Solving Some of the Problems of Aging

by Ray Peat, Ph.D.
Ray Peat's Letter

In the 1970's a strange "Pine-sol" type disinfectant with insecticide was widely promoted in Mexico, and nearly every bathroom, bus, and public room in the country smelled of that rank, un-pinelike substance. One morning I woke around 3 AM smelling Pinosol, and as I was trying to decide where the smell was coming from, I realized that I could smell it only while exhaling - it was coming from inside me. From then on, I began to wake up every night, usually between 2 and 4 AM. I knew that many old people like to get up and start their day a little before dawn, but after this experience I began to notice that many younger people have - and are disturbed by - a similar alteration of their sleep rhythm.

Around the time of my Pinosol experience (in 1979) I happened to find a dead bug in my Nescafe bottle, and it occurred to me that this was the first bug of any kind that I had seen since I arrived in Jalapa. Walking to the outskirts of the town, where there were forests, I found a reasonable number of insects, but I couldn't find one in the city. This fact, combined with my awareness that my tissues were soaked with insecticide, (and other discomforts) caused me to quit my job at the university and return to Oregon. As I was driving across the desert, I noticed that I would smell Pinosol whenever it was meal-time. Apparently low blood sugar, causing fat mobilization, would cause the insecticide to be released into my blood. I had been back in Oregon for several weeks before I quit smelling it at meal-times and in the middle of the night. But even when I couldn't smell the chemical I kept waking around 3 AM, and I got in the habit of drinking milk or orange juice to raise my blood sugar enough to lower my adrenalin (and cortisol) so that I could return to sleep.

Since I had already spent years investigating the effects of light on hormones and health, I began to see that the existing knowledge regarding the involvement of stress and glucocorticoid hormones in the aging process meshed perfectly with my concept of "winter-sickness" and the role of inadequate light in the stress-related diseases such as the premenstrual syndrome, colitis, osteoporosis, and depression.

Besides looking for the precise ways in which light acts on us (such as by preserving the function of the essential respiratory enzyme, cytochrome c), I also considered the dietary factors which might exacerbate the problem of light deficiency (such as an excess of unsaturated fats) and the possibility of other therapies, including drugs, that might be more practical and economical than hormone supplementation.

When various kinds of cells are deprived of energy (mast cells are often studied) they tend to produce (and secrete) histamine (among other substances). Unsaturated fats promote the release of histamine, while short-chain saturated fats, and glucose, inhibit it. When mice are killed by a variety of methods, they are found to have very high tissue histamine levels, so the high-histamine phenomenon seems to be about as generalized as shock. People who suffer from nocturnal asthma are known to have their highest blood level of histamine around 4 AM. Some inhibitory cells in the brain (including those involved in the "coma" state of protective inhibition) secrete acetylcholine. The similarity of the effects of histamine and acetylcholine are such that many people used to think of histamine as the "systemic cholinergic" hormone equivalent to acetylcholine. As a result of their similarity, any chemical which interferes with one of these "transmitter substances" is likely to interfere with the other, though not necessarily in the same way.

People who are awake in the dark have higher levels of cortisol than when they are asleep in the dark, that is, sleep is a partial defense against the stress of darkness. The cortisol (an adrenalin) secreted in darkness, or other stress, has the important function of maintaining the blood sugar level. The fact that cortisol causes the destruction of tissue to convert to glucose is the reason that stress and hypoglycemia are destructive. In 1971 I found that none of the sexually mature hamsters in our lab had any detectable thymus glands during the winter, though they all had them in the summer. Since estrogen and testosterone, the other thymus-shrinking hormones, are lower in the winter, I inferred that it was cortisone which caused their loss of thymus in the winter.

The main inhibitory "transmitter" substance in the brain is GABA (gamma amino butyric acid), which is closely related to aspartic and succinic acids. GABA has many anti-stress effects, besides the direct brain-quieting action. For example, it causes a sequestration of insulin, keeping some sugar from being turned into fat, and it promotes progesterone formation, which protects many systems from damaging hyperactivity.

Succinic acid was found by Szent-Györgyi to stimulate tissue respiration. Others found that it promotes the production of protective steroids, and more recently it was found to be the best material for chelating and removing aluminum from mitochondria. Succinic acid was identified as a major component of Vladimir Filatov's biogenic stimulators of tissue regeneration. Finding food sources rich in this material (especially in combination with the closely related butyric acid) would be desirable.

I experimented with various herbs known to have antihistamine and anticholinergic action, with the thought that they would help to sustain blood sugar through the night. (For example, insulin secretion is stimulated by acetylcholine from cholinergic nerves, and lowering its action during the night would decrease the need for adrenalin and cortisol.) My best results so far have been with a combination of the mildly sedative Jimson weed and the stimulant Ephedra; in combination, it seems that their antihistamine and glucose sustaining effects predominate, allowing comfortable sleep without the dry-mouth effect of their anticholinergic action.

It is now clear that both stress and an excess of the glucocorticoid hormones cause brain damage (as well as damage to all other organs). Marion Diamond's work with rats (confined or free) showed that stress causes very general brain damage, including to the cortex, and others have shown specific damage to the hypothalamus, the hippocampus, and other brain areas.[1] (Nerve cells are replaced by connective tissue cells. I think the damage is analogous to the viral (or "prionic") disease, scrapie; brain tissue from a scrapie infected young animal is antigenically similar to tissue from an old animal without the infection.)

Excessive cholinergic action in itself can cause brain damage.[2] The anticholinergic drugs, amantadine (Symmetrel) and atropine (related to the substances in Jimson weed) have been used to treat Parkinson's diseases. Atropine used to be listed as antidote for many poisons, probably because of its stabilizing effect on the nerves. It also promotes the formation of the protective hormone progesterone. Efficient energy production keeps the body from moving either to the "cholinergic" extreme or to the glucocorticoid extreme. When the mitochondria are damaged, the protective steroid pregnenolone (which is made in the mitochondria from cholesterol) can't be produced. In young people, the brain contains a very high concentration of pregnenolone and its derivatives, DHEA and progesterone, all of which stabilize cells and protect against the effects of cortisol, but in old age these fall to about 5% of their normal concentration, leaving the brain exposed to the destructive action of cortisol. The protective hormones can be used directly, or their synthesis can be promoted by using succinic acid, thyroid, vitamin A, and the atropine-type drugs, and maintaining adequate cholesterol. (T. Shimamoto, et al. have reported that low cholesterol is associated with a high incidence of stroke, especially hemorrhagic stroke.)

Since excessive excitation of cells (relative to the energy that's available) causes cells to die (in the brain, as elsewhere), it is important to consider as many of the natural means of inhibition as possible, while doing everything possible to sustain energy production. Succinic acid and butyric acid seem to be involved in both the energy sparing and the energy producing processes. The amino acids taurine and glycine are also considered to be inhibitory transmitters in the brain. Gelatin, which is extremely rich in glycine, is often added to fruit juice to take at bedtime as a sleep-supporting drink. Several of the local anesthetics including procaine and lidocaine, have cell-protecting action. Their anti-inflammatory or antihistamine function is probably caused by a more general cell-stabilizing effect. For example, lidocaine is used to prevent heart arrhythmia, and it can prevent tired heart cells from taking up too much calcium (which depletes cellular energy, in a deadly vicious circle). When taken orally at bedtime they act directly on the intestine (especially if there is inflammation anywhere in the intestine) to normalize its function, and even an occasional dose can have a long-lasting effect on the general health.

D. O. M.

The Wise One

Estrogen, too, causes brain damage. Its prenatal effect on the brain has been known for many years. Marian Diamond found that estrogen, like the stress of confinement, causes the cortex and other parts of the brain to be smaller than normal; she also found that progesterone, opposing estrogen, enlarges the cortex.

It has been suggested that estrogen's nerve-damaging action is caused by way of elevated glucocorticoid hormones. (In the "hamster lab" where I worked, other people showed that estrogen causes enlargement and hyperactivity of the adrenal cortex.)

When I first suggested that "aging is estrogenic," or that estrogen promotes aging changes, it was because of a large number of biochemical similarities in aging and in the state of estrogen dominance, and the absence of any detectable biochemical differences between the states, except their history.[3] For example, in both states the oxygen tension is relatively low, and as a result, unsaturated lipids are rapidly changed into "age pigment" or lipofuscin through lipid peroxidation.

Insomnia and hot flushes commonly occur around the time of menopause. These and other symptoms of menopause can be produced by an excess of cortisol, as in Cushing's syndrome.[4] The increase of cortisol during the night is probably responsible for "night sweats." When progesterone is deficient, cortisol - even in "normal" amounts - has a stronger effect.

The animal evidence is now clear, showing that it is largely the prolonged exposure to estrogen which causes reproductive aging.[5] Treatment with progesterone can prolong fertility,[3,6] as well as controlling symptoms such as insomnia and osteoporosis.

Until we know how to modify the environment (especially the radiant spectrum in the region of 600 nm to 1200 nm) to minimize the stress of winter and nighttime, the use of nutrition and hormone balancing techniques can control symptoms and minimize the cumulative damage that is occurring while we have the symptoms.

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