Ray Peat's Newsletter

"The people have no voice because they have no information." Gore Vidal

 Raymond Peat P.O. Box 5764 Eugene OR 97405 **May 2020**

This Novel Flu Season

The argument:

A failure of energy metabolism limits the ability of cells to return from an excited active state to a stable resting state. Unresolved excitation causes cells to emit signals indicating the need for repair, inflammatory signals. Pre-existing inflammation is associated with high altitude sickness and the ability to get sick from a corona virus, as well as chronic diseases. This implies that treatment for a so-called "coronavirus infection" should be to reduce cellular excitation and inflammation and normalize energy production. It also implies that these treatments will have favorable effects on cell aging.

The conditions that produce inflammation activate the adaptive exosome system, a retrotransposon system involving a massive block of our DNA, which overlaps with the virus production mechanism. Current approaches to preventing viral disease dangerously ignore this fundamental physiological-genetic system. An important implication of this system's involvement in health and disease is that we are not defined "somas" produced once by our DNA, but rather adaptive, epigenetic, ongoing creative beings.

U.S. history has repeatedly hinged on words that didn't correspond to facts, for example the bombing of Vietnam based on the fictional Tonkin Gulf incident, or the invasion of Iraq based on the yellowcake uranium and other fictional weapons of mass destruction. To explain the present destruction of the normal US economy it would be reasonable to look for some clear image to indicate that China's new variant corona virus was more dangerous than preceding strains of the virus, but there has been no public information about how to distinguish infections with this new virus from other acute lung problems. According to official medical views, no specific treatment or test was known when the WHO declared the pandemic, so the FDA has bypassed its normal regulations for both tests and drugs. A test, to be useful in diagnosis, determining the exact cause of symptoms, would have to show whether any of the common respiratory disease organisms was present, and naturally, any test has to be tested itself. The CDC has observed that half of the positives on an antibody test, in a population with low prevalence, could be false. A muddle of tests has created confusion even among experts; on May 21, the CDC acknowledged that it was mixing together their counts of antibody tests and PCR virus tests.

In March and April, several Stanford professors were arguing that the lethality of the new virus was very similar to that of the familiar influenzas, about 0.25% of those infected. The latest figures from the CDC, published inconspicuously on May 22, were similar, assuming that 35% of infected people could be symptom free; if a higher percentage of infections are symptom free, then the infection-death rate is even lower.

With no public explanation of the pathophysiology of the "new disease," the vacuum was filled by rumors that it was a virus escaped from germ warfare labs, alternately said to be from Wuhan or Fort Detrick, and several broadly circulated articles denied that such a virus was even possible to engineer, conflicting with articles in major journals in recent years describing exactly that engineering (de Haan, et al., 2008; Graham and Baric, 2010). In the absence of empirical information about the nature of the disease, but with the

rumors creating fear of a uniquely horrible disease, hospitals have been instructing doctors to treat patients with breathing problems in very aggressive and invasive, and standardized, ways.

A couple of doctors in the US said publicly that those treatments aren't appropriate for the real disease. Cameron Kyle-Sidell has made two videos observing that his patients' symptoms resemble those of people with high altitude pulmonary edema, **a feature of which is very low carbon dioxide as well as low oxygen.** Another doctor in New York, Isaac Solaimanzadeh, suggested using calcium channel blockers and acetazolamide to treat the new disease, because of their therapeutic effect in high altitude pulmonary edema. He didn't mention it, but both of these drugs can correct the tissue deficiency of carbon dioxide.

In Germany, Luciano Gattinoni (Gattinoni, et al., 2020) pointed out that the standard ventilation protocol wasn't conforming to the best knowledge of respiratory physiology. He observed that in one conventional hospital the mortality of respiratory patients was 60%, while in a nearby hospital following his more rational method, the mortality of respiratory patients was zero.

High altitude physiology is obviously confusing to the many doctors who have scoffed at the comparison of the new disease to high altitude pulmonary edema. This is because of the way physiology is taught. At low altitude, when a tissue's oxygen consumption increases beyond the blood's ability to deliver oxygen, as in an intensely working muscle, the tissue activates the glycolytic process, converting glucose to lactic acid as a source of additional energy. Carbon dioxide is seen as nothing but a waste disposal problem. This view has led to the concept of the "high altitude lactate paradox," referring to the fact that maximal exertion at high altitude doesn't increase lactic acid production in the normal way. Neglecting the role of carbon dioxide in suppressing the formation of lactic acid, they also neglect all of its other essential metabolic effects, including its role as the factor whose absence results in the syndromes of altitude sickness, and ventilator-induced lung damage (Sinclair, et al., 2002; Cummins, et al., 2010; Contreras, et al., 2012).

This CO2-negligent approach to physiology has affected medicine for 100 years. When Otto Warburg discovered that aerobic glycolysis is the defining feature of cancer, the presence of a little extra lactate in the blood, displacing CO2, didn't appear to most doctors and biologists to be medically important, though a little extra carbon dioxide could arouse concern. Ignoring that 30 years of slightly elevated lactate might lead to cancer or other degenerative disease, those who taught physiological chemistry also had little interest in the idea of chronic metabolic hyperventilation—losing a little too much CO2 even at sea level. **Cumulative injury of all sorts contribute to a background of inappropriate excitation and inflammation.**

In studies related to asthma, it has become well known that abnormally low CO2, hypocapnia, constricts the airways, and elevated CO2, hypercapnia, relaxes them (El Mays, et al., 2011; Choudhury, et al., 2012); various mechanisms, affecting intracellular calcium, are known to be involved. The causes of relative hyperventilation continue to be disputed.

The basic principles of respiration, the Bohr and Haldane effects, describe the physical equilibria of oxygen and CO2 in people who have adapted to living at different altitudes. The Haldane effect describes the fact that increased oxygen pressure decreases the amount of carbon dioxide retained by hemoglobin, and decreased oxygen pressure increases the amount of CO2 retained. A steady increase of retained CO2 with increasing altitude occurs in those who adapt. People who fail to adapt experience a loss of CO2, with an increase of lactate.

It has become increasingly common to treat altitude sickness with carbon dioxide. **A few people have argued for a long time that mechanical ventilation would be less harmful if a mixture of CO2 and O2 were used** (Laffey and Kavanagh, 1999; Kregenow and Swenson, 2002), analogously to the therapeutic effect of CO2 in high altitude sickness (Harvey, et al., 1988).

In a state of chronic stress, oxidative energy production is low, and mediators of inflammation are likely to be chronically increased; there is typically a chronically increased production of lactate, and/or decreased oxidation of it. In this state, the increased ventilation caused by high altitude will cause an increased loss of carbon dioxide, increasing the pH of the

blood, which increases the formation of lactic acid. The lactate increases the leakiness of capillaries and loss of fluid, and decreases the ability of oxygen to diffuse from the alveolus to the erythrocyte. Since carbon dioxide diffuses many times more rapidly than oxygen, this diffusion barrier results in low blood CO2 at the same time as hypoxia. Even at sea level, an increase of lactate immediately increases the lungs' diffusion barrier.

Thinking of the infection as the disease, and therefore considering the "receptor," "entry," and replication of the virus to be sufficient to explain the damage to infected cells, tissues, and organs, and defining the disease as an inflammation of the respiratory tree and lung, the hospital system went into action. Failing to think of the intestine (which is infected as easily as the nose and lungs), the meaning of events throughout the organism, including the lungs, is misunderstood. The infection can serve as one of the factors increasing inflammation and stress, suppressing energy function, but the relevant disease to be treated is that unstable state of counter-productive, energy-depleting excitatory and inflammatory signals.

Healthy individuals aren't harmed by the presence of the virus, so the nature of the defect that makes some people susceptible should be the focus of attention. Some important factors have already been identified: living at high altitude provides 3- or 4-fold protection (Arias-Reyes, et al., 2020), and being a young woman is even more protective. In Italy, 70% of the deaths are men, but deaths increase sharply among post-menopausal women.

The lungs are especially sensitive to activation of the so-called "calcium channels," i.e., calcium uptake by cells, by hypoxia, causing constriction of blood vessels, but increased carbon dioxide, which increases during adaptation to altitude, reverses the hypertension caused by hypoxia (Baudouin and Evans, 1993; Chuang, et al., 2011). Calcium channel blockers, paralleling that effect of CO2, are effective treatments for high altitude pulmonary hypertension. Like acetazolamide, the other recognized treatment for altitude sickness, calcium channel blockers inhibit carbonic anhydrase, facilitating the body's retention of CO2. To the medical scoffers who deny that CO2 has a constructive physiological role, the exaggerated pulmonary constriction at high altitude is the cause of the lung failure, while in the respiratory distress caused by Covid-19 that contriction is a consequence of the disease (Luks and Swenson, 2020), and neither is a result of a CO2 deficiency.

The presence of lactate corresponds to some degree of reductive excess in cells, and the degree of reduction regulates the "calcium channels," controlling the excitatory effects of intracellular calcium (Wang, et al., 1997; Iesaki and Wolin, 2000; Schach, et al., 2007). Reduction by stress and/or lactate "activates the channels," tightening vascular smooth muscle, and activating a wide range of other cell activities, including inflammation, exosome secretion, and viral replication (Savina, et al., 2003; Chen, et al., 2019). Exosome production during stress is part of the body's normal restorative function (Zhang, et al., 2017); it's only when protective factors such as progesterone and carbon dioxide are lacking that their production becomes counter-productive.

Progesterone and its neuroactive metabolites including tetrahydroprogesterone or allopregnanolone, are very effective "calcium channel blockers" (Todorovic, et al., 2004; Pathirathna, et al., 2005; Hu, et al., 2007). A major function of progesterone is the inactivation of the estrogen receptor; estrogen and its "receptor" are powerful activators of cellular calcium uptake (Sarkar, et al., 2008).

Studies of progesterone's effects on recovery of nerve function after traumatic brain damage have found that vitamin D increases its effectiveness. By improving calcium homeostasis, opposing the effects of the parathyroid hormone which activates calcium channels, vitamin D (25-hydroxycholecalciferol) is coming to be considered a neurosteroid (Groves, et al., 2014; Gezen-Ak and Dursun, 2019), as well as an essential factor in immunity (Pfeffer and Hawrylowicz, 2012).

Intracellular calcium is essential for all aspects of the viral cycle—entry, gene replication, maturation, and release—while also disturbing the cell's own functions. "Evidence has emerged that pharmacologically targeting the calcium channel or calcium release from the endoplasmic reticulum … can obstruct virus lifecycles" (Chen, et al., 2019).

A few doctors recognize that progesterone supplementation might seem reasonable for preventing or treating the corona virus problem, though they don't seem to know about its already established antiviral effects (Pfahler, et al., 1987; Muñoz, et al., 2007; Hall, et al., 2016), or the mechanisms involved. Other doctors (Sharon Nachman), following their cliché thinking instilled by estrogen industry advertising, and believing that estrogen is "the female hormone" that explains women's health advantages, have begun a study, treating the corona infection in men with estrogen patches. Old men's estrogen levels, especially if their health is poor, can be higher than that of women of the same age, while their progesterone is always lower.

Nitric oxide is a powerful oxidant that can destroy viruses, and it happens to dilate blood vessels. Doctors have almost unanimously recommended it to treat the corona virus infection; however, it is associated with inflammation (Weidinger, et al., 2015), and promotes fibrosis, and fibrosis is a sequela of coronavirus disease. An increased amount of nitric oxide in the exhaled breath is a clear predisposing factor for high altitude sickness (Ren, et al., 2015). Progesterone is a respiratory stimulant that increases the hypoxic ventilatory response, and a low hypoxic ventilatory response is another predisposing factor to high altitude sickness. Progesterone inhibits the formation of nitric oxide (Wolfson, et al., 2015), while estrogen increases it (Lima, et al., 2014).

For years, corona viruses have been known to bind to the angiotensin converting enzyme 2 (ACE2), and that enzyme has been known to have protective effects, destroying angiotensin, and losartan, an angiotensin receptor blocker, has been known to be protective against corona viruses. Angiotensin increases intracellular calcium, and losartan lowers intracellular calcium. **In reaction to the new corona virus, a few groups responded quickly, treating successfully with antiinflammatory things—losartan, cinanserin (a serotonin antagonist), aspirin, and azithromycin or erythromycin, which lower intracellular calcium. Aspirin's effects overlap those of losartan, and it downregulates the angiotensin receptor, ATR1** (Mitra, et al., 2012).

Meanwhile, medical media, such as Lancet, immediately warned against the use of anti-angiotensin drugs, as if the authors and editors hadn't been reading respiratory physiology in recent years. This is because of the stupefying effects of the receptor dogma. Having identified ACE2 as the "coronavirus receptor," nothing physiological matters. Graded, holistic effects, involving simultaneous changes in many "receptors," in which rising inflammation can lead to viral replication, suggesting many safe therapeutic interventions, simply don't fit into the paradigm of product "development" and marketing.

The closed, authoritarian nature of the medical profession makes it a perfect tool for political manipulation. Obstructing the use of rational treatments, the profession has been mobilized to promote the militarization of the national response to the latest respiratory virus, the history of which shows the massive involvement of the US military. Ralph Baric's publications on the corona virus, as well as dissenting opinions among virologists and in government (Nature, Nov. 12, 2012; The Scientist Magazine, Nov. 16, 2012), make it clear that military-motivated gain of function virus research has been able to override a presidential moratorium, and the actions of Eric Schmidt and his National Defense Commission on Artificial Intelligence (proposing responses to growing Chinese power), and his recent appointment by Governor Cuomo to help reorganize New York's schools, health system, and economy, offer new perspectives on the government's surprising actions. The fact that Italy and Iran last year signed an agreement to participate in China's expansive trade plan might be relevant to evaluating the meaning of this novel flu season.

Since the recognition that only 1% or 2% of our DNA consists of "our genes," and that around 48% shows features specifying retroviruses, many geneticists are suggesting that retroviruses, transferring their RNA information into our DNA, are our ancestors. The reason for this crazy thought is probably to avoid as far as possible the radical abandonment of the Central Dogma of genetics, that information flows only from nucleic acids to proteins. Now that the protective and adaptive functions of exosomes and retrotransposons have been clarified, the more obvious inference might be that we are the ancestor of retroviruses, though the real implication is that we are essentially

adaptive, epigenetic, creative beings. The "germ line" is everywhere, not insulated in the gonads.

Vaccine adjuvants are designed to produce systemic inflammation, and that involves some degree of activation of our innate immunity with its epigenetic adaptive potential. **Recognizing that a barely recognizable background of inflammation predisposes to develop serious sickness from a corona virus, it's important to consider the role of the recent great expansion of the influenza vaccination campaigns in Italy and the US, especially directed at older people, in the current increased incidence of corona infections.** Several studies, designed to judge the effectiveness of the influenza vaccine, reported that the vaccine might be about 45% effective in reducing influenza infections, but that the vaccinated people were much more likely to have other respiratory infections, including corona virus infections.

Focus on the induction of antibodies by vaccines to define immunity has led to a dangerous disregard for the basic facts of health. The present testing of a vaccine containing the RNA that specifies the most destructive spike protein of the corona virus, the part that inactivates our protective ACE2 enzyme, is being done in a culture that avoids consideration of the meaning of our massive endogenous system of RNA-responsive reverse transcriptases and retroelements. The consequences of incorporating the spike protein of the virus into our genetic repertoire are hard to imagine. **The mindless activation of our huge epigenetic system of retroelements, with no knowable benefits, should be stopped.**

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