“Relatively mild stress” depresses cellular immunity in healthy adults

Ronald Glaser
Department of Medical Microbiology and Immunology and Comprehensive Cancer Center, Ohio State University College of Medicine, Columbus, Ohio 43210

Janice K. Kiecolt-Glaser
Department of Psychiatry, Ohio State University College of Medicine, Columbus, Ohio 43210

Ader & Cohen (A & C) have provided an excellent discussion of conditioned immunopharmacological responses. Their work in this area is clearly outstanding. They suggest, however, that relatively mild stress or conditioned stress may be capable of exerting their subtle effects only in an already immunocompromised host. Though such speculation is consistent with data obtained in some studies with rodents as discussed by A & C, it is in conflict with the human experimental data discussed below.

Work from our laboratory has demonstrated the immunosuppressive effects of commonplace acute “stressful” events in otherwise healthy adults. For example, we found replicable and significant decrements in natural killer (NK) cell activity in medical student blood samples obtained on the day of examinations in comparison to baseline samples obtained one month previously (Kiecolt-Glaser, Garner, Speicher, Penn, Holliday & Glaser 1984; Kiecolt-Glaser, Glaser, Strain, Stout, Tarr, Holliday, & Speicher, in press). Self-report data documented the significantly greater distress associated with examinations. Other immune functions were also responsive to this relatively mild stressful event, including the transformation of B lymphocytes by Epstein-Barr virus (Kiecolt-Glaser, Speicher, Holliday & Glaser 1984), the percentage of helper T lymphocytes (Kiecolt-Glaser et al., in press), and the production of interferons by lymphocytes stimulated with concanavalin A (Con A).

Additional demonstrations of the immunodepressing effects of acute stress in otherwise healthy adults are seen in data from Jemmott, Borysenko, Borysenko, McClelland, Chapman, Meyer, and Benson (1983), who showed that alterations in salivary immunoglobulin A in dental students were related to high and low stress periods. Acute stress-related alterations in humoral immunity have also been shown in nonhuman primates (Coe, Wiener, Rosenberg & Levine, in press).

A & C characterize as “subtle” the immunological consequences of relatively mild stress or conditioned stress. Although the size of conditioned effects is generally small (while having survival value, as described by A & C), the effects of relatively mild stress are frequently of considerable magnitude. For example, the production of interferon by lymphocytes stimulated by Con A declined from a baseline value of 2003.03 U/ml 6 weeks before final examinations to a mean of 80.00 U/ml on the day of final examination in 40 second-year medical student blood samples (data submitted for publication). Similarly, exam-related decrements in natural killer (NK) cell activity have ranged from 16% to 43%, depending on the subject sample, the NK target cell used, and the effector:target-cell ratio across three samples of medical students; the modal decrease is around 33% of baseline values.

In further work, we have assessed the possible enhancement of immune function by simple positive interventions (Kiecolt-Glaser, Glaser, Williger, Stout, Messick, Sheppard, Ricker, Romisher, Briner, Bonnell & Dennerberg 1985). Forty-five
geriatric residents of independent living facilities were randomly assigned to one of three protocols: (1) progressive relaxation training, (2) social contact, or (3) no intervention. Subjects in the relaxation and social contact protocols were seen individually three times a week for a month. Blood samples and self-report data were collected at baseline before the intervention began, at the end of the one-month intervention, and at a one-month follow-up. There was a significant increase in NK cell activity in the relaxation subjects at the end of the month-long intervention without significant changes in the other two groups; NK cell activity returned to near baseline levels in the relaxation group at the follow-up, when subjects reported little continued relaxation practice. There was also a significant decrease in antibody titers to herpes simplex virus in the relaxation group at the end of the intervention, a change which was maintained at follow-up. Lower antibody titers to latent herpes viruses probably reflect better cellular immune system control of virus latency (Glaser, Kiecolt-Glaser, Speicher & Holliday, in press; Glaser & Gottlieb-Stematsky 1982).

Taken together, these data suggest that the immune system in otherwise healthy individuals is responsive to relatively commonplace stressful events (and perhaps positive events) across populations. These data are not consistent with the hypothesis that the effects of relatively mild stress may be evidenced only in an immunocompromised host, in contrast to the rodent data discussed by A & C. Although the functioning of the immune system is similar across mammalian species, there are also a number of important differences, including the greater sensitivity of the rodent immune system to the immunosuppressive effects of the adrenal glucocorticosteroids (Claman 1972). Moreover, it is not clear how to compare the physical stressors used in animal studies with the cognitive stressors that are of primary interest in human psychoneuroimmunology.

Immune function is depressed by commonplace aversive events in otherwise healthy adults. Recent data suggest that more profound distress may be associated with dysfunction at the molecular level, in the speed and quality of DNA repair (Kiecolt-Glaser, Stephens, Lipet, Speicher & Glaser, in press). The health-related consequences of such alterations are not yet known.