Psychoneuroimmunoendocrinology describes the unity of mental, neurological, hormonal, and immunological functions, addressing the impact of cognitive images of the mind (whatever its elusive definition) on the central nervous, endocrine, and immune systems. It encompasses biofeedback and voluntary controls, impacts on physiology of thought and belief, past/present stress, placebos, social relationships, and “energy medicine.” This column highlights clinical applications of cogent studies from these arenas of holistic medicine in the new millennium.

The Immune System in Infectious Transmissible Disease

Influenza Vaccination Responses and Stress
Anxiety, depression, and stress were measured by appropriate psychological instruments in spousal caregivers of dementia patients (median age 73 years) and 67 controls (median age 68) of comparable socioeconomic status. Salivary cortisol concentrations were measured in early morning, noon, and evening. Participants received a trivalent influenza vaccine, and IgG antibody titers to each strain were measured on days 0, 7, 14, and 28. Mean scores of emotional distress were significantly higher in caregivers at each time-point than in controls (all p<0.0003). Mean salivary cortisol concentrations, calculated as the area under the curve (AUC), were 16.0 and 11.2 in caregivers and controls, respectively, at six months (p=0.0001). Sixteen percent of 50 caregivers and 39% of 67 controls had a fourfold increase in at least one of the IgG titers (p=.007). Stressed elderly caregivers of spouses with dementia had increased activation of the hypothalamic-pituitary-adrenal axis and a significantly diminished antibody response to influenza vaccine.


COMMENT: One consequence of stress on the immune system was a poor antibody response to injected influenza virus vaccine vs. controls not faced with this stress. Studies of effectiveness of vaccines for a variety of purposes rarely address inter-individual differences. The physical and psychosocial stress to which subjects are exposed at any given time can vary immune responsiveness to vaccine challenge several-fold.

Immunity and Stress
Men whose wives had terminal breast cancer were found to have normal responsiveness of T- and B-cells to phytohemagglutinin, concanavalin A, and pokeweed mitogen antigenic challenge. A number of weeks after the deaths of their spouses, this response was severely compromised (PHA p<.04; ConA p<.005; and PWM p<.003).


COMMENT: This is further demonstration of the potential for unmanaged stress to compromise immune responses. Optimal resistance to attack by invaders (bacterial, viral, fungal, parasitic, toxic) depends on an intact immune system. The ability of invader to defeat the host is down-regulated by an intact, rapidly reacting immune system. The stressful aspects of lifestyle compromise this process.

Immunity and Grief
Twenty-six persons whose spouses had died were found to have significantly decreased mitogenic T-cell phytohemagglutinin responses at eight weeks, but not at two weeks, post-bereavement vs. controls who had not suffered death of a spouse (2p<.05). No significant hormonal changes resulted from the stress of the grief reaction, and white blood cell counts remained unchanged.


COMMENT: Response to mitogenic challenge, a measure of the immune system’s ability to respond to assault by infectious and toxic agents, was significantly compromised at eight weeks following the death of a spouse. The stress due to the loss of loving and companionable relationships can therefore significantly affect individual responses to pandemic and epidemic infectious disease transmission. We return to the age-old question debated by Pasteur and Bernard in the 1870s: which is most important, the agent (virus, bacterium, toxin) or the “territory? Pasteur is said to have confessed on his deathbed, “Alas, Bernard is right; the territory is everything.” Why do some resist the pandemic virus better than others? It appears that their immune systems are intrinsically stronger and more resistant.

Immunity, Guided Imagery, and Relaxation
This study measured the effects of relaxation and guided imagery on cellular immune function. During a period of ten days, ten healthy subjects underwent a single one-hour relaxation procedure and one combined relaxation and guided imagery procedure, during which subjects were instructed to imagine their immune system becoming very effective. Even though no major changes in the composition of the major mononuclear leukocyte subsets could be demonstrated, a significant increase in natural killer function followed.

COMMENT: These data suggest that relaxation and guided imagery might have a beneficial effect on immune defenses. This is the next step following the demonstration of reduced immune function in the presence of stress as illustrated in the studies above. Can the immune system be up-regulated with appropriate therapeutic techniques? This study appears to answer in the affirmative. Relaxation and guided imagery were effective in enhancing natural killer cell function in these healthy subjects.

Immunity and Humor

Ten randomly selected volunteers viewed both a Richard Pryor humorous videotape and a didactic lecture on anxiety presented in random-order, crossover fashion. All rated the Pryor tape more humorous than the lecture (p<.001). Scores on the Coping Humor Questionnaire were correlated with salivary IgAs prior to viewing (p<.05), indicating that the salIgA was related to the subjects' perception of their use of humor as a coping device. Salivary IgA significantly increased from 58 before viewing the humorous videotape to 67 mg/dl afterward; sIgA in the control time with the didactic lecture rose from 57 to 58 mg/dl with the lecture tape (NS).


COMMENT: All of us in academia should note the fact that the immune system remained unchanged during a probably uninspiring didactic lecture! Au contraire, the immune system salivary IgA rose a significant 16% after viewing Richard Pryor. Students on campuses who are repeatedly exposed to didactic learning only may be more susceptible to epidemics of infectious disease.

Immunity and Hypnosis

Twenty hypnotizable subjects, ages 22-85, significantly (p<.05) increased the in vitro proliferative responsiveness of their lymphocytes to pokeweed mitogen (which stimulates both T- and B-cells) when given the suggestion under trance that their white blood cells were like “powerful sharks” destroying “weak germs.”


COMMENT: Organized medicine has left a 150-year trail of inability to apply the recorded incredible success of James Esdaile, a Scottish surgeon (1808-1859) who applied hypnotherapy to his surgical subjects. The common 15%-20% mortality of the time due to postoperative infections was reduced in his hands to about five percent, so striking as to make him the envy of the surgical profession who denigrated his results and failed to employ his methods. This study may explain why Esdaile achieved his outstanding reduction in postoperative mortality. By whatever mechanism, the immune system can respond to the suggestion of better function, particularly when given in the alpha brain-wave state of relaxation.
Immune System

Immunity and Hypnosis II

Of 57 children, in those randomized to practice self-hypnosis, salivary Immunoglobulin A rose to 12.6 units from 7.75 at baseline after three 30-minute sessions, during which they learned self-hypnosis to suggest to themselves that they increase their immune substance in saliva as they chose: (p<.007) vs. a rise from 7.8 to 9.25 units (NS) in those spending equivalent time with an instructor without any hypnotic procedure. Differences between groups was significant (2p<.01).


COMMENT: Previously in this column, I have referred to this wonderful study of children’s ability to achieve results in the mind-body world resisted by skeptical adults. These children were successful after only three sessions of hypnotherapy training. Both children and adults learn better and more quickly by experiencing a process rather than being told about it. The power of suggestion has few limits, even though there are gaps in explaining the mechanisms by conventional science. More and more, research is making its way into the literature measuring the effect of intention. It reminds me of one explanation for the disparity of results reached by different experimenters dealing with tiny aspects of matter by invoking the Heisenberg uncertainty principle: that the experimenter affects the results of the experiment.

Immunity and Imagery

In two randomly selected groups of healthy college students, mean salivary IgA increase was 32 mg/dl in the group treated with exposure to 17 minutes of focusing on immune system imagery while a music tape played in the background vs. a rise of 16 mg/dl in quietly sitting controls (2p<.0001). Instances of tachycardia, breathing problems, and bruxism decreased significantly in the imagery group vs. no change in controls.


COMMENT: Effects here were similar to those detailed above under hypnosis. While not formally defined as hypnosis, the parameters utilized involved background soothing music and suggestions, both of which contribute to induction of the alpha-state of reduced basal brainwave cycling to the range of 8-13 Hz. In this relaxed state, subjects are almost uniformly more suggestible, and images presented have a tendency to gain greater traction for inducing change. Also important is the Psychosynthesis principle: “Images or mental pictures and ideas tend to produce the physical conditions and the external acts that correspond to them; images likewise tend to awaken emotions and feelings that correspond to them” (Assagioli R. The Act of Will. New York:Viking, 1973). Stated differently: images evoke coherent physiological, biochemical, and emotional responses. Functional MRI scanning and PET scanning will soon shed more light on how the brain patterns accomplish this.

Immunity and Emotional Expression

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 banal control topics during four consecutive daily sessions. The day after completion of the writing, participants were given their first hepatitis B vaccination, with booster injections at one and four months after the writing. Blood was collected before each vaccination and at a six-month follow-up. Compared with the control group, participants in the emotional expression group showed significantly higher antibody levels against hepatitis B at the four- and six-month follow-up periods (p<.05). Other immune changes evident immediately after writing were significantly lower numbers of circulating T-helper lymphocytes (p<.05) and basophils (p<.01) in the treatment group.


COMMENT: The finding that a writing intervention influences immune responsiveness provides strong support for a link between emotional disclosure and health. The responsiveness of the immune system to challenge by hepatitis B vaccinations improved after writing about emotional traumas. One has to assume that the writing in some way helped resolve the feelings about the original emotional traumas still residual in the system. Some authorities believe that maintaining strong feelings about past emotional traumas requires significant energy; once released, higher levels of energy assist all bodily systems including the immunological.

Skin Tests and Hypnosis

Eight volunteers underwent skin testing for type I and type IV reactions before and after hypnosis. Histamine skin-prick testing after hypnosis accompanied by suggestions of decreased flare showed significantly less erythema (p<.02). The size of the wheel did not change. In a second study of tuberculin skin testing, a suggestion was made under hypnosis in a healthy volunteer to increase the post-hypnotic reaction in one arm and decrease it in the other, significant differences in erythematous area and palpable induration were apparent (p<.01) consistent with the suggestions. Laser doppler measurements showed a 19% difference in erythema and a 44% difference in dermal infiltrate thickness.


COMMENT: The power of suggestion includes the ability to perform simultaneous, differential effects on different parts of the body. The ability to distinguish sides with differing suggestions still defies explanation but has been repeatedly shown. Mystery still challenges us.

Immunity and Stress

Salivary Immunoglobulin A determinations were done in 15 healthy undergraduates five days before exams, during exams, and fourteen days following their last final exam. Secretory IgA levels were much lower during exams (p<.0001). Students reporting more social support at the pre-exam time had consistently higher sIgA levels than their peers with less social support (p<.05).


COMMENT: This is consistent with the theories that stress reduces chemical immunity and that social support enhances health. Greater susceptibility to viral and bacterial
invasion during times of stress has been well documented. Although there is little present cogent research, one suspects that eventually stress will be shown to play a role in parasitic infections as well.

Skin Test Responses and Stress
Sixteen, final-year, psychology undergraduate students about to take their final examinations and fourteen controls from research and administrative staff with a similar age distribution were randomly recruited to complete the 30-item Recent Perceived Stress Questionnaire and to have the Multitest CMI skin test, which simultaneously imprints the dermis with seven delayed hypersensitivity antigens (tuberculin, tetanus, diphtheria, Streptococcus, Candida, Tricophyton, and Proteus), applied to a forearm. Dermal indurations were read at 48 hours. Mean perceived stress score for the students was 72.7 vs. 58.5 for the controls. The stress group immune response to challenge was significantly weaker than the control group, whose stress levels were much lower (p=.024).

COMMENT: We tend to think of immune skin-testing as providing consistent results. The global results of skin-testing for these seven antigens found significant reductions in reactions in stressed subjects. In other words, their immune systems were less reactive in responding to challenge. Medicine needs to find ways to individualize diagnostic and treatment approaches in recognition of great differences from person to person as shown by Dr. Roger Williams 50 years ago. The current terminology describes these differences as genetic pleomorphisms.

Robert Anderson is a retired family physician whose practice took a holistic turn as decades passed. He has authored five major books: Stress Power!, Wellness Medicine, The Complete Self-Care Guide to Holistic Medicine (co-author), Clinician's Guide to Holistic Medicine (McGraw Hill, 2001), and The Scientific Basis for Holistic Medicine, (6th edition, 2004), available from American Health Press, holos@charter.net. Anderson was the founding president of the American Board of Holistic Medicine, past president of the AHMA, and former Assistant Clinical Professor of Family Medicine at the University of Washington. He is currently an Adjunct Instructor in Family Medicine at Bastyr University.

Robert A. Anderson, MD, FAAFP, FACPM
614 Daniels Drive NE
East Wenatchee, Washington 98802-4036 USA