Aging, Free Radicals and Stress

Stress increases circulating catecholamines, which in turn inhibit both magnesium-calcium and sodium-potassium ATPase, leading to increases in cellular calcium and sodium and loss of potassium and magnesium. Metabolism of catecholamines produces free radicals. Targets of this free radical activity include potential damage to neuronal receptors, atherosclerosis, oncogenic deterioration and a variety of other organ tissue damage.


COMMENT: Demopoulos demonstrated the biochemical connection with stress and the known relationship to foreshortened longevity. Perceptions, past experience, beliefs, attitudes and emotional states have the potential to contribute to higher catecholamine levels and thus higher free radical levels, and thus increased incidence of “diseases” which truncate life prematurely. This is why it is essential for practitioners to understand the benefits of a broad bio-psycho-social-spiritual approach to patient experience.

Aging and Stress

Review: The elevation of cortisol that occurs with stress tends in the young to return to baseline quickly; in the old it has a propensity to remain much higher and return to baseline much more slowly. Chronic stress accelerates the aging process. Stress leads to increased corticosteroid synthesis which down-regulates the neuronal loss in the brain, especially hippocampal; neuroreceptor loss provides negative feedback which decreases corticosteroid synthesis. The hyperadrenal corticoidism suppresses immunity, causes muscle atrophy, increases bone calcium loss, increases blood glucose and hyperlipidemia, leads to steroid diabetes, contributes to atherosclerotic cardiovascular disease and Alzheimer’s disease.


COMMENT: Sapolsky, renowned authority in this field, delineates the mechanisms which support his premise that stress accelerates aging. The pathways involved chronically elevated catecholamines and corticosteroids. Some of the learned behaviors, among many, which neutralize these effects by reducing peak levels of catecholamines and corticosteroids with stress and their baseline levels in times of relative calm, include prayer, meditation, appropriate breathing techniques, reflective time in Nature, humor and laughter, and quiet times of appreciating great art, literature and music. Written prescriptions for the practice of these skills will have an effect on a fairly wide spectrum of patients and will emphasize their importance in the total mix of therapeutic initiatives.

Aging, Corticosteroids and Stress

Four, 12 and 18 month-old rats were trained for six months in a two-way shuttle escape task inducing anxiety stress and elevated corticosteroid levels. The two younger groups showed increased evidence of neurophysiological aging without neuronal loss (p<0.005); the older group showed no further age-related physiological changes but exhibited significant neuronal cell loss (p<0.001). The aged stress group showed significantly more decrease in hippocampal neuron density than controls (p<.02). A limit in physiological changes was reached, after which no further change was incurred; neuronal cellular loss, however, continued steadily. This suggests that 6 months of moderate daily stress accelerates functional as well as anatomic markers of hippocampal aging. If data are extrapolated to mammals, chronic stress in the young and mid-aged could alter neurophysiological mechanisms important for normal memory and cognition. In the aged, chronic stress may promote neurodegeneration.


COMMENT: Perhaps greatly accelerated neuronal degeneration in Alzheimer’s patients occurs in a subset of persons particularly susceptible to stress. Hippocampal loss has been shown in PTSD subjects whose stress is traceable to the Vietnam War. It certainly becomes incumbent to recognize stress and proactively deal with it to forestall proximate and distant downside effects. The patient needs to be disabused of her/his belief that s/he has no control over the cascade of stress effects. The entrée into the therapy which begins to address the management of the stressful issues can comfortably begin with biofeedback, which convinces many skeptical patients by its demonstrable results.

Disease Incidence and Attitude

At a mean age of 25, 99 Harvard graduates completed a Content Analysis of Verbatim Explanations and the Attributable Style Questionnaire developed by the author and used to identify a pessimistic explanatory style. This style, embracing a belief that bad events are caused by stable, global and internal factors, significantly predicted poor health at age 40-65, even after adjustment for mental and physical
Health at age 25. Correlations at each age bracket were: 45: (p<.01); 50: (NS); 55: (p<.05); and 60: (p<.02).

COMMENT: At every age bracket except 50 year-olds, a pessimistic explanatory style for life events predicted poor health for pre-retirement subjects. Pessimism, as shown below, has a large downside effect on longevity.

**Longevity and Optimism**

Eight hundred forty (840) general medical Mayo Clinic patients, mean age 35, were divided at baseline into optimists (n=124), mixed (n=518), or pessimists (n=197) on the basis of their answers to 298 MMPI questions: 86% were available for followup 30 years later. After all adjustments, optimists were living a mean of 19% longer than pessimists (p=.01).


**COMMENT:** I have referred to this seminal study before. The 19% advantage to optimists translates to roughly 14 additional years of life. This dwarfs the extended years of life attributable to conquering cancer, wiping out heart disease or eliminating trauma.

Can a pessimist be converted to an optimist? It is often not easy, but attitudes can be learned or “caught” from acquaintances, relatives, friends and medical practitioners. I have often had success by prescribing a two to three week arbitrary behavior shift utilizing the “as if” technique. The patient is asked to monitor his/her attitudes. On finding any pessimistic flavor at any given time, the task is to shift to an optimistic attitude as if it were already incorporated. Another way of looking at this is to play the “what if game on the positive rather than the negative side of the ledger. My experience is that a three-week experience becomes very convincing, but it must be reinforced by a practitioner who is himself or herself, optimistic.

**Longevity and Suspiciousness**

Higher scores on a measure of suspiciousness (closely related to the Cook Medley hostility scale) predicted greater 25-year mortality risk in a sample of 500 older men and women during a follow-up averaging 15 years. This association remained significant after controlling for age, sex, physician’s ratings of functional health, smoking, cholesterol, and alcohol intake. The suspiciousness factor was also associated with physician’s ratings of health at the initiation of follow-up.


**COMMENT:** These findings add to the weight of evidence that implicates a set of negative interpersonal attitudes in the domain of hostility, anger, cynicism, and mistrust as a prospective marker of individuals at risk for adverse health outcomes. Patients who harbor these negative attitudes and emotions can be gently nudged toward awareness when a depth of rapport has been established. In the patient whose suspicion and hostility is worn on their sleeves, the establishment of a deep degree of trust takes longer.

**Immunity, Compassion and Anger.**

In 30 healthy volunteers, salivary IgA, heart rate and mood were measured before and after experiencing loving care or anger which were induced in two ways: by self-induction and by viewing video tapes. Anger produced a significant increase in heart rate (p<.01) and total mood disturbance (p<.05) and an insignificant immediate increase in IgA followed by significant decreases in IgA at 1, 2, 3 and 6 hours (p<.01), and 4 and 5 hours (p<.05). Positive emotions (care and compassion), however, produced a significant immediate increase in salivary IgA of 41% (p<.05).

Thus, in contrast to care and compassion, anger produced a significant inhibition of IgA at one to five hours after the experience. The C/C group experienced dramatic decreases in tension/anxiety, anger/hostility, fatigue, confusion and an increase in vigor (p<.05). Self-induction techniques were more potent than external methods in induction of IgA changes.


**COMMENT:** The observation of one’s attitudes and emotions is a powerful therapeutic option in and of itself. The degree of disidentification required to observe oneself illustrates the psychological principle “Everything from which I disidentify I can control.” So if one observes one’s emotions, a degree of control over them is immediately apparent. We cannot have an emotion and be that emotion at the same time. The adoption of or identification with positive emotions in this study was immediately strengthening of a measurement of immunity. Improved immunity is consistent with better quality and quantity of life.

**Rheumatoid Arthritis and Laughter**

In 26 rheumatoid arthritis women patients age 43-66, mean duration of disease 19.4 years, and 31 healthy female controls, exposure to Rakugo (traditional Japanese comic stories) for an hour in the early afternoon resulted in: decrease in negative mood (observational analogue face scale) from 7.2 to 2.1 (p<.01) vs. controls from 7.4 to 2.4 (p<.01); decreased pain (visual subjective analogue scale) from 4.7 to 2.1 (p<.01); decreased tension (visual subjective analogue scale) from 4.5 to 2.1 (p<.01) and an immediate increase in sIgA 41% (p<.01) vs. controls. Laughter produced a significant increase in heart rate (p<.01) and total mood disturbance (p<.05) and an insignificant immediate increase in IgA followed by significant decreases in IgA at 1, 2, 3 and 6 hours (p<.01), and 4 and 5 hours (p<.05). Positive emotions (care and compassion), however, produced a significant immediate increase in salivary IgA of 41% (p<.05).

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Longevity and Emotional Disclosure

On the basis of a theory of inhibition and psychosomatics, it was predicted that the more individuals disclosed personally traumatic experiences, the better their long-term health following the disclosure. Thirty-three Holocaust survivors talked for 1-2 hours about their personal experiences during World War II while skin conductance level (SCL) and heart rate (HR) were continuously monitored. Each videotaped interview was rated by independent judges once every minute on the degree to which the survivor's experience was traumatic. For each subject, the trauma ratings were correlated with minute-by-minute SCL and HR readings. Based on previous research, negative trauma-SCL correlations are indicative of high personal disclosure, whereas positive trauma-SCL correlations suggest low disclosure. Approximately 14 months after the interview, self-reports of the subjects' health were collected. Controlling for pre-interview health problems, degree of disclosure during the interview was found to be positively correlated with long-term health after the interview.

Survival and Self-Evaluations

Baseline evaluations in 2,800 persons over age 65 assessed lifestyle; level of medical care available; external resources (family, community); "internal" resources (optimism, depression, attitudes and feelings); physical disability; biological risk factors; presence of overt disease; and self-assessed ratings of health. Four years later, those with self-assessed ratings of "poor" health were 6.7 times as likely to have died vs. the "excellent" self-rated group regardless of the status of any of the other factors.

Reversal of Atherosclerosis with Meditation

Psychosocial stress influences the development and progression of atherosclerosis. Carotid intima-media thickness (IMT) is a valid surrogate measure for coronary atherosclerosis, is a predictor of coronary outcomes and stroke, and is associated with psychosocial stress factors. Sixty subjects completed pretest and post-test carotid IMT data determined by ultrasound. Hypertensive subjects were randomly assigned to either the Transcendental Meditation program or a health education group. Mean maximum IMT from 6 carotid segments determined by B-mode ultrasound was used to determine baseline IMT values and those taken 6-9 months later. Age and pretreatment IMT were found to be predictors of post-test IMT values and were used as covariates. The TM group showed a significant mean decrease of .098 mm vs. an increase of .054 mm in the control group (2p=.038).

Ref:
Paychosom Med 1989 Sep; 51(5):577-89

COMMENT: This describes an underused technique that lends itself to use by many practitioners who may feel ill prepared to dabble in the psychosocial realm of the counselor. I have observed few if any downside results of this approach, and on the upside, dramatic progress is often apparent. The Pennebaker approach has now been widely used, with impressive results in organic disease as reported by Smyth (Smyth JM et al. JAMA 1999; 281:1304) in rheumatoid arthritis and asthma. Practitioners can confidently incorporate this approach in addition to other conventional and integrative/holistic approaches to organic and functional illness, anticipating lengthened survival.
COMMENT: Practice of the Transcendental Meditative state appeared to significantly reduce carotid atherosclerosis compared to progression in controls in hypertensive African Americans. The dropout group was large, although attrition rate for meditators and controls was equal; one would certainly like to see confirmation of these results in larger studies by other groups and with other meditative approaches. In the meantime, using my "why-not" approach, given the many other beneficial results of meditation and understanding the theoretical basis by which reversal of atherosclerosis is possible, development of this skill in patients should be strongly encouraged.

Temperament and Health

Temperament, an expression of innate biological endowment, provides a more global portrayal of an organism than an aggregate of separate characteristics alone. Of 172 students, irritable-demanding-moody temperament had the greatest 30-year risk of premature disease and mortality; spontaneous-outgoing-active types had the least risk with cautious-reserved-quiet-undemanding types scoring in the intermediate range (p<.01).

Betz BJ, Thomas CB. Individual temperament as a predictor of health or premature disease. Johns Hopkins Med J 1979; 144:81

COMMENT: Temperament appears to be a variable of predictive potential of individual stamina, or of vulnerability to premature disease and death. Stella Chess' evaluation of temperament in the newborn nursery and high correlation with health factors 20 years later is evidence that genetic predisposition is an important determinant (Chess S, Thomas A. Can J Psychiatry 1990; 35:557). Identical twin studies also demonstrate that personality differences, "identical" notwithstanding, also play a role in longevity. So, are we victims of our heredity? Perhaps, unless we recognize the detrimental aspects and do something about them, in which case they may be neutralized and overcome.

Survival and Hostility

In 2,200 subjects, high college-age hostility vs. low hostility carried a relative risk of 1.22 for being a smoker 30 years later (95% CI 1.05-1.41); 1.2 (1.03-1.39) for consuming >2 alcoholic drinks/d, 1.18 (1.03-1.34) for perception of low social support, 1.19 (1.08-1.32) for achieving less than expected in career, 1.37 for achieving <median US income (1.07-1.74) and 1.16 (1.06-1.28) for unsatisfying relationships, 1.33 (1.16-1.52) for depression, and 1.20 (1.03-1.41) for appraisal of family life changing for the worse. Gain in hostility from college years to adulthood 30 years later increased odds ratios for obesity to 1.38 (1.14-1.68), perception of inadequate social support 1.18 (1.03-1.34), sense of having achieved <expected 1.58 (1.39-1.79) and depression 1.92 (1.59-2.30).

Signorli IC et al. Patterns of change in hostility from college to midlife in the UNC Alumni Heart Study predict high-risk status. Psychosom Med 2003; 65:738

COMMENT: High hostility at college age and increase in hostility from college to midlife predicted a full range of increased behavioral health risks. Linked with the temperament studies, above, it is apparent that the psychosocial health/disease effects often outweigh the biomedical elements in predicting sickness, health and longevity. Can these behaviors, once apparent, be modified? Of course they can. The determinants are the insights of the patient and the skills of the attending physician or counselor. The trained and skilled physician can introduce the possibilities of change through the strength of the therapeutic relationship which is the crux of the healing bond between patient and practitioner.

Parental Caring

In the 35-year Harvard Mastery of Stress Study in which 398 college women and men completed the Harvard Parental Caring Scale (HPCS), the SCL90R, and the Marlowe-Crowne (MC) scale (measure of defensiveness) at baseline, positive ratings of parent care predicted substantially reduced incidence of cardiovascular disease, ulcers, and alcoholism in mid-life. High HPCS parental caring ratings were associated with reports of markedly reduced symptoms in women and men (p<.00002). The relationship between HPCS and symptoms was strongest in the least defensive subjects. Positive perceptions of love and caring from parents in childhood, typically the most important source of social support for children, were associated with greatly reduced psychiatric and somatic symptoms. Defensiveness may play a modest protective role psychologically in reducing the conscious awareness of symptoms accompanying low perceptions of parental love and caring.


COMMENT: Childhood experience casts a long shadow. The authors do not mention controlling for learned negative behaviors which may have resulted from low quality parenting and increase symptoms as adults. Nonetheless, their data is very strong and complements the prior work of Carolyn Bedel Thomas at Johns Hopkins (Shaffer JW et al. J Behav Med 1982; 59:143). Identification of these perceptions in patients in their 20s and 30s gives opportunity for psychological "work" to neutralize the effects of these adverse childhood and juvenile experiences.

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, former Assistant Clinical Professor of Family Medicine at the University of Washington and is currently an Adjunct Instructor in Family Medicine at Bastyr University.