

Ray Peat's Newsletter

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Lungs, shock, inflammation, and aging

There is a growing effort by the food and drug industries, and many physicians, to promote the use of certain polyunsaturated fatty acids, those with their double bonds farthest from the acidic end of the molecule. These fats, which are found in fish, algae, and many vegetables, are the most easily oxidized of the common fatty acids. With stress, such as premature birth, and with aging, these fats produce free radical decomposition products at a high rate. They contribute to "shock lung" and to multiple organ failure.

After I had done my dissertation on the changes in oxygen metabolism that occur during aging and under the influence of estrogen, and not long after I had seen the therapeutic effects of progesterone in epilepsy, arthritis, depression, and multiple sclerosis, I met a woman who was disabled with some kind of inflammatory muscle and joint disease. Her face, arms, and upper torso were emaciated, but her hips and thighs were huge. This pattern of fat distribution is typical of the extreme and prolonged influence of estrogen.

In discussing her health history, she said that her movement problems began at the age of 21, when her physician-father began giving both her and her mother regular injections of estrogen.

Having a doctor in the family, they had the most complex medical studies done in trying to diagnose their problems. The thing that stood out in her description of the tests was the pulmonary oxygen diffusion test, which she said showed that both she and her mother had oxygen diffusing capacity that were "95% below normal." I think she might have meant that they were in the lowest 5 percent of the population, since I can't think of

another interpretation that would be compatible with life. Right around that time, I read a study in which mice were given a large dose of estrogen, which, after just 40 minutes, caused a similarly radical decrease in their oxygen diffusing capacity.

In the late 1960s, I had been interested in the use by athletes of a drink made by foaming oxygen into a solution of gelatin, to increase their blood oxygenation and their performance. I tried to talk to a few physician-researchers about this, and they firmly said that it was nonsensical, because "blood is always fully oxygenated when it leaves the lungs." Looking in the science library at the university, I found a recent (c. 1968) study in which the blood's oxygenation was found to decline with aging, commonly down to about 50%. But despite the mouse study, I didn't find any studies regarding estrogen's effects on oxygen diffusion in humans. I believed that the reason was the same as the denial that athlete's blood might not be fully oxygenated, namely, a stupefying degree of authoritarianism and a need to absolutize anything that was in a medical textbook.

About 15 years later, I visited a friend who was 82 years old, who lived in Toluca, Mexico. When I first saw him, I could see that he didn't recognize me. He was sitting down, breathing heavily, and his face was purplish. He had been diagnosed as having emphysema, and hadn't been able to work for several weeks. Since he was very fat, I guessed that he might be suffering from the

"... at a maximum level of exertion, the heart at high altitude is relying less on glycolysis (anaerobic energy production), and getting more of its energy from oxygen, than it would at sea level." This means that sea-level metabolism is more like cancer metabolism, because of the high oxygen/carbon dioxide ratio.

same sort of estrogen-provoked diffusion problem that I had run across previously. I left his daughter some progesterone and pregnenolone to give him, and left Toluca for several days. The next time I saw him, his skin had a better color, and his humor had returned. When I came back again two weeks after he had started taking progesterone and pregnenolone, his color was entirely normal, he had resumed working in his office (in a building that didn't have an elevator), and he insisted on taking me around the city, causing me to pant because of the altitude, about 8,500 feet above sea level.

In the 1950s, Gilbert Ling found that, under the influence of increased carbon dioxide, excitable cells don't "depolarize" electrically¹ to the extent that they do under a normal atmosphere. This principle has been applied to treat epilepsy, by breathing air with a few percent of carbon dioxide added, and more often, the principle has been used in the "diagnosis" of epilepsy, by using hyperventilation to induce seizures, by displacing too much carbon dioxide. Carbon dioxide spontaneously forms carbamino groups by reacting with the amino groups in proteins, and increasing the oxygen pressure causes the carbon dioxide to be displaced.

The binding of the acidic carbon dioxide to the protein molecule shifts electrons in the protein, making it more acidic. This shift in the protein changes the way the protein interacts with other molecules, including water, sodium, potassium, and calcium. Under the relatively acidic conditions when carbon dioxide is abundant, with the cell proteins' average electrons slightly "retracted," free radical production is inhibited, and cells are more resistant to radiation damage or other excitatory damage.

Carbon dioxide, along with the carbonic acid it forms as it reacts with water, regulates the organism's handling of water.

Carbon dioxide's association with cells has many effects, including the regulation of hormones and nerve transmitters. For example,

carbon dioxide causes cells to bind serotonin, so that a loss of carbon dioxide causes serotonin to be released, with the effect that blood vessels become more permeable, and leak fluid (including serum proteins) into the surrounding spaces.

In the lungs, this leakage of fluid is very inconvenient.

In any tissue, the leakage of serum creates an additional barrier to the diffusion of oxygen from the blood to the tissue cells. The hypoxic cells release lactic acid and other mediators of inflammation, and the walls of the capillaries and other blood vessels thicken, making the proper circulation of the blood more difficult. These effects are usually overlooked in the brain and the heart, but in the lung they are hard to miss. Following a stressful death, the lungs are waterlogged, with a great increase in weight, a condition called "shock lung" or "wet lung."

The antiexcitatory action of carbon dioxide is opposed by oxygen, so oxygen can, in this context, be considered as a cell excitatory agent. At increased pressure, pure oxygen causes seizures, and even at normal pressure, the lungs are more likely to be damaged when there is more oxygen. Since the lungs' delicate membranes are in direct contact with air, it's obvious that they are in a vulnerable situation, easily losing too much carbon dioxide in the presence of excessive oxygen.

At high altitudes, once a person has adapted to the lower oxygen pressure, the tissues retain more carbon dioxide, and this prevents cells from being activated to the same extent that's possible at low altitude, so there is less lactic acid produced. The carbon dioxide makes the blood circulate more easily, so the heart works less to circulate the blood at the same rate that it would circulate at sea level, or even at a higher rate, and even **at a maximum level of exertion, it is relying less on glycolysis (anaerobic energy production), and getting more of its energy from oxygen, than it would at sea level.**

¹ In the normal resting state, a cell is "polarized." In the depolarized state, a cell is vulnerable, and if it is too frequently depolarized, it can be damaged or killed in the process called "excitotoxicity," and other related degenerative processes. Cancer cells are chronically "depolarized," and this is related to their low-efficiency metabolism.

Some people, who have a respiratory problem at sea level, react to high altitude by breathing so hard that they lose even more carbon dioxide than they were losing at low altitude, and they may develop lung edema, and even brain edema and seizures. With lung edema, breathing becomes harder, and the heart works harder. It has been discovered repeatedly over the years that altitude sickness can be treated successfully with supplemental carbon dioxide. The now-standard treatment for mountain sickness is the drug acetazolamide, which causes the body to retain carbon dioxide. Despite the drug's success in preventing and curing altitude sickness, there is a weird reluctance to acknowledge that mountain sickness is produced by an insufficiency of carbon dioxide. The same drug is now often used to treat sleep apnea, despite the textbooks' opinion that sleep apnea is caused by too much carbon dioxide, rather than by the alkalosis resulting from insufficient carbon dioxide.

If we think of the presence of lactic acid as evidence of metabolic inefficiency, then an athlete, or anyone who exercises strenuously, has a low degree of efficiency, especially at sea level. Despite the presence of oxygen that isn't being consumed at a maximum rate, glycolysis becomes very intense, producing lactic acid that apparently helps to limit the full use of the available oxygen. It is probably the high oxygen pressure, wasting carbon dioxide, that turns on the lower efficiency lactic acid-producing glycolysis.

"Hypoxemia of exercise," the failure of the blood to be fully oxygenated during strenuous activity, is very similar to the chronic hypoxemia that occurs in the "respiratory distress syndrome." Women athletes have a greater tendency to exercise hypoxemia than men. In the luteal phase, when progesterone should be dominant, women breathe more effectively than during the estrogen-dominated follicular phase of the cycle. Since estrogen, like exercise, causes blood vessels to leak fluid, this isn't surprising. Stress, such as exercise or sickness, causes a significant rise of estrogen, along with the other mediators of inflammation, even in men.

Both exercise and estrogen dominance cause fatty acids to be liberated from the tissues. The

unsaturated fatty acids increase the permeability of capillaries, and the ratio of unsaturated fatty acids to saturated fatty acids corresponds closely to the degree of lung malfunction and respiratory distress. (Baughman, et al., 1984) The medium chain saturated triglycerides, extracted from coconut oil, can be used for intravenous feeding without causing the respiratory distress and lung damage produced by the unsaturated vegetable oils that were formerly used.

The long chain polyunsaturated fatty acids, including linoleic, linolenic, arachidonic, and docosahexaenoic (DHA) acids, cause mitochondrial breakdown, thyroid suppression, vascular permeability, brain edema, and increased radiation sensitivity.

DHA is the most unstable of these unsaturated fatty acids. But there is at present a very powerful marketing campaign which argues that DHA should be added to baby formula and should be taken by adults, because we supposedly "evolved on a diet rich in n-3 fatty acids," and because our tissues generally contain a much lower concentration of the n-3 fats than of the n-6 fats.

There is evidence that the low ratio of these n-3 fatty acids, such as DHA (docosohexaenoic acid), to the n-6 fats, such as arachidonic acid, is the result of the fact that the n-3 fats are extremely unstable, and break down rapidly in the tissues, producing lipid peroxides, free radicals, and the characteristic ethane, which can be measured in the breath. Stress accelerates the decomposition of these fats, and the resulting ethane can be detected in higher amounts during respiratory distress, and in premature babies and in older people.

Mead Johnson has announced that it will add DHA to their baby formula, arguing that it is an essential nutrient for eye and brain development. But animals that are fed a diet that is "deficient in" DHA are less susceptible to eye damage than animals that have "sufficient" DHA. But more generally, animals that are deficient in *all of the so-called "essential fatty acids"* are extremely resistant to all sorts of injury, shock, and poisoning.

Since all of the polyunsaturated fats inhibit thyroid function, and since the thyroid hormone is essential for the development of the brain and

lungs, increased use of polyunsaturated oils will increase the incidence of hypothyroidism, leading to the birth of more premature babies with lung disease. With a high concentration of polyunsaturated fats in the lungs, the exposure of the newborn's lungs to oxygen will create an inflammatory reaction. This is probably why the respiratory distress of prematurity usually takes a few days to appear. Considering what is known about oxygen, lungs, and DHA, I think it would be reasonable to say that increased use of DHA would be the ideal way to increase infant lung disease.

The unsaturated fats and estrogen contribute to the increased release of serotonin and nitric oxide (NO). Nitric oxide is produced during inflammation, and, like ethane, can be detected in the breath when the lungs are inflamed. Nitric oxide, as a pro-inflammatory free radical, stimulates the peroxidation of the unsaturated fats. Both NO and serotonin inhibit mitochondrial respiration, shifting metabolism toward glycolysis.

Since the processes that damage the lungs are so similar in aging, stress, and prematurity, I think an examination of the factors that cause premature birth will be useful for understanding the general problem of "lung stress."

Preeclampsia, or a syndrome of pregnancy induced hypertension, occurs in about 10% of pregnancies, and it's the main cause of maternal death and sickness of the newborn.

Thomas Brewer, about 50 years ago, made it clear that a protein deficiency is the main cause of preeclampsia. Protein deficiency causes a general inflammatory condition, with increased serotonin.

In women with preeclampsia, there are abnormally high levels of serotonin, nitric oxide, and lipid peroxidation.

In a study of more than 3000 women (Clausen, et al., 2001), the consumption of sugar and polyunsaturated fat was strongly associated with the development of preeclampsia. Women who don't eat enough protein are likely to substitute sugar and fat for the absent protein, so this study is consistent with Brewer's work, but it's very important to see that it was polyunsaturated fats, not saturated or monounsaturated fats, that caused the problem. Eclampsia (pregnancy-related

seizures) and preeclampsia are caused by oxidative stress, produced by the excessive unstable fats. The increased serotonin and nitric oxide are exactly what would be expected to result from the high consumption of polyunsaturated fats, especially with a deficiency of protein in the diet.

Protein deficiency, like an excess of polyunsaturated fats, causes a thyroid deficiency. Supplements of thyroid, given during gestation, accelerate the maturation of the baby's lungs, and prevent the respiratory distress syndrome.

The use of adequate protein and saturated fats during pregnancy will prevent many of the problems of pregnancy and infancy, but since the unsaturated fats remain stored in the tissues for many years, and are mobilized during stress, it's important to eat correctly long before pregnancy. The requirement for vitamin E remains high for years after the diet has contained an excess of the polyunsaturated fats.

The diet which protects the developing fetus happens to be the diet that protects adults from all sorts of stress, and prevents many of the worst symptoms of aging.

Supplemental thyroid, pregnenolone, and progesterone can partly make up for defects in the diet, by maintaining a better balance between carbon dioxide and lactic acid, and by restraining the various mediators of stress, such as NO, serotonin, and estrogen.

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plasma MDA and lipid peroxides increased ($P < 0.001$ and $P < 0.05$, respectively). Breath alkane output did not change significantly and vitamin E intake did not prevent the increase in lipid peroxidation during menhaden oil supplementation. The results demonstrate that supplementing the diet with n-3 fatty acids resulted in an increase in lipid peroxidation, as measured by plasma MDA release and lipid peroxide products, which was not suppressed by vitamin E supplementation.

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