darkened basement room using a personal computer. The procedure for participants in the emotional writing group followed the detailed instructions outlined previously (Pennebaker, 1989) and included the following directions:

> *During each of the 4 writing days, I want you to write about the most traumatic and upsetting experiences of your whole life. You can write on different topics each day or on the same topic for all 4 days. The important thing is that you write about your deepest thoughts and feelings. Ideally, whatever you write about should deal with an event or experience that you have not talked about with others in detail.*

Participants in the control group were instructed to write on different aspects of their use of time on each of the 4 days. They were asked to write about the following topics on successive days; what they had done in the previous 24 hr, what their plans were for the next 24 hr, the next week, and the following 12 months. Each day in their writing, control participants were asked to write in a purely descriptive and objective way with minimum use of emotions. The treatment group comprised 11 female and 9 male participants, whereas the control group had 8 female and 12 male participants; this was not significantly different from the expected distribution, $\chi^2(1, N = 40) = 0.90$, *ns*.

The blood for immunological assays was collected on the day after completion of the 4 days of writing, which was immediately before the participants' first hepatitis B vaccination (HBvax-II, 10 micrograms). Subsequently, blood was collected at the same time of day (between 11 a.m. and 1 p.m.) immediately before the 1- and 4-month booster vaccinations and finally at a 6-month follow-up.

Physiological Recordings

Skin conductance was measured continuously during the writing using the CARMEN software program, which allows the linking of typed text with measures of autonomic activity (Pennebaker & Uhlmann, 1994). Electrodes were attached to the first and third fingers of both hands to record skin conductance level (SCL) with a J & J Model T-68 temperature–galvanic skin response module that included two IG-3 preamplifiers.

Before and After Writing Assessments

Before and after each writing session, participants completed a six-item mood rating and a six-item physical symptom rating. Items such as "sad," "anxious," "pounding heart," and "dizzy" were rated on a 7-point scale ranging from *not at all* (1) to *a great deal* (7). After writing, participants also completed an essay evaluation measure that asks them to report on the same 7-point scales the extent to which their writing was personal, meaningful, and revealing of their emotions and how much they had held back from previously discussing this material with others.

Content Analysis of Writing

Objective measures of essay content were obtained from the Linguistic Inquiry and Word Count (LIWC; Francis & Pennebaker, 1994) text analysis program. This program analyzes text on a word-by-word basis and classifies words into four high-level categories comprising emotional expression (e.g., negative emotionality, guilt, depression), cognitive strategies (e.g., insight, causation, acceptance), content domains (e.g., friends, university, sex) and language composition (e.g., pronouns, self-references, past tense verbs).

Immunological Assays

At each blood sampling, 15 ml of blood was collected into EDTA (anticoagulant) tubes for cellular assays and 5 ml was collected into a dry tube for serum antibody tests. Blood in the dry tubes was allowed to clot at 4° Celsius for 4 hr and then was centrifuged at 1000 × g for 5 min, and the serum was collected and stored frozen at −20° Celsius.

From the anticoagulated blood, two 1-ml samples were removed for hematological and cell surface marker tests, and the rest was diluted with an equal volume of physiological saline, layered onto Sepalymph, and centrifuged at 1500 × *g* for 30 min. Mononuclear cells were collected from the interface, washed twice in culture medium (RPMI 1640 containing 5% fetal calf serum), counted in a hemacytometer and then assayed for natural killer cell activity.

Hematological and Lymphocyte Surface Markers

Measurement of white blood cells, red blood cells, and platelet count, together with white blood cell differential counts were determined using a Bayer Technicon H1 Hematology Analyzer. Proportions of mononuclear cells in the blood bearing the CD4 (T helper lymphocytes), CD8 (T cytotoxic–suppressor lymphocytes) and CD56 (NKH1; natural killer cells) markers were determined using flow cytometry in a Coulter EPICS Profile II Analyzer with the following monoclonal Coulter antibodies: Fluorescein-antiCD4, Rhodamine-antiCD8, and Phycoerythrin-antiCD56. Absolute numbers of CD4, CD8, and CD56 cells were calculated using these proportions and the total lymphocyte counts.

Natural Killer (NK) Cell Assays

A standard 4-hr chromium release method (Coligan, Kruisbeek, Margulies, Shevach, & Strober, 1990) with eight serial twofold dilutions of purified mononuclear cells with K562 target cells was used to assay natural killer cell activity. This gave effector to target ratios of from 100:1 down to 0.8:1. Percent specific lysis was calculated at each cell concentration, and then lytic units per 10^7 mononuclear cells and per 10^7 NK (CD56) cells were calculated using the logistic transformation method (Bryant, Day, Whiteside, & Herberman, 1992).

Hepatitis B Antibodies

All serum samples were stored frozen at −20° Celsius and then all assayed for anti-hepatitis B antibodies at the same time. Antibodies against HBsAg (subtypes ad and ay) were quantitated using an IMx AUSAB kit (Abbott Laboratories) in a standard microparticle enzyme immunoassay (EIA) system.

Results

Experimental Manipulation

Before looking at differences between treatment and control groups on immune variables, we examined participant ratings concerning their writing, analysis of the text itself, and skin conductance level changes as a check of the experimental manipulation. The content of topics in the treatment condition were predominantly about the disruption of romantic or family relationships (45%), followed by parental divorce (10%), the death of a loved one (10%), professional direction (10%), physical or psychological abuse (7.5%) and other miscellaneous topics (17.5%). Analysis of the text in both treatment and control groups by the LIWC text analysis program was conducted using a series of Condition × Day repeated measures analyses of variance (ANOVAs). These revealed strong differences between conditions, with the treatment group higher on the expression of negative emotions, $F(1, 39) = 163.2$; anxiety, $F(1, 39) = 64.9$; anger, $F(1, 39) = 34.4$; and depression, $F(1, 39) = 30.9$ (all $ps < .001$). In treatment participants, there was also higher use of the cognitive strategy categories of insight words, $F(1, 39) = 264.1$; causation, $F(1, 39) = 87.4$; and acceptance, $F(1, 39) = 15.4$ (all $ps < .001$).

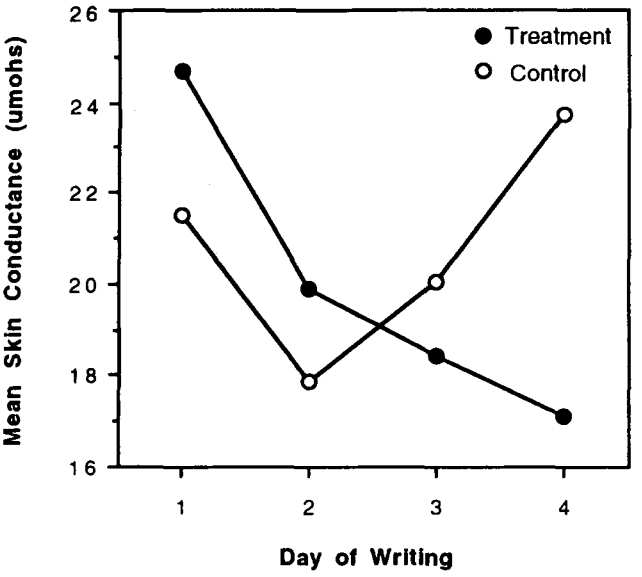

Figure 1. Mean skin conductance levels over writing days in treatment and control groups.

Participant ratings of their writing each day also supported the strength of the experimental manipulation. Participants in the treatment condition rated their writing to be more personal, $F(1, 39) = 7.0$; to be more meaningful, $F(1, 39) = 6.2$; and to cover topics they had held back from discussing, $F(1, 39) = 5.3$ (all $ps < .01$). Changes in mean skin conductance over the course of writing in the treatment and control groups are shown in Figure 1. SCL exhibited a steady and significant decline over the 4 writing days for participants in the treatment group, whereas mean SCL for control participants decreased initially but increased toward the end of writing. A 2 × 4 (Condition × Day) repeated measures ANOVA yielded a significant interaction effect for mean SCL, $F(1, 39) = 3.4$, $p < .05$, supporting the observation that the treatment group had a significant drop in mean SCL over the course of the 4 days of writing.

Psychological Changes and Symptom Reports After Writing

Analysis of the participants' brief symptom and mood checklists completed after writing showed no difference before writing between the treatment and control groups on any of the items averaged across sessions. However, in the checklist completed immediately after writing, there were significantly higher levels reported for "sadness," $F(1, 38) = 26.6$, $p < .001$, and "guilt," $F(1, 38) = 4.7$, $p < .05$, in the treatment group. Participants in the treatment group also reported significantly higher scores for "pounding heart," $F(1, 38) = 8.2$, $p < .01$, after the writing sessions.

Changes in Hepatitis B Antibodies and Other Immune Variables

All participants were selected on the basis of having no immunity to the hepatitis B virus when screened using a solid-

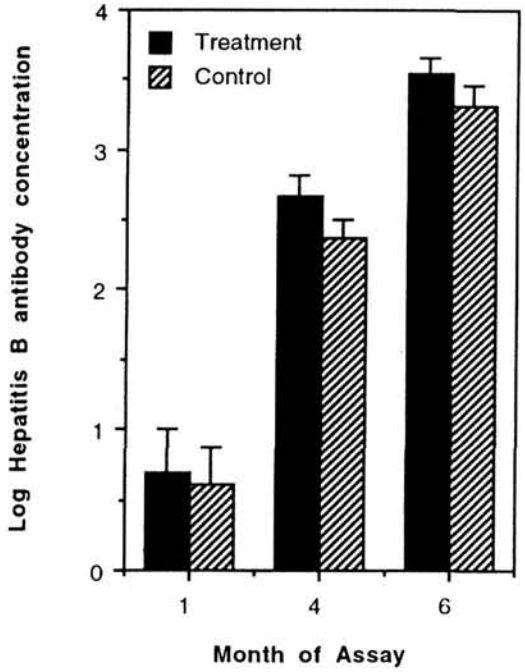

Figure 2. Mean (and *SEM*) log hepatitis B antibody concentrations in treatment and control groups.

phase ELISA screening method before the start of the study. However, using a more sensitive analysis, IMx microparticle EIA, we found that 5 participants (2 control and 3 treatment) had low but detectable levels of anti-hepatitis B antibodies in the first blood sample before the first vaccination. This indicated that these participants, at some stage, had been exposed and developed antibodies to the virus and would, therefore, be likely to mount a secondary (or memory) response rather than a primary response to the vaccine. The kinetics of antibody development in primary and secondary response are different so to control for this, log hepatitis B antibody concentrations were standardized at each of the three postwriting periods separately for the 35 participants with no previous antibodies to hepatitis B and for the 5 participants with low initial titers. The standardized hepatitis B antibody scores were then subjected to a 2 (Condition) × 3 (Assay Period) between-within repeated measures ANOVA. As can be seen in Figure 2, a significant (Condition × Period) interaction emerged, $F(2, 76) = 3.83, p < .05$, indicating that the treatment group had increasingly higher levels of hepatitis B antibodies over time compared with control participants. To assess whether the 5 participants who were initially antibody positive displayed different patterns of response, we computed a 2 (Condition) × 2 (Initial Status [antibody negative versus antibody positive] × 3 (Period) between-within repeated measures ANOVA on the standardized hepatitis B scores. As before, the Condition × Period interaction attained significance, $F(2, 72) = 7.32, p < .01$. Neither the Initial Status × Condition interaction nor the Initial Status × Condition × Period interaction attained significance. However, when the 5 antibody-positive participants were excluded from the analysis, the overall Condition × Period interaction was not significant, $F(2, 66) = 2.21, p = 0.11$. The pattern of means, however, was identical with or without the 5 participants. Table 1 presents data comparing the treatment and control groups on lymphocyte subsets, natural killer cell activity and basophil numbers. Analysis of these immune variables the day after writing showed that, compared with the control group, the treatment group exhibited significantly reduced numbers of CD4 (T helper) lymphocytes, $F(1, 39) = 5.5, p < .05$, but no differences in numbers of CD8 (T cytotoxic–suppressor), CD56 (natural killer) lymphocytes, or natural killer cell activity. There was also a significant decrease in circulating basophil numbers in the treatment group, compared with those in the control group, $F(1, 39) = 6.3, p < .05$. The CD4 and basophil effects were transient, however, and no differences were apparent by the time of the second blood sample 1 month later. There were no significant associations between these short-term immune phenotype effects and the longer term antibody changes. None of the other immune or hematological measures showed any significant differences between the groups.

Discussion

The results of this study confirm that expression of emotions concerning stressful or traumatic events can produce measurable effects on human immune responses. More importantly, the data demonstrate that such changes can influence the outcome of a vaccination program with important clinical relevance to participants. Participants in the emotional writing group developed a small but significantly higher level of antibodies against the hepatitis B vaccine than did control participants, indicating that changes in immune function prompted by emotional disclosure may have potentially important health consequences for the development of protection against infectious diseases. However, caution should be exercised in generalizing from this result beacause of the possibility that primary and secondary antibody responses are differentially affected by emotional disclosure. A secondary response occurs in individuals who have been exposed previously to a specific antigen (in this case, the hepatitis B virus). As well as generally displaying different characteristics from primary responses, secondary responses are subject to a different spectrum of immunological control mechanisms (e.g., helper *T* lymphocyte requirements, cytokine influences) but insufficient data is known about these mechanisms to ascribe the effects of emotional disclosure to any particular immunoregulatory pathways at this stage. Although differing effects on primary and secondary pathways are conceivable, it was not possible to examine this further in our study because of the small numbers of participants undergoing a secondary response (i.e., those who were hepatitis-B-antibody positive at the outset).

It is important to note that this experiment was conducted using young, healthy participants vaccinated according to a standard protocol designed to produce maximal immunity to hepatitis B in more than 90% of healthy individuals. The significant difference in antibody concentrations between treatment and control groups, therefore, does not indicate an impaired immune response to the vaccine in the control participants. However the results suggest that in more marginal situations, such as in individuals with compromised immune

Table 1
Means (and SEM) for CD4+, CD8+, and CD56+ Basophil Numbers and Natural Killer (NK) Cell Activity Between Treatment and Control Groups the Day After 4 Days of Writing and at Subsequent Test Times

Test time and group	CD4	CD8	CD56	NK activity	Basophil
Day after writing					
Treatment	0.85 (0.05)*	0.55 (0.07)	0.35 (0.07)	185.4 (18.4)	0.061 (0.007)**
Control	1.12 (0.10)*	0.63 (0.06)	0.31 (0.03)	198.6 (21.4)	0.081 (0.005)**
Follow-up periods					
1 month					
Treatment	0.83 (0.06)	0.59 (0.06)	0.21 (0.03)	207.1 (17.7)	0.057 (0.006)
Control	0.94 (0.08)	0.61 (0.05)	0.24 (0.04)	238.2 (36.6)	0.072 (0.007)
4 months					
Treatment	0.80 (0.05)	0.54 (0.05)	0.27 (0.05)	226.2 (17.7)	0.054 (0.005)
Control	0.97 (0.07)	0.56 (0.04)	0.22 (0.04)	190.2 (18.3)	0.068 (0.007)
6 months					
Treatment	0.84 (0.06)	0.57 (0.05)	0.18 (0.03)	196.4 (12.6)	0.053 (0.006)
Control	0.90 (0.08)	0.50 (0.04)	0.17 (0.03)	181.6 (13.0)	0.062 (0.006)

* $p < .05$. ** $p < .01$.

systems or with vaccines that stimulate the immune system less effectively, emotional disclosure may be of critical importance for the development of antibodies.

The writing itself produced skin conductance changes consistent with emotional disclosure, with a decrease in the mean SCL over each writing day in the disclosure group, and this was supported by participant reports and linguistic analysis of the text. The increase in SCL in the control group on the last day of writing may be explained by the fact that the writing on this day focused on their plans for the year, which included major medical school examinations. The changes in CD4 lymphocyte and basophil numbers immediately after the writing intervention are more difficult to interpret because of a lack of baseline data for these particular variables as they were not the primary focus of the study. Statistically significant differences between the emotional disclosure and control groups were found in the CD4 (helper) but not CD8 (cytotoxic–suppressor) *T* lymphocyte, CD56+ (NK) populations or for natural killer cell activity. These differences in CD4+ lymphocyte populations had disappeared a month later and are consistent with the treatment group participants' reports of increased levels of distress in terms of higher levels of sadness and guilt immediately after writing (Glaser et al., 1985; van Rood, Bogaards, Goulmy, & van Houwelingen, 1993). It is difficult to conclusively determine in the present study whether these short-term immune changes were due to the immediate effects of disclosure, but the psychological effects were consistent with a recent report on the emotional changes after personal traumatic disclosure (Murray & Segal, 1994). There was also a significant transient elevation in circulating basophil numbers in the treatment group immediately after the intervention. Although the numbers of basophils in the blood is normally very low and small changes should be not be overinterpreted, basophils are important elements in allergy reactions and so it would be useful to assess in future work whether emotional disclosure interventions have any effects on allergic symptoms.

The finding that emotional disclosure may influence an individual's immunity to infection is consistent with previous reports on the health benefits of disclosure. Studies of college students have mostly shown a decrease in medical center visits in the weeks after a writing intervention (Pennebaker, Colder, & Sharpe, 1990; Pennebaker & Francis, 1994). Illness in these studies is operationally defined as any presenting complaint to a medical center that could be attributed to an acute infection or other internal cause unrelated to an injury. As upper respiratory tract infections and other viral complaints are among the most common presenting complaints at university health centers, any intervention with an impact on resistance to infection is likely to affect the number of health center visits in such a population.

The immune system is a complex process requiring cooperation and sequential engagement of a variety of elements. The rationale for prophylactic immunization is that it mimics the way the immune system is stimulated by the antigens of infectious agents, and there is some experimental evidence that the effectiveness of immunization is subject to psychosocial influences. For example, in an animal study, mice stressed by sleep deprivation failed to develop protective immunological memory when immunized with influenza virus antigen (Brown, Pang, Husband, & King, 1989). Evidence from studies in humans shows that response to vaccination can be modulated by psychosocial factors measurable both at the time of immunization and during the course of the response (Glaser et al., 1992; Jabaaij et al., 1993). Our study extends these findings by demonstrating that an active psychological intervention can modulate the immune response to a vaccine. Given the widespread use of vaccinations as preventative health measures, the influence of psychological factors on response to vaccines is an important area of psychoimmunology in need of further attention.

The study provides further support for models that propose that emotional suppression is important in development of illness (Greer & Watson, 1985; Gross, 1989; Pennebaker, 1989). The data from this study are consistent with the proposition that the inhibition of emotional thoughts may diminish the abil-

ity of the immune system to respond effectively to antigens, be they infectious organisms or abnormal cells. The mechanisms mediating the relationship between emotional expression and immune competence require further investigation from two directions. First, a clearer understanding of the nature of emotional expression itself is desirable to distinguish the types of emotional expression that produce immune changes. To this end, more intensive investigation of the type of emotions and trauma disclosed and the links to autonomic nervous system function would be beneficial. Second, increased attention should be given to the immune changes immediately around the time of writing to identify the immune variables most sensitive to emotional disclosure and their role in modulating immune behavior.

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