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Social Relationships and Susceptibility to the Common Cold

Sheldon Cohen

Social relationships are thought to have both negative and positive influences on the ability of our bodies to resist infection. On the negative side, social conflicts are a common cause of stressful environments, including chronic problems at home and work and acute major stressful life events involving family, friends, and workmates. Laboratory studies have found that experimentally induced marital conflicts suppress cellular components of immune function (Kiecolt-Glaser et al., 1993) and epidemiologic studies have linked family conflict with higher risk for naturally acquired upper respiratory infections (Clover, Abell, Becker, Crawford, & Ramsey, 1989; Meyer & Haggerty, 1962). On the positive side, social relationships provide many benefits, including facilitating the motivation to care for oneself, allowing for more effective regulation of emotional responses, and providing support in the face of stressful events (Cohen, 1988; Thoits, 1983). The most provocative evidence that links social relationships to better physical health is the well-established association between participation in multiple social domains (family, friends, work, group memberships) and decreased mortality (e.g., Berkman & Syme, 1979; House, Robbins, & Metzner, 1982). This relation has been reported in multiple prospective studies and has a relative risk (isolated people are approximately two times more likely to die during follow-up) that is comparable in magnitude to the relation between smoking and mortality (e.g., House, Landis, & Umberson, 1988).

The research reported in this chapter assesses the role of social conflicts and social participation in susceptibility to upper respiratory infections. In our studies, we characterize the social environments of healthy volunteers. Subsequently, we expose them to a virus that causes a common cold. Approximately 40% of those exposed develop a verifiable illness. Hence, we can ask whether the status of their social environment before exposure predicts whether their bodies are able to resist infection.

This work is unique in two ways. First, because we intentionally expose healthy volunteers to a controlled dose of virus and quarantine them after exposure, the associations we find between the social environment and illness cannot be attributed to social interaction-based differences in exposure to infectious agents. Second, closely monitoring volunteers (in quarantine) throughout the course of our studies allows us to assess behavioral and biological pathways that might link the social environment to disease susceptibility.

Figure 7.1 presents the plausible pathways that link social conflicts to disease susceptibility, and figure 7.2 presents the pathways that link social participation to susceptibility. The figures are meant only as heuristics for understanding how the social environment gets into the body and, therefore, include only those pathways that start in the social environment and terminate in the ability to resist infectious illness. There are no assumptions implied about other possible pathways.

As apparent from figure 7.1, social conflicts are thought to act through their negative impact on emotions and cognitions. Negative cognitive and emotional

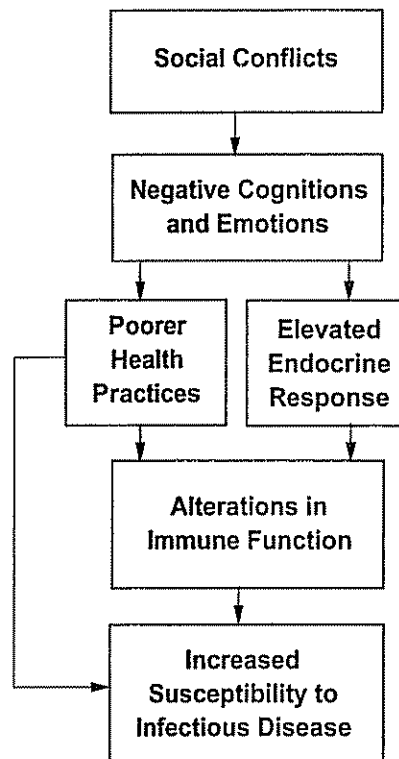


Figure 7.1 Plausible pathways linking social conflicts to disease susceptibility. The figure includes only those pathways that start in the social environment and terminate in the ability to resist infectious illness. There are no assumptions implied about other possible pathways.

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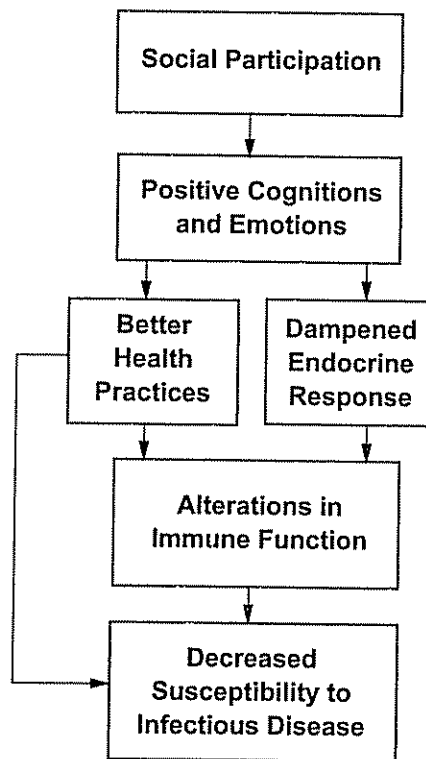


Figure 7.2 Plausible pathways linking social participation to disease susceptibility. The figure includes only those pathways that start in the social environment and terminate in the ability to resist infectious illness. There are no assumptions implied about other possible pathways

states can result in behavioral coping strategies, such as increased smoking and decreased exercise and sleep, which may compromise health. Poor health practices can operate directly on an outcome (e.g., cigarette smoke results in inflammation of the nasal mucosa) or by suppressing the immune system's ability to protect the body against infectious agents. Negative emotions have also been linked with increases in the release of a number of hormones, including epinephrine, norepinephrine, and cortisol. Elevated levels of these hormones have been found to suppress the immune system's ability to recognize, mark, and destroy infectious agents (Rabin, Cohen, Ganguli, Lyle, & Cunnick, 1989).

As shown in figure 7.2, positive social relationships can result in a range of positive cognitions and emotions, including feeling needed, feelings of self-worth and control, and feelings of well-being and calmness. Clearly, having greater self-esteem and control can result in increased motivation to care for oneself and, in turn, better health practices. However, the relation between positive psychological states and endocrine and (especially) immune pathways is more controversial. There is evidence that positive relationships have acquiescent effects on hor-

monal systems (see reviews in Seeman, Berkman, Blazer, & Rowe, 1994; Uchino, Cacioppo, & Kiecolt-Glaser, 1996) In theory, this might alter immune function in a positive manner. There is, however, little evidence that positive emotions are associated with enhanced immunity (see review in Cohen & Herbert, 1996)

Associations between the social environment and immune regulation provide the underpinning for a biologically plausible argument for how external social stimuli get inside the body and influence our ability to resist infectious agents (e.g., figs. 7.1 and 7.2). However, evidence for the role of the immune system in linking the social environment to disease is indirect at best. The central problem is the lack of measures of immune function (other than specific antibody to the infectious agent) that reliably predict susceptibility to infectious disease in healthy humans (e.g., Cohen & Herbert, 1996). Our failure to find immune markers of host resistance is usually attributed to the limited access we have to the internal organs, such as the spleen, lymph nodes, and gut, where most immune tissue is found. Instead, when studying humans, we are generally limited to assessing the function of white blood cells circulating in the blood. More convincing evidence that psychosocial effects on immune regulation may influence susceptibility to disease is provided by the prospective epidemiologic studies of the relation between social conflicts and upper respiratory illness (Clover, Abell, Becker, Crawford, & Ramsey, 1989; Meyer & Haggerty, 1962). However, these studies are subject to a range of alternative causal explanations. For example, a conflict at home might result in the seeking of social support from friends, fellow workers, or family members. The increase in social interactions results in an increased probability of *being exposed* to infectious agents. Hence, it is difficult to know whether associations between social conflict and illness reported in naturalistic settings are attributable to exposure to infectious agents or to the competence of the immune system in fighting off infection.

Pittsburgh Common Cold Study

The data we present comes from a study of susceptibility to the common cold run in Pittsburgh, Pennsylvania, between 1993 and 1996. Detailed presentations of the procedures and results of this trial are published elsewhere (Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997; Cohen, Frank, Doyle, Skoner, Rabin, & Gwaltney, 1998). After completing a stressful life events interview and a questionnaire that assesses social participation and social ties, 276 (125 men and 151 women) healthy volunteers, aged 18 to 55, were exposed to one of two viruses that cause the common cold. The association between the social environment measures and the subsequent development of biologically verified clinical disease was examined with use of controls for baseline (before exposure to the virus) amount of antibodies to the experimental virus, body mass, season of the year (fall or spring), and various demographic factors. In further analyses, we examined the possible role of several behavioral and biological pathways in linking the social environment and susceptibility to infection.

Experimental Plan

All volunteers came to the hospital for medical eligibility screenings. Social networks, select health practices (smoking, alcohol consumption, exercise, sleep quality, diet), demographic factors, and body weight and height were also assessed at the screening and used as baseline data for those who were found to be eligible. Eligible subjects returned to the hospital both four and five weeks after screening to have blood drawn. An assessment of a marker of immune function—natural killer cell activity—was based on both blood draws, and an assessment of antibodies to the experimental virus was based on the second blood draw. A personality questionnaire was administered twice, once at each blood draw. Volunteers returned an additional time during the period after initial screening but before being exposed to the virus to complete an intensive stressful life events interview.

Subjects were quarantined within one week after the second blood draw. Baseline assessment of self-reported respiratory symptoms and two objective indicators of illness (nasal mucociliary clearance and nasal mucus production) were assessed during the first 24 hours of quarantine (before viral exposure). Urine samples for hormone assessment and information on dietary intake were also collected at this time.

At the end of the first 24 hours of quarantine, volunteers were given nasal drops that contained a low infectious dose of one of two types of rhinovirus (RV39 [$N = 147$] or Hanks [$N = 129$]). Two viruses were used in order to assess whether predictors of susceptibility are equivalent across different rhinovirus types.

The quarantine continued for five days after exposure. During this period, volunteers were housed individually but were allowed to interact with each other at a distance of three feet or more. Nasal secretion samples for verifying infection by virus culture were collected on each of the five days. On each day, volunteers completed a respiratory symptoms questionnaire and were tested for objective markers of illness with the same procedures as those used at baseline. Approximately 28 days after challenge, another blood sample was collected for verifying infection by determination of changes in antibodies to the challenge virus. All investigators were blinded to subjects' status on social network, personality, endocrine, health practice, immune, and prechallenge antibody measures.

Standard Control Variables

We used eight control variables, which might provide alternative explanations for the relation between social environmental characteristics and illness. These included the antibody to the experimental virus at baseline, age, body mass index (weight in kilograms divided by the square of height in meters), whether the trial was conducted in the fall (November) or spring (April and May), race, gender, viral type (RV39 or Hanks), and education.

Measures of Social Stress and Social Participation

We used a semistructured life events interview, the Bedford College Life Events and Difficulties Schedule (LEDS) to assess both social and nonsocial life events (Brown & Harris, 1989; Harris, 1991). The LEDS uses strict criteria for whether or not an event occurs, classifies each event on the basis of severity of threat and emotional significance, and makes a distinction between events and ongoing chronic difficulties (stressors). Raters blind to the individual's subjective response to an event are provided with extensive information regarding each event and the context in which it occurred; they then rely on thorough "dictionaries" to rate events. The dictionary ratings are based on the likely response of an average person to an event that occurs in the context of a particular set of biographical circumstances. We focus on the traditional LEDS outcomes: the occurrence of severe events (less than four weeks in duration) and chronic difficulties (more than four weeks). We also calculate separate scores for events and difficulties that involve social conflicts and those that do not.

Social network participation was assessed by questionnaire. The Social Network Index assesses participation in 12 types of social relationships (Cohen et al., 1997): relationships with a spouse, parents, parents-in-law, children, other close family members, close neighbors, friends, workmates, schoolmates, fellow volunteers (e.g., charity or community work), members of groups without religious affiliations (e.g., social, recreational, professional), and members of religious groups. One point is assigned for each kind of relationship (possible score of 12) for which respondents indicate that they speak (in person or on the phone) to someone in that relationship at least once every two weeks. The total number of persons with whom they speak at least once every two weeks (number of network members) was also assessed.

Infection and Illness

Infectious diseases result from the growth and action of microorganisms or parasites in the body (see Cohen & Williamson, 1991). Infection is the multiplication of an invading microorganism. Clinical illness occurs when infection is followed by the development of symptoms characteristic of the disease.

Infection We used two common procedures for detecting whether volunteers were infected by the experimental challenge virus. In the viral isolation procedure, nasal secretions, which were collected daily, were inoculated into cell cultures, which stimulated replication of the specific virus. If the virus was present in nasal secretions, it grew in the cell cultures and could be detected. Alternatively, one can indirectly assess the presence of a replicating virus by looking at changes in serum antibody levels to that virus from before exposure to several weeks after. An invading microorganism (i.e., infection) triggers the immune system to produce antibodies. Because each antibody recognizes only a single type of microorganism, the production of antibodies to a specific infectious agent is evidence for the presence and activity of that agent.

Nasal washes were performed daily during quarantine to provide samples of nasal secretions for virus culture. Serum samples were collected both before and 28 days after exposure to the virus to assess both prechallenge levels (standard control factor) and the amount of change in antibodies to the experimental virus (marker of infection).

Objective Signs of Illness On each day of quarantine, we assessed two objective signs of illness—mucus weights and mucociliary clearance function—and one subjective measure, self-reported symptoms. Mucus weights were determined by collecting used tissues in sealed plastic bags. After correcting for the weight of the bag and the mucus weight at baseline, the postchallenge weights were summed across the five days to create an adjusted total mucus weight score.

Nasal mucociliary clearance function refers to the effectiveness of nasal cilia in clearing mucus from the nasal passage toward the throat. Clearance function was assessed as the time required for a dye administered into the nose to reach the throat (nasopharynx). Each daily time was adjusted for baseline, and the adjusted average time in minutes was calculated across the postchallenge days of the trial.

Subjective Symptoms of Illness On each day of quarantine, subjects rated the severity of eight symptoms (congestion, runny nose, sneezing, cough, sore throat, malaise, headache, and chills) during the previous 24-hour period. Ratings ranged from 0 (none) to 4 (very severe) for each symptom. The symptom scores were summed for each day. Finally, after adjusting (subtracting) baseline symptoms, daily symptoms were summed across the five postchallenge days to create a total symptom score. Subjects were also asked each day if they had a cold.

Defining Colds Volunteers were considered to have a cold if they were *both* infected and met illness criteria. They were classified as infected if the challenge virus was isolated on any of the five postchallenge study days or if there was a substantial rise (fourfold increase in antibody titer) in serum antibody level to the experimental virus. The illness criterion was based on selected *objective* indicators of illness: a total adjusted mucus weight of at least 10 grams or an adjusted average mucociliary nasal clearance time of at least 7 minutes. By basing the definition of illness entirely on objective indicators, we were able to exclude interpretations of our data based on psychological influences on symptom reporting. Mean total adjusted symptom score for those with colds (infected and meeting the objective criterion for illness) was 19.28 (sd = ± 14.7) versus 5.67 (sd = ± 8.1) for those without colds ($t(274) = -9.88, p < .001$).

Relative Risk We use odds ratios to estimate the relative risk of developing a cold. An odds ratio approximates the odds that the disease outcome (common cold) will occur in one group as compared to another. We report the odds ratios comparing those with 4–5 and 6 or more roles to those with 3 or fewer and comparing those who experienced stressful life events to those who did not. All odds ratios we report are adjusted for the standard control variables. In each case, we report the corresponding 95% confidence intervals (CI [95%]).

Social Networks and Susceptibility

Figure 7.3 presents the rate of colds found for each of the three social network groups. These are observed rates and are not adjusted for the standard controls. As apparent from figure 7.3, the rate of colds decreased as social network diversity increased. The adjusted odds ratios were 4.2 (CI [95%] = 1.34, 13.29), 1.9 (CI [95%] = 1.00, 3.51), and 1, respectively. There were no interactions between the standard control variables and social network diversity in predicting colds. Hence, the relations were similar for the two virus types, different preexposure antibody levels, age, gender, race, education, body mass, and across the two seasons.

Total number of network members was not associated with colds ($p < .12$). Moreover, entering the number of network members into the first step of the regression equation along with standard controls did not reduce the association between diversity and colds ($p < .01$). Hence, the diversity of the network is more important than the number of network members, and its association with colds is independent of the number of members.

Acute Stressful Life Events, Chronic Difficulties, and Susceptibility

There were 179 subjects with at least one severe acute event that occurred within one year of the study. Acute stressful life events were not, however, associated with developing a cold. There were 75 subjects with a chronic difficulty that lasted one month or longer. Those with such difficulties were 2.2 times more likely to develop a cold (CI [95%] = 1.08, 4.34) than those without. Moreover, there were no interactions between any of the standard control variables and

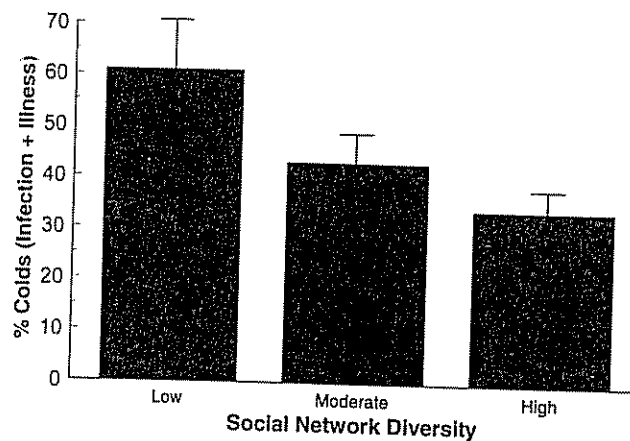


Figure 7.3 Observed incidence of colds by social network diversity. Low diversity is described as 1–3 types of social relationships, moderate 4–5, and high 6 or more. Error bars indicate standard errors.

chronic difficulties in predicting colds. Hence, the relations were similar for the two virus types, different preexposure antibody levels, age, gender, race, education, body mass, and across the two seasons.

As discussed earlier, we were primarily interested in whether interpersonal conflict increased susceptibility to infectious illness. Difficulties were categorized into three domains: interpersonal, work, and other. As is apparent from figure 7.4, having either work or interpersonal chronic difficulties was associated with greater risk for colds in comparison with those with no difficulties and other types of difficulties.

We considered the possibility that difficulties at work were in fact interpersonal difficulties as well. To pursue this issue, we had each of the 30 (one-month criterion) chronic difficulties coded for interpersonal content (criteria from Johnson, Monroe, Simons, & Thase, 1994). Only 2 of the 30 were found to be interpersonal conflicts at work, while 27 were attributable to unemployment or underemployment and 1 to a failing business.

Finally, we considered the possibility that those with a work or an interpersonal difficulty had more difficulties than those with another type of difficulty. The differences between groups did not approach significance (1.2 difficulties for work, 1.3 for relationships, and 1.1 for other). Nor was there an association between number of difficulties (for those with at least one difficulty) and colds.

Pathways Linking Social Networks and Stressful Life Events to Susceptibility

Preliminary analyses indicated that those with low levels of social participation were more likely to be smokers and less likely to exercise. Similarly, those with enduring difficulties were more likely to be smokers. There were also marginal asso-

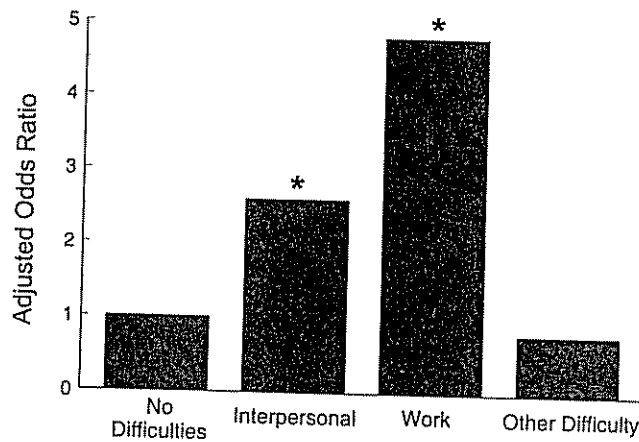


Figure 7.4 Adjusted odds ratios contrasting persons with interpersonal, work, and other chronic difficulties to those with no chronic difficulties; * $p < .05$

ciations between having a difficulty, less exercise, and poorer sleep efficiency. All of these health practices were also associated with susceptibility to colds with smokers, those getting less exercise, and those with poor sleep quality all at greater risk. However, these health practices could explain only a small fraction of the relation between these characteristics of the social environment and susceptibility to infectious illness. Neither the hormones nor immune measures were associated with either social network or social conflict measures and hence neither could operate as a pathway that linked the social environment to illness susceptibility.

Personality as an Alternative Explanation

The Big Five personality factors are thought to represent the basic structure of personality (e.g., Goldberg, 1992). The factors are commonly described as introversion-extroversion, agreeableness, conscientiousness, emotional stability, and openness. We found that only introversion-extroversion was associated with susceptibility to colds. Those with scores below the median (introverts) were at greater risk (adjusted OR = 2.7, CI = 1.45, 4.92). Although none of the personality factors were associated with chronic difficulties, introversion was associated with lower levels of social network diversity ($p < .002$). However, the relation between network diversity and colds occurred above and beyond (independent of) the association of introversion and colds.

Conclusions

On the one hand, enduring interpersonal conflicts were associated with greater risk for developing an illness among those exposed to a virus. These were severe conflicts, which lasted at least a month, and included ongoing problems with spouse, family, and friends. On the other hand, having more types of social relationships was associated with less susceptibility to viral-induced illness. Interestingly, the diversity of types of relationships, not the total number of relationships, is what mattered. The associations between these characteristics of the social environment and illness susceptibility were substantial. Those with interpersonal conflicts were 2.5 times more likely to develop an illness than those without, and those who were relatively isolated (1-3 social relationships) were 4.2 times more likely to develop illness than those with very diverse networks (6 or more relationships). In contrast, the biggest effect of health practices was a threefold risk for smokers in comparison to nonsmokers. Interestingly, social conflicts and social participation had independent relations with illness susceptibility. Moreover, there was no interaction between social conflicts and social participation, so that a diverse social network did not operate to protect people from the influences of enduring social conflicts.

What can account for the relations between these characteristics of the social environment and susceptibility to infectious illness? In figures 7.1 and 7.2, we presented a number of plausible pathways. A key mediator in both models is emotional and cognitive response. In fact, social participation was associated with more positive affect (both state and trait, not reported here), but positive af-

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fect was not associated with susceptibility. Unexpectedly, neither positive nor negative affect was associated with chronic difficulties in this study. We used the POMS, a well-established measure of affect, and, therefore, we feel that from a measurement perspective we made a reasonable attempt. However, there are a number of earlier studies that have shown that those with chronic difficulties are at greater risk for depression (Brown & Harris, 1989). We did not measure relevant cognitive mediators, such as feelings of personal control and self-esteem, and hence cannot say whether they play a part.

Other mediators proposed in both models included health behaviors and the function of the endocrine and immune systems. However, when we measured these potential pathways, none could account for the relations we found. In the case of health practices all five of the measures operated as risk factors for illness. Smokers, those abstaining from alcohol, those with poor sleep efficiency, those with few days of exercise, and those with low dietary intake of vitamin C were at greater risk for developing colds. However, health practices could account for only a small part of the relations between the social environment and host resistance. Because the health practice measures were all related to susceptibility in the expected manner, we are confident that we did a good job of assessing this pathway. As a consequence, it seems unlikely that these health practices play a major role in linking social environments to resistance to infectious illness. Although we assessed the health practices that we thought would be most likely to provide pathways, it is possible that other practices, such as caffeine intake, use of mouthwash, or regular hand washing, might link the social environment to illness susceptibility.

Those with elevated levels of epinephrine and norepinephrine were similarly at greater risk for developing colds. Again, however, levels of these hormones did not provide any additional explanation of the relations between the social environment and colds. To our surprise, these hormones were not even associated with the social environment measures. Because epinephrine and norepinephrine were assessed during the 24 hours before viral exposure, they might have been indicating a stress-type reaction to the beginning of quarantine rather than a base level of response to the participants' background social environments. In our current work, we are attempting to get better background levels by measuring hormones several times during the weeks before volunteers report for quarantine. This is a case where obtaining reliable measurements (multiple measures) at appropriate points in time is essential.

We chose natural killer cell activity as our primary marker of immune function for two reasons. First, natural killer (NK) cells are surveillance cells, which identify infected (and otherwise altered cells) and kill them. In theory, higher levels of natural killer cell activity should help limit infection and prevent illness. Second, there is evidence that chronic psychological stress is associated with suppression of NK activity (reviewed in Herbert & Cohen, 1993). However, NK activity did not operate as a pathway that linked the social environment to illness susceptibility in our study. We mentioned earlier that measuring immunity in the blood is not always the most appropriate procedure, and this may be the problem here. In theory, NK activity in the lung might be the essential issue in the case of respiratory infections. It is also possible that NK activity in the blood might make a dif-

ference, but that the immune system's ability to compensate for deficits in single subsystems obscured any relation. At any rate, we found no evidence for immune mediation of the relations between the social environment and infectious illness. Again, we think that this may be attributable to problems in measurement. We are unsure that we can ever adequately assess immune-mediated host resistance in this setting, but we still think that the immune system is a key player in linking the social environment to susceptibility to upper respiratory infections

Note

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References

- Brown, G. W. & Harris, T. O. (Eds.) (1989). *Life events and illness*. New York: Guilford.
- Clover, R. D., Abell, T., Becker, L. A., Crawford, S., & Ramsey, C. N. (1989). Family functioning and stress as predictors of influenza B infection. *Journal of Family Practice*, 28, 536-539.
- Cohen, S. (1988). Psychosocial models of the role of social support in the etiology of physical disease. *Health Psychology*, 7, 269-297.
- Cohen, S., Doyle, W. J., Skoner, D. P., Rabin, B. S., & Gwaltney, J. M., Jr. (1997). Social ties and susceptibility to the common cold. *Journal of the American Medical Association*, 277, 1940-1944.
- Cohen, S., Frank, E., Doyle, W. J., Skoner, D. P., Rabin, B. S., & Gwaltney, J. M., Jr. (1998). Types of stressors that increase susceptibility to the common cold. *Health Psychology*, 17, 214-223.
- Cohen, S., & Herbert, T. B. (1996). Health psychology: Psychological factors and physical disease from the perspective of human psychoneuroimmunology. In J. T. Spence, J. M. Darley, & D. J. Foss (Eds.), *Annual review of psychology* (Vol. 47). El Camino, CA: Annual Review.
- Cohen, S., Tyrrell, D. A. J., & Smith, A. P. (1991). Psychological stress and susceptibility to the common cold. *New England Journal of Medicine*, 325, 606-612.
- Cohen, S., Tyrrell, D. A. J., & Smith, A. P. (1993). Life events, perceived stress, negative affect and susceptibility to the common cold. *Journal of Personality and Social Psychology*, 64, 131-140.
- Cohen, S., & Williamson, G. M. (1991). Stress and infectious disease in humans. *Psychological Bulletin*, 109, 5-24.
- Doyle, W. J., McBride, T. P., Swartz, J. D., Hayden, F. G., & Gwaltney, J. M., Jr. (1988). The response of the nasal airway, middle ear and Eustachian tube to provocative rhinovirus challenge. *American Journal of Rhinology*, 2, 149-154.
- Evans, P. D., & Edgerton, N. (1991). Life-events and mood as predictors of the common cold. *British Journal of Medical Psychology*, 64, 35-44.
- Evans, P. D., Pitts, M. K., & Smith, K. (1988). Minor infection, minor life events and the four day desirability dip. *Journal of Psychosomatic Research*, 32, 533-539.

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- Glaser, R., Rice, J., Sheridan, J., Fertel, R., Stout, J., Speicher, C. E., Pinsky, D., Kotur, M., Post, A., Beck, M., & Kiecolt-Glaser, J. K. (1987). Stress-related immune suppression: Health implications. *Brain, Behavior, and Immunity*, 1, 7-20.
- Goldberg, L. R. (1992). The development of markers for the Big-Five factor structure. *Psychological Assessment*, 4, 26-42.
- Harris, T. O. (1991). Life stress and illness: The question of specificity. *Annals of Behavioral Medicine*, 13, 211-219.
- Herbert, T. B., & Cohen, S. (1993). Depression and immunity: A meta-analytic review. *Psychological Bulletin*, 113, 472-486.
- House, J. S., Landis, K. R., & Umberson, D. (1988). Social relationships and health. *Science*, 241, 540-545.
- House, J. S., Robbins, C., & Metzner, H. L. (1982). The association of social relationships and activities with mortality: Prospective evidence from the Tecumseh Community Health Study. *American Journal of Epidemiology*, 116, 123-140.
- Johnson, S. L., Monroe, S., Simons, A., & Thase, M. E. (1994). Clinical characteristics associated with interpersonal depression: Symptoms, course and treatment response. *Journal of Affective Disorders*, 31, 97-109.
- Kiecolt-Glaser, J. K., Malarkey, W. B., Chee, M., Newton, T., Cacioppo, J. T., Mao, H.-Y., & Glaser, R. (1993). Negative behavior during marital conflict is associated with immunological down-regulation. *Psychosomatic Medicine*, 55, 395-409.
- Meyer, R. J., & Haggerty, R. J. (1962). Streptococcal infections in families. *Pediatrics*, 29, 539-549.
- Rabin, B. S., Cohen, S., Ganguli, R., Lyle, D. T., & Cunnick, J. E. (1989). Bidirectional interaction between the central nervous system and immune system. *CRC Critical Reviews in Immunology*, 9, 279-312.
- Seeman, T. E., Berkman, L. F., Blazer, D., & Rowe, J. W. (1994). Social ties and support and neuroendocrine function. *Annals of Behavioral Medicine*, 16, 95-106.
- Stone, A. A., Bovbjerg, D. H., Neale, J. M., Napoli, A., Valdimarsdottir, H., & Gwaltney, J. M., Jr. (1993). Development of common cold symptoms following experimental rhinovirus infection is related to prior stressful life events. *Behavioral Medicine*, 8, 115-120.
- Thoits, P. A. (1983). Multiple identities and psychological well-being: A reformulation and test of the social isolation hypothesis. *American Sociological Review*, 48, 174-187.
- Uchino, B. N., Cacioppo, J. T., & Kiecolt-Glaser, J. K. (1996). The relationship between social support and physiological processes: A review with emphasis on underlying mechanisms and implications for health. *Psychological Bulletin*, 119, 488-531.
- Wethington, E., Brown, G. W., & Kessler, R. C. (1995). Interview measurement of stressful life events. In S. Cohen, R. C. Kessler, & L. Underwood Gordon (Eds.), *Measuring stress*. New York: Oxford University Press.
- Whiteside, T. L., Bryant, J., Day, R., & Herberman, R. B. (1990). Natural killer cytotoxicity in the diagnosis of immune dysfunction: Criteria for a reproducible assay. *Journal of Clinical Laboratory Analysis*, 4, 102-114.

Commentary

Ted Robles

During the 1980s and 1990s, Cohen has provided important contributions to our understanding of emotions, social relationships, and health. In particular, the

viral challenge research described in the present chapter provides a method of studying the roles of multiple psychosocial factors on actual health outcomes. The most unique and important contribution of Cohen's work is the use of clinical illness as a dependent variable. Moreover, the viral challenge studies are of high rigor and control, which also contribute to the importance and value of this research.

In addition to empirical contributions, this commentary focuses on Cohen's theoretical contributions to our understanding of the relationships between psychosocial factors and health outcomes. Specifically, fundamental empirical questions presented by Cohen in his theoretical work are relevant to researchers in health psychology, psychoneuroimmunology, and behavioral medicine. Emphasis will be given to these questions with respect to Cohen's own work as a marker of how the viral challenge research has furthered knowledge of psychosocial influences on health. This commentary also draws from other researchers in this volume and illustrates how their work can strengthen viral challenge research. Suggestions for future directions are provided in the concluding section.

Theoretical Contributions

Many of Cohen's contributions to health psychology, psychoneuroimmunology, and behavioral medicine have been in the theoretical domain. Specifically, Cohen has contributed to how we conceptualize the relationships among social relationships, stress, and health. A major paper published in *Health Psychology* entitled "Psychosocial Models of the Role of Social Support in the Etiology of Physical Disease" suggested several plausible models that might link psychosocial factors, stress, social support, and disease etiology and progression (Cohen, 1988). In addition to presenting different models of these relationships, Cohen differentiated between two components of social support: structural (the existence of a social network) and functional (the purpose and function of the social network). These concepts, along with constructs such as social integration and perceived availability, continue to be important in current research.

The most influential aspect of Cohen's 1988 article is the definition of two models that relate social support to health: the *main effect* model and the *buffering* model. The main effect model states that social support is beneficial regardless of whether or not one is under stress. Persons with high levels of social support should consistently have better health, regardless of stress level, compared to persons with low levels of social support. Social integration as a relevant measure of social support is associated with this model. The stress-buffering hypothesis states that social support is beneficial only when the person who is receiving support is under stress and that stress buffering occurs only when one's level or quality of support matches one's needs for support. Perceived social support as a relevant measure of social support is associated with this model. Cohen suggested several directions for future research, including more accurate and consistent verification of disease, more psychometrically valid measures of stress and social support, and the need for more prospective data

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on onset of disease and risk. These points later served as basic principles to guide the viral challenge research.

Another influential publication was a chapter by Cohen in the *Handbook of Human Stress and Immunity*. Cohen presented five important empirical questions to guide research on social relationships, stress, and health (Cohen, 1994). These questions are described below, with a statement of the implied research directive following each question:

1. *What psychosocial factors influence immune function?* We need to develop a better understanding of which particular psychosocial factors (e.g., life events, behavior, social relationships) influence immune function.
2. *Which parameters of immunity are subject to psychosocial influence?* The immune system is a complex system, with wide diversity in types of immune cells and immune responses. A broader range of immune function measures must be used to assess the role of psychosocial factors in immune function variability.
3. *Which parameters of immunity are critical in susceptibility to infection and viral reactivation?* Although this question is specific to infectious disease, it addresses the importance of translating findings related to immune function to health outcomes. Immune measures chosen in a research design should be related to some aspect of disease susceptibility and resistance.
4. *What are the hormonal mechanisms that link psychosocial factors to immune function?* Numerous endocrine hormones have the capability to alter immune function. Future research must not solely examine relationships between specific endocrine hormones and immune function but how such relationships are moderated by psychosocial influences.
5. *What are the behavioral mechanisms that link psychosocial factors to immunity?* Another mechanism of psychosocial influence is on behaviors related to health, including exercise, diet, smoking, and alcohol use. Research on the relationships between psychosocial factors and immunity must account for such behaviors.

These questions will be used to assess the progress made by Cohen's viral challenge work in a later section.

Empirical Contributions

The main findings from the Cohen chapter and results from previous viral challenge work will be briefly summarized. The specific methods and results derived from these studies are elaborated elsewhere (e.g., Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997). The first viral challenge study (Cohen, Tyrell, & Smith, 1993) examined relationships among negative life events, perceived stress, and negative affect on both subjective and objective indicators of infection with the common cold virus. The authors found that negative life events were associated with

greater rates of clinical illness as measured by increased symptoms. Perceived stress and negative affect were associated with clinical illness as measured by higher rates of infection rather than greater symptoms. Overall, these relationships persisted after accounting for a number of control variables, including age, gender, prechallenge serostatus, and education.

A follow-up study (Cohen et al., 1995) examined the role of negative affect in the development of the common cold and focused on the roles of state and trait negative affect on clinical signs and self-reported symptoms. Cohen and colleagues found that both state and trait negative affect were associated with greater cold symptoms and that the influence of state and trait negative affect was mediated through different pathways. State negative affect was associated with objective markers of disease progression—actual disease severity. In contrast, trait negative affect was associated with higher symptom reporting through increased illness complaints and not objective signs.

Results from the subsequent Pittsburgh Common Cold Study are reported in this volume and elsewhere (Cohen et al., 1997; Cohen et al., 1998). Briefly, this study employed a more sophisticated measurement strategy, including measures of immune function, endocrine hormones, objective symptomatology, and social integration; the Big Five personality dimension scale; and most important, a new measure of psychological stress: the Life Events and Difficulties Schedule (LEDS; Brown & Harris, 1989).

The main finding from the Pittsburgh study was that as social network diversity increases, the risk of developing a cold decreases (see fig. 7.3). In addition, acute stressful life events were not associated with developing a cold, while chronic difficulties were. Persons with a chronic difficulty that lasted one month or longer were 2.2 times more likely to develop a cold compared to persons with no chronic stressors. Work difficulties, specifically unemployment or underemployment, were particularly associated with risk of developing a cold. With respect to the biological measures, prechallenge measures of urinary cortisol, epinephrine, and norepinephrine and prechallenge measures of NK cell activity did not operate as pathways that linked social integration to susceptibility to colds. Health practices could account for a small fraction of the relationship, and of the personality measures, only extroversion was associated with susceptibility to colds, such that introverts had a higher risk of developing a cold.

Assessing the Viral Challenge Research

Having briefly summarized the theoretical and empirical contributions of Cohen, we now turn to the question: how has the viral challenge research furthered our understanding of emotion, social relationships, and health? Answers to this question will be framed in terms of the conceptual guidelines and empirical questions put forth by Cohen.

The main effect model and the buffering model are prominent theoretical contributions, which relate social support and health (Cohen, 1988). The former views social support as continually beneficial to health, whereas the buffer model

views social support as beneficial only in the presence of stressors. The latter views social support as beneficial only in the presence of stressors. The latter

Testing the model results from both studies show that social support is perceived with a way to test focus on components of stressors on health. Testing the model results from both studies show that social support is perceived with a way to test focus on components of stressors on health. Testing the model results from both studies show that social support is perceived with a way to test focus on components of stressors on health.

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1. What psychological challenge research, socially, social integration, perceived chronic stressors, the viral challenge factors?
2. Which pathways and viral responses are related to illness (cellular questions, viral challenge)?
3. Which pathways and viral responses are related to illness (cellular questions, viral challenge)?
4. What are the immune function, epinephrine, and norepinephrine levels of the Pittsburgh study with development was found none of the life stressors, social support

views social support as beneficial to health only during times of stress and when support is perceived as appropriate. Does the viral challenge work provide us with a way to test either model? Prior reports (Cohen et al., 1997, 1998) separately focus on components of the model: the role of social support and the role of life stressors on health outcomes.

Testing the main effect and buffering models requires an integration of the results from both studies and an analysis that allows for examination of the interactions among life stressors, social support, and health outcomes. Moreover, the Stress \times Social Support interaction necessary for the stress-buffering model requires a large sample size to test (Cohen & Wills, 1985), which is difficult to achieve in the viral challenge studies. Most important, as described earlier, measures of social integration are more informative to the main effect model, whereas measures of perceived social support and its interaction with life stress are more relevant to the buffering model. The viral challenge research utilizes social integration as a measure of social support but does not include measures of perceived social support. As such, the viral challenge research does not adequately test the stress-buffering model.

The questions outlined in Cohen (1994) also serve as another framework for evaluating the contributions of the viral challenge research to our understanding of emotions, social relationships, and health.

1. *What psychosocial factors influence immune function?* The viral challenge research clearly shows that aspects of social networks—specifically, social integration—are associated with health outcomes. In addition, perceived stress, negative affect, introversion, and the presence of chronic stressful life events influence susceptibility to colds. However, the viral challenge research is only beginning to link the same psychosocial factors to immunity by itself (Cohen, Doyle, & Skoner, 1999).
2. *Which parameters of immunity are subject to psychosocial influence?*
3. *Which parameters of immunity are critical in susceptibility to infection and viral reactivation?* Response to cold infection involves numerous responses from the immune system repertoire. The Pittsburgh study utilized one functional measure (NK cell activity) and enumerative measures (cell subset counts) of immunity. In order to address both of these questions, other functional aspects of immunity must be examined in viral challenge research.
4. *What are the hormonal mechanisms that link psychosocial factors to immune function?* The Pittsburgh study utilized 24-hour urinary cortisol, epinephrine, and norepinephrine measures, providing thorough coverage of the hormones associated with stress and immunity. In the Pittsburgh study, norepinephrine levels above the median were associated with developing symptoms of a cold, and a similar but weaker association was found with epinephrine. However, in the pathway analyses, none of the hormone measures were associated with social support or life stress measures, and they did not operate as pathways that linked social support or life stress to susceptibility to colds. In addition, similar to

the measures of immunity, the endocrine measures were taken prior to viral challenge. In future research, daily sampling would provide data on changes in endocrine functioning during quarantine.

5. *What are the behavioral mechanisms that link psychosocial factors to immunity?* A number of health-related behaviors were associated with susceptibility to colds, including smoking, poor sleep efficiency, abstinence from alcohol, and low vitamin C intake. In the pathway analyses, all of the health behavior measures accounted for a small portion of the relationship between social support and susceptibility to colds. However, answers to the questions of the extent of the relationships between health behaviors and immunity have not yet been examined.

Overall, the viral challenge studies provide insight into the psychosocial variables that are implicated in susceptibility to illness. To delineate the mechanisms through which the identified psychosocial variables operate, further research, as indicated above, is needed.

Future Directions

How might the work of other contributors to this volume extend or inform viral challenge research? Answers to this question are organized around the major themes that are pertinent to all of the chapters in this volume.

Positive and Negative Emotions

Cohen's work has focused primarily on aspects of negative emotional experience. For instance, the LEDS examines the negative aspects of stressors not positive aspects or events. In addition, susceptibility and symptoms of illness have been linked to state and trait negative affect. At the same time, positive emotions are implicit in discussions of social support. In the differentiation of social support into its structural and functional components, positive emotion should play a role in the functional aspects of social support. Measures of perceived social support, which tap into the degree to which one's needs are met by one's level of social support, also deal with positive emotion. In models of the relationship between psychosocial factors and illness, positive emotion should play a role in the main effect and the buffering models. However, employing measures based on a circumplex model (arrays multiple variables in a circular, two-dimensional space) of emotion did not show any significant effects of positive emotion on viral challenge outcomes.

Thus, future work should examine positive emotions, particularly as they play a role in supportive social relationships. In this volume, Ryff et al. and Reis focus on the nature of interpersonal relationships in the context of emotional well-being. Ryff devotes an entire dimension of emotional well-being to "positive relationships with others" and has shown that the quality of interpersonal relationships, particularly spousal relationships, are highly associated with self-reported

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health status (chap. 5). Using concepts from attachment theory and intimacy theory, Reis (chap. 3) proposes that positive emotions have prime importance in emotional well-being and maintenance of social ties. Assessing the quality of social relationships in the viral challenge paradigm would help researchers gain a richer understanding of the emotional dynamics that underlie particular social relationships as well as providing additional pathways that relate social relationships to health. Understanding the positive and negative emotional aspects of social relationships may also shed light on the question of the main effect and buffering models, which relate social support to health.

Gender Differences

Gender was utilized as a control variable in the viral challenge studies. However, work by Seeman indicates that the efficacy and provision of social support differs between genders. Specifically, women seem to be more reactive to negative social interaction, as shown by higher levels of urinary cortisol (chap. 6) and norepinephrine (Kiecolt-Glaser, Glaser, Cacioppo, & Malarkey, 1998). Moreover, Kiecolt-Glaser et al. showed that physiological changes due to marital conflict persisted longer in women compared to men. Gottman and colleagues (Carstensen, Gottman, & Levensen, 1995) have also observed gender differences in affect. This evidence suggests that social support differentially affects men and women, in both the supporter and the person receiving social support. The viral challenge paradigm provides a particularly interesting forum within which gender differences in social support and underlying physiological effects could be examined.

Mechanisms

Much of the analysis in the viral challenge studies is devoted to delineating pathways through which social support and stressful life events operate to affect susceptibility to illness. The analysis then addresses the question of mechanisms via health practices, hormones, and markers of immune system function. More diverse measures of immunity and endocrine function, which may be more relevant to infection with the common cold, should be utilized. Specifically, measures of immunoglobulin A (IgA) and G (IgG) in the nasal epithelium are potential markers of the immune environment within the main locus of infection. Another avenue, following from Cohen et al. (1998), would be measures of chemical mediators of inflammation, such as cytokines and bradykinins, which are partially responsible for cold symptoms. Perhaps psychosocial factors play a role in this realm of inflammation and symptoms in addition to the cell-mediated or humoral-mediated immune responses typically measured in psychoneuroimmunology (PNI) research. This work has begun, as Cohen and colleagues recently examined relationships among perceived stress, cold symptoms, and the proinflammatory cytokine IL-6 (Cohen, Doyle, & Skoner, 1999). In addition, salivary cortisol measures with diurnal sampling (as Cohen points out, urinary cortisol is not the ideal method for measuring cortisol) are an important direction for neuroendocrine assessment. Overall, sampling of immune function and endocrine

measures should be taken more frequently to track the time course of physiological changes over the duration of the quarantine.

An additional physiological measure that warrants consideration is cardiovascular reactivity. Cardiovascular reactivity has been identified as a moderating factor in changes in immunity in response to laboratory stressors (Herbert et al., 1994) and has been linked to long-term alterations that result from chronic stress (Cacioppo et al., 1998). In terms of social support, numerous studies have shown the positive effects of social support on cardiac reactivity and, conversely, the negative impact of interpersonal conflict on cardiovascular functioning (Uchino, Cacioppo, & Kiecolt-Glaser, 1996). Utilizing cardiovascular reactivity in viral challenge research will also allow for the assessment of the role of sympathetic nervous system activity in susceptibility to colds.

Cumulative Effects

The influence of cumulation of life stressors is a central component of the viral challenge research. The LEDS data showed a significant increase in the risk of developing colds in individuals with chronic life stressors that endured for more than six months. However, it is conceivable that some of these stressors began as acute stressors (i.e., supervisor reprimanding employee), which accumulated over time to develop into chronic, daily stressors or threats (i.e., supervisor constantly belittling employee). This possibility could be considered by including checklist-type measures of life events and relating such measures back to the LEDS data. Another aspect of cumulative effects pertains to the persistence of poor social relationships, stemming either from a lack of social ties or a high level of social conflict. Note that stressors that stem from interpersonal conflicts were associated with increased risk for developing colds (Cohen et al., 1998). Once again, assessing the qualitative aspects of social relationships in future research would provide a deeper understanding of the dynamic role of social support, especially with respect to cumulative effects.

Multiple Methods

The viral challenge paradigm is an excellent illustration of the use of multiple methodologies to assess objective and subjective signs of clinical illness, psychosocial factors, and underlying biological mechanisms. Further research could include assessments of psychosocial variables during the quarantine itself, as opposed to just prior to viral challenge. To shed light on the main effect and buffering models, future research could also examine the interactions between social support and stressful life events. The social support construct needs further research to assess functional support and emotional support across diverse types of relationships. In addition, the daily diary approach used by Reis could be utilized in the quarantine setting to track the efficacy of interactions with others in one's social network. A recent study integrated a portable daily diary (via handheld computer) with portable ambulatory blood pressure and heart rate monitoring, such that the cardiovascular readings were recorded simultaneously with the

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diary entries (Kamarck et al., 1998). Although no consistent findings were shown to link an aspect of social interaction (social conflict) with cardiovascular activation, integrating the methodology with the controlled environment of the viral challenge may prove promising and would provide ecological data on both social interaction and cardiovascular measures.

Multiple Relationships

The viral challenge research has opened doors to understanding the roles of different types of relationships in health outcomes. Future work in this area could differentiate among spousal, familial, and work-related relationships. Previous work by Cohen has addressed this, particularly in terms of stressful life events. However, it would be useful to extend the viral challenge work on social integration to specific relationship types (e.g., spouses, friends, coworkers) and to include measures of functional support. Finally, based on previous theoretical concepts proposed by Cohen, attention should also be turned to perceived social support. The buffering hypothesis warrants the use of perceived social support measures, which could be extended to specific relationships and associated expectations from each.

The viral challenge paradigm itself can also be improved upon. For example, aspects of the actual quarantine likely interact with those same psychosocial variables assessed at baseline; that is, factors such as perceived stress and negative affect may be elevated over the course of the quarantine and may thus influence susceptibility. Tracking these day-to-day changes in affect may provide ways to tease apart such interactions.¹ Linking these psychological changes to day-to-day endocrine and immune changes may be particularly valuable to understanding the progression of infection as it relates to changes in psychosocial factors. Finally, the LEDS, while a good measure of duration and severity of life stressors, employs raters, who use dictionaries to evaluate the time course, onset, and degree of social stress of the subject-identified stressors. Previous work has shown that the individual's appraisal of an external event as "stressful" contributes to the "stressfulness" of the event. Utilizing subjective ratings of the degree to which an event is stressful to the individual could be useful in pathway modeling and in answering theoretical questions about the relationships among stressful life events, social support, and health.

In conclusion, the contributions of Cohen and colleagues to our understanding of the role of social relations in susceptibility and resistance to infection have been extensive. This commentary points to numerous future directions for the viral challenge paradigm, some ensuing from Cohen's own observations and others from the perspectives and findings of other contributors to this volume.

Note

1. Of particular note is Cohen et al. (1995), which reported that state negative affect, which was measured each day of the quarantine, was associated with objective markers of cold symptoms and illness.

References

- Brown, G. W., & Harris, T. O. (Eds). (1989) *Life events and illness*. New York: Guilford.
- Cacioppo, J. T., Berntson, G. G., Malarkey, W. B., Kiecolt-Glaser, J. K., Sheridan, J. F., Poehlmann, K. M., Bureson, M. H., Ernst, J. M., Hawkley, L. C., & Glaser, R. (1998) Autonomic, neuroendocrine, and immune responses to psychological stress: The reactivity hypothesis. In S. M. McCann & J. M. Lipton (Eds), *Annals of the New York Academy of Sciences. Vol 840. Neuroimmunomodulation: Molecular aspects, integrative systems, and clinical advances* (pp 664-673). New York: New York Academy of Sciences.
- Carstensen, L. L., Gottman, J. M., & Levensen, R. W. (1995). Emotional behavior in long-term marriage. *Psychology and Aging, 10*(1), 140-149.
- Cohen, S. (1988). Psychosocial models of the role of social support in the etiology of physical disease. *Health Psychology, 7*, 269-297.
- Cohen, S. (1994). Psychosocial influences on immunity and infectious disease in humans. In R. Glaser & J. K. Kiecolt-Glaser (Eds), *Handbook of human stress and immunity* (pp 301-319). San Diego, CA: Academic.
- Cohen, S., Doyle, W. J., & Skoner, D. P. (1999). Psychological stress, cytokine production, and severity of upper respiratory illness. *Psychosomatic Medicine, 61*, 175-180.
- Cohen, S., Doyle, W. J., Skoner, D. P., Fireman, P., Gwaltney, J. M., Jr., & Newsom, J. T. (1995). State and trait negative affect as predictors of objective and subjective symptoms of respiratory viral infections. *Journal of Personality and Social Psychology, 68*, 159-169.
- Cohen, S., Doyle, W. J., Skoner, D. P., Rabin, B. S., & Gwaltney, J. M. (1997). Social ties and susceptibility to the common cold. *Journal of the American Medical Association, 277*(24), 1940-1944.
- Cohen, S., Frank, E., Doyle, W. J., Skoner, D. P., Rabin, B. S., & Gwaltney, J. M. (1998). Types of stressors that increase susceptibility to the common cold in healthy adults. *Health Psychology, 17*(3), 214-223.
- Cohen, S., Tyrell, D. A. J., & Smith, A. P. (1993). Life events, perceived stress, negative affect and susceptibility to the common cold. *Journal of Personality and Social Psychology, 64*, 131-140.
- Cohen, S., & Wills, T. A. (1985). Stress, social support, and the buffering hypothesis. *Psychological Bulletin, 98*(2), 310-357.
- Herbert, T. B., Cohen, S., Marsland, A. L., Bachen, E. A., Rabin, B. S., Muldoon, M. F., & Manuck, S. B. (1994). Cardiovascular reactivity and the course of immune response to an acute psychological stressor. *Psychosomatic Medicine, 56*, 337-344.
- Kamarck, T. W., Shiffman, S. M., Smithline, L., Goodie, J. L., Paty, J. A., Gnys, M., & Jong, J. Y. (1998). Effects of task strain, social conflict, and emotional activation on ambulatory cardiovascular activity: Daily life consequences of recurring stress in a multiethnic adult sample. *Health Psychology, 17*(1), 17-29.
- Kiecolt-Glaser, J. K., Glaser, R., Cacioppo, J. T., & Malarkey, W. B. (1998) Marital stress: Immunologic, neuroendocrine, and autonomic correlates. In S. M. McCann & J. M. Lipton (Eds), *Annals of the New York Academy of Sciences Vol 840. Neuroimmunomodulation: Molecular aspects, integrative systems, and clinical advances* (pp 656-663). New York: New York Academy of Sciences.
- Uchino, B. N., Cacioppo, J. T., & Kiecolt-Glaser, J. K. (1996) The relationship between social support and physiological processes: A review with emphasis on underlying mechanisms and implications for health. *Psychological Bulletin, 119*(3), 488-531.

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