Psychoneuroimmunoendocrinology
Review and Commentary
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Psychoneuroimmunoendocrinology describes the impact of cognitive images of the mind on mental, neurological, hormonal and immunological functions. It encompasses biofeedback and voluntary controls, impacts on physiology of thought, attitude and belief, past/present stress, placebos, social relationships and "energy medicine." This column highlights clinical applications of cogent studies from these arenas of integrative holistic medicine.

Septicemia and Prayer
This was a double-blind, parallel group, randomized, controlled trial of an intervention involving intercessory prayer. 3393 adults whose bloodstream infection was detected at one hospital between 1990 and 1996 were randomized to either a control group or an intervention group. A remote, retroactive intercessory prayer was said for the well-being and full recovery of the intervention group. Mortality was 28.1% in the intervention group and 30.2% in the control group (p = 0.4 = NS). Length of stay in hospital and duration of fever were shorter in the interventionees vs. controls (p = 0.01 and 0.04, respectively).

Leibovici L Effects of remote, retroactive intercessory prayer on outcomes in patients with bloodstream infection: randomised controlled trial. BMJ 2001; 323:1450

Comment: The essentially subjective nature of prayer and "remote healing" makes controlled research difficult to accomplish. Controls may have had prayers offered for them unbeknownst to the researchers. Survival favored the prayer group, but results were not statistically significant. However, duration of fever and length of hospital stay did significantly favor the intervention prayer group. Much further research is necessary in this arena.

H. Pylori and Stress
Helicobacter pylori infection (HI) is a risk factor for development of peptic ulcers. Psychological stress (PS) too may play a role in the pathogenesis of this condition. However, no interaction between PS and H. pylori infection has been established in the development of peptic ulcer. Colonization by H. pylori is the first step in the infection of the gastric mucosa. In this mouse study, the authors examined H. pylori colonization of the stomach after psychological stress. The mice were subjected to PS in a communication box test, in which they observed other mice experiencing a physical stressor (electrical stimulation) before they were inoculated with H. pylori.

H. pylori colonization in the stomach of psychologically stressed mice was significantly greater than in the control mice (p < 0.05), and histological examination showed that the gastric mucosal injury in the stressed mice was more extensive than in control mice (p < 0.05). To explore the underlying mechanisms, the authors administered RU486 (a type II glucocorticoid receptor antagonist) to antagonize the effect of endogenous corticosterone: this decreased colonization by H. pylori in the psychologically stressed mice.


Comment: H. pylori infection of the stomach in these BALB/c mice was augmented by prior exposure to psychological stress. The effect appeared to be mediated by glucocorticoids, which would be increased by the stress. A number of prior studies have shown that stressed subjects, including humans, are more susceptible to subsequent acute viral and bacterial infections. In humans, the acute or chronic nature of the stress and the upregulation of stress management skills may also explain differences in outcomes.

Immune Function in the Aging
Aging is associated with a natural dysregulation in immune functioning, which may be amplified when it occurs in the context of chronic stress. Family dementia caregiving provides an excellent model to study the impact of chronic stress on immune functioning among older individuals. Empirical data suggest that the stress of caregiving dysregulates multiple components of innate and adaptive immunity. Elderly caregivers have poorer responses to vaccines, impaired control of latent viruses, exaggerated production of inflammatory mediators, and accelerated cellular aging compared with noncaregiving older adults. The chronic stress-induced immune
dysregulation observed among older caregivers appears to be of sufficient magnitude to affect health. Furthermore, evidence suggests that chronic stress leads to premature aging of the immune system.


Comment: Alzheimer’s caregiving has become a prototypical or classical example of chronic stress in humans. Numerous examples of immunity decline in noncaregiving elderly can be cited. As an example, the long-term immunity conferred by having chicken pox as a youngster declines in many elderly to the point that subjects are susceptible to resurgence of the herpes virus manifesting as herpes zoster or shingles. As highlighted in this review, the unrelenting stress of dementia caregiving appears to further erode the immune system to make caregivers more susceptible to a wide variety of infections. Practitioners can help aging patients and aging caregivers reduce risk of this decline by emphasizing the upregulation of stress-management skills with lifestyle interventions, including physical exercise, a whole-foods diet, appropriate nutritional supplements, and mind-body techniques such as biofeedback and meditation.

Stress and Influenza Vaccine Responsiveness

Immunization against potentially epidemic diseases is a widely used public health initiative. At the individual level, however, not everyone is protected by immunization, and increases in antibody titers may fail to reach protective levels. Studies suggest that psychological stress may contribute to these individual disparities. This meta-analysis of 13 studies examined the influence of psychological stress on antibody responses following influenza vaccination, and involved 1158 men and women. In five studies, the increased antibody levels of caregivers following vaccination were compared with those of noncaregivers. The remaining studies focused on associations between self-reported stressful life events or perceived stress and increased antibody titers following vaccination. The analysis revealed a significant negative association between psychological stress and antibody responses to influenza vaccination. While effect sizes were similar across different indicators of stress, antibody responses to the A/H1N1 and B-influenza types appeared to be more sensitive to stress than the A/H3N2 type. Results revealed significant negative associations between stress and peak antibody titers in both young and older groups.


Comment: Not only are stressed individuals more susceptible to influenzalike illness, but, as shown in this meta-analysis, they are also less likely to respond to attempts to decrease their susceptibility through vaccination. It is not definitely known whether responses to immunizations can systematically be improved in large populations by stress-management training. One would suspect, however, that the possibility obtains, based on individual case reports of
self-hypnosis and meditation successfully both increasing and decreasing immune responsiveness to immune challenge.

Qi Gong and Immune Responses

Qi gong is a type of Chinese psychosomatic exercise that integrates meditation, slow physical movements, and relaxed breathing, to which numerous physical and mental benefits have been classically ascribed. Of 29 naïve subjects, 13 were allocated to a control group and 16 to an experimental group who underwent qi gong training by a qualified instructor, consisting of half an hour/d practice for one month. At termination, qi gong subjects showed significantly lower total leukocyte and eosinophil counts, number and percentage of monocytes, and lower complement C3 concentration.

Comment: This study has weaknesses, including being short-term and not describing randomization of assignment to groups. Nonetheless, after one month’s practice, significant immunological changes emerged in the qi gong group compared with controls who did not practice qi gong. Qi gong is a physical and mental training program for health, martial art, and self-enlightenment commonly practiced in Asia and becoming increasingly popular in America. Other Asian disciplines, including tai chi chuan and many varieties of yoga, are being increasingly subjected to controlled research, with findings of significant health benefits.

Prolonged Infection, Immune Downregulation, and Lack of Social Support

Negative affect and lack of supportive interpersonal relationships loom large in the picture of modulation of immune dysregulation. Immune dysregulation may be one core mechanism for a spectrum of conditions associated with aging, including cardiovascular disease, osteoporosis, arthritis, type 2 diabetes, certain cancers, and frailty and functional decline; production of proinflammatory cytokines that influence these and other conditions can be stimulated directly by negative emotions and indirectly by prolonged infection. The ability to unwind after stressful encounters downregulates the total stress burden. Prolonged intrusive ruminations following a stressful trauma appear to provide one avenue for persistent immune downregulation, including reduced natural killer cell activity. Higher salivary immune responses are associated with days of more positive mood. Higher social support is robustly associated with higher NK cell activity and mitogenic leukocyte responsiveness in those under stress, whereas chronically abrasive close personal relationships are seen to provoke persistent immune downregulation. Differences in perceptions of the same event provoke different endocrine and immune responses. Benefits of disclosure-based interventions vary depending on the degree to which subjects become emotionally and cognitively involved in the process, reorganize the meaning of the traumatic event, and reduce avoidance of the issue.

Humor and Lymphocyte Blastogenesis

Cortisol inhibits mechanisms such as interleukin-2 expression and proliferation of lymphocytes. Laughter and humor decrease the classical hypothalamic-pituitary-adrenal-cortical response. Ten healthy male volunteers watching a humorous 60-minute videotape were compared with five controls who did not. Blood samples drawn from an indwelling catheter before, during, and after the viewing found that cortisol fell during laughter and humorous expression during the humorous video as well as afterward (p = .008), and lymphocyte blastogenesis increased from baseline and after viewing (p = .003). Non-watching controls remained unchanged.

Comment: Immune responsiveness, including blastogenesis, is important in repelling invasion of the human body by potentially pathogenic microorganisms. Stress raises cortisol, which diminishes these protective responses. Laughter is here shown to enhance the responses that assist the body’s protective mechanisms. Author Norman Cousins’s experience with using humor as an agent to overcome his ankyllosing spondylitis also speaks to the benefits of reducing inflammatory responses. Some authorities believe that he was misdiagnosed and actually had reactive arthritis. Whatever inflammatory process he had was definitely mitigated by humor.

Robert Anderson is a family physician who has authored several major books: Stress Power!, Wellness Medicine, Clinician’s Guide to Holistic Medicine and The Scientific Basis for Holistic Medicine. Anderson founded the American Board of Integrative Holistic Medicine, and is a past president of the AHMA, past assistant clinical professor of family medicine at the University of Washington, and present adjunct instructor in The Art of Primary Care at Bastyr University.