Ray Peat's Newsletter

We can't possibly hope to reform that which we do not understand. Julian Assange

Copyright 2016 **Raymond Peat P.O. Box 5764 Eugene OR 97405** **September 2016**

Dangers of sadistic science: Determinism vs process thinking

It's very common for people to talk about cancer as a localized disease, until it metastasizes, when it becomes a multitude of localized instances of that cancer. Occasionally, symptoms can appear in association with a tumor that involve abnormal function of a tissue or organ in which there are no cancer cells, and this is called a "paraneoplastic" syndrome—something which isn't cancer, but is caused by cancer. The idea of cancer as a "systemic disease" (as opposed to a localized disease) hardly fits into the contemporary medical culture, but several decades ago some people thought that processes throughout the body—in the digestive system, the nervous system, immune system, blood, kidneys, hormones, etc.—underwent changes that allowed tumors to form.

An advantage of thinking of cancer as a localized disease is that it fits into a deterministic view of the world, in which intrinsic defects in the molecules and cells of a tumor can explain its abnormal structure and behavior. These intrinsic defects could include "cancer genes" that were inherited, or genes that have been randomly altered during a person's life. The idea has led to attempts at "gene therapy," but the main focus has been on ways to identify the defective cells and to destroy them.

If the essence of cancer isn't within the tumor, then a more complex kind of thinking about causality is needed, in which extrinsic factors are taken into account. The nature of the organism, and how it interacts with its environment, become relevant to the issue of understanding cancer.

The ideology of mechanistic causality that motivated the hostile rejection of Pasteur's and Warburg's holistic metabolic ideas still exists in the Cancer Establishment. In 1971, the War on Cancer accelerated the search for a mutated gene or virus that was responsible for the "uncontrolled proliferation" of cancer cells. There has been increasing awareness that misconceptions about the nature of cancer accounted for the failure of the War on Cancer to produce objective results, and hundreds of publications in the last few years have focused on changes in metabolic pathways as the cause of cancer (e.g., Dang, 2012; Stine and Dang, 2013; Altman, et al., 2016). This shift has been paralleled by a growing understanding of the metabolic meaning of inflammation, and an awareness of the role of inflammation in all the degenerative diseases.

> **The evil that is in the world almost always comes of ignorance, and good intentions may do as much harm as malevolence if they lack understanding. – Albert Camus**

In 2015 Dr. Soon-Shiong, a Los Angeles cancer billionaire, enlisted Vice President Biden in a publicity campaign (Cancer Moonshot) to promote the doctrine of gene mutation as the cause of cancer. Describing the Cancer Moonshot, Doug Lowy, Acting Director of the National Cancer Institute, says "cancer is a disease of the genome." The role of the government in this consortium, besides providing publicity, is to accelerate the approval of new cancer drugs. Sanjay Gupta is an integral part of Soon-Shiong's corporate publicity program. The White House has directed the Department of Defense and 12 other government agencies to participate.

Historically, after ordinary observation and science have identified an environmental cause of

cancer, industries associated with the presence of the causative factor have invested heavily in a kind of science that challenges the validity of the link, usually arguing that the real cause is likely to be a pre-existing genetic defect in the victim. A tremendous effort has gone into producing studies showing that smoke, estrogen, asbestos, and radiation *might not really* be carcinogic, mutagenic, or otherwise toxic. In each of these cases, an industry gained 50 or more years of freedom from regulation by arguing that if it isn't absolutely certain that their product will kill you, you shouldn't worry about it. Devra Davis's book, *The Secret History of the War on Cancer*, describes some of the methods used to keep the public from worrying. The doctrine of genetic determinism, of an innate propensity to develop a particular disease, has been very effective in distracting attention from actual avoidable causes of disease. The researchers, teachers, and doctors who have promoted this doctrine have generally believed it themselves.

An exploratory, receptive attitude has become very uncommon among people with a career in science; the people who fund research want to be sure that something concrete will be achieved, and researchers who don't question well established assumptions are more likely to be funded than someone who wants to explore the implications of an unpopular assumption. A lack of curiosity is probably valued in proportion to the authoritarianism of a situation and the degree of a person's need for approval from the authorities. A need for "certainty" displaces an interest in possibilities.

Erich Fromm, in his 1941 book *Escape from Freedom*, wrote about sadism and masochism as aspects of the authoritarian character, striving, respectively, to control or to be controlled by others. In the hierarchical governments of the middle ages, one's place in society was largely hereditary, but the changes of the social order produced by the industrial revolution led to new ways of imposing, or challenging, authority. Natural science developed knowledge of ways to control nature, but the new knowledge became a challenge to religious and monarchic authority. At the same time, the ruling classes began finding ways to use "science" to defend their interests. Darwin's cousin, Francis Galton, coined the term "eugenic" in explaining his ideas for improving the human species by controlled breeding, essentially by limiting the reproduction of the inherently inferior lower classes. In biology, the idea of inborn, hereditary traits of inferiority and superiority implied that improvement came by eliminating the inferior.

In the authoritarian societies that were the contemporary background for Fromm's study of character, social control in many cases involved literal sadism, such as performing surgical experiments on prisoners without anesthetic. Their intellectual framework was shared by many prominent biologists in England and the United States. The population-engineering of the eugenics movement became the genetic engineering of the molecular biologists.

Power always thinks it has a great soul and vast views beyond the comprehension of the weak; and that it is doing God's service.... – John Adams

Two famous experiments strongly influenced Anglo-American thinking about biology through much of the 20th century, leading in the 1950s to the Central Dogma of molecular biology, and to the free radical theory of aging. In the 1880s, August Weismann argued that germ cells are immortal, while the other "somatic" cells are mortal, and wear out from use, and that these two "cell lines" are perfectly isolated from each other, preventing information from the somatic cells from entering the germ cells. Francis Crick's Central Dogma simply restated Weismann's doctrine. Weismann's experiment, which he thought disproved the inheritance of acquired traits, involved the amputation of the tails of 1,592 mice, over 22 generations.

In the 1920s, Raymond Pearl refined Weismann's idea of "wearing out" with his "rate of living" theory of aging. Pearl sprouted cantaloupe seeds in a dish, and observed that the seed sprouts that grew fastest died soonest (the growth of a sprout involves the conversion of nutrients stored in the seed into active cells, depleting the

nutrients). In the 1950s, Denham Harman proposed that a high rate of living shortens the lifespan in the same way that ionizing radiation or a toxic excess of oxygen does, by accelerating the formation of free oxygen radicals that cause cumulative damage, especially to DNA molecules.

Weismann's mouse mutilation and Pearl's seed sprouting were remarkably stupid experiments, which had absolutely nothing to do with the claims based on them, but they were fantastically successful propagandistically, and they resonated over the years with the prejudices of millions of professors, editors, and authorities of all sorts.

Pearl undoubtedly knew that death from starvation (providing the seeds nothing but water) didn't say anything about death resulting from aging, which results from a progressive inability to adaptively assimilate available resources. In Weismann's time, it was commonly understood that Lamarck believed that the changes of an organism's form and function that were acquired in the process of *adapting* to a particular environment could be passed on to subsequent generations. Although it's possible that Weismann hadn't read Lamarck and ignored the basic role of biological *need* in his idea of adaptation, it's much more likely that both he and, a generation later, Pearl, understood that even a bad metaphor was good enough when the audience had a strong need to be convinced.

In 1954, Barry Commoner's research group described their measurements of free radicals in living tissues. Until then, the official view was that free radicals were very toxic and completely incompatible with life. It was around this time that it occurred to Denham Harman that the production of free radicals in the process of oxidative metabolism might be a mechanism to explain the degenerative processes of aging. Harman's earlier work as a Shell petroleum chemist (including work on insecticides) defined his view of biological free radicals.

He suggested that the mitochondrion is "the true biological clock" of aging, Although supplementing antioxidants could reduce some diseases in his experimental animals and increase their average lifespan, he found that they didn't increase the maximum lifespan. He concluded that supplemented antioxidants couldn't penetrate to the mitochondrial matrix, and that free radicals produced there damaged the mitochondrial DNA, resulting in metabolic errors that increased the rate of free radical production, leading to a constant acceleration of the rate of decline.

This statement of the "rate of living" in terms of damage to the genes of somatic cells appealed to mainstream biologists, who were just learning about the new DNA double-helix model of the gene, and who were already committed to the "wear and tear" theory of aging and cancer, involving random "somatic mutations," which were thought to be caused mostly by radiation. An extrinsic cause of age-associated diseases, ionizing radiation, had been replaced by an intrinsic, inescapable cause, mitochondrial respiration.

By 2006, at the age of 90, Harman seemed to be fully convinced that mitochondrial deterioration was unavoidable, an "inborn aging process (IAP)." Since his original theory proposed toxic free radicals as the cause of cancer as well as aging, the "IAP" would suggest that cancer too is ultimately the result of an inborn tendency, though he had found that antioxidants could reduce the cancer death rate in animals. His experiments in the 1960s and '70s contributed to the use of vitamin E and vitamin C, and to the development of increased optimism about the possibility of radically extending the maximum lifespan.

For example (1961), he found that the most highly unsaturated fats were the most carcinogenic, and (1976) he showed that peroxidation damages brain function, increasing learning errors. DHA, the most peroxidizable of the fatty acids, accumulates in the brain with age, and peroxidation corresponds to reduced function (1977). In 1989, he observed that the age pigment, lipofuscin, "is increased by vitamin E deficiency and by increased intake of polyunsaturated fatty acids." Unfortunately, he saw those facts as mere epiphenomena to the "inborn aging process." His view of science excluded a creative/damaging role for the environment.

Free radicals do cause the kinds of damage that Harman described, but those reactions don't necessarily follow from the free radical processes that are intrinsic to life energy production. The harmful reactions are consequences of

interference with the intrinsic mitochondrial reactions, so they illustrate the opposite of the "rate of living" theory: A higher, less impeded, rate of living results in a lower rate of aging (Speakman, et al., 2004; Speakman, 2005).

Harman's work with free radicals in petroleum chemistry had convinced him that their reactions were always random, and, following established assumptions about the nature of cells, he neglected to consider that reactive unpaired electrons might have a constructive, non-random, role in cell metabolism.

The recent recognition of a constructive biological role for unpaired electrons provides an opportunity for a return to the exploratory approach to science that W.F. Koch, Warburg, and Szent-Gyorgyi exemplified. In the paradigm of mainstream authoritarian biology, organisms are products of their inherited relatively timeless components, the genes. In the newer developing paradigm, organisms use their inherited resources creatively, modifying themselves to optimize their use of the environment as well as modifying the environment to meet their needs.

Most medical publications seek to confirm the old paradigm, even when they are dealing with fundamentally unsolved problems such as cancer, dementia, and aging itself. The new paradigm sees the organism's contacts with the environment as the focus of attention, and with experience as the subject matter, a radical empiricism tends to replace argument from the authority of "well established assumptions."

For organisms capable of intense oxidative metabolism, the daily cycle of light and dark, and longer cycles of changes of food supply, are stresses that can be handled by adjusting the metabolic rate, in sleep, torpor, hibernation or estivation. Early in life, there is a great difference in oxygen consumption between day and night, but in old age there is less difference, with decreased daytime oxygen consumption, and a decrease in both the amount and the depth of sleep. This corresponds to the increasing amount of polyunsaturated fat in the brain, especially the n-3 DHA.

Newborn babies are said to often be "deficient in essential fatty acids," and they spend most of their time sleeping. When animals are fed a diet lacking the so-called "essential fatty acids" their oxygen consumption is very high, representing a retention of a more juvenile physiology, and their sleep is deeper, with a longer duration of slow wave sleep (Dzoljic, 1978). This is the phase of sleep in which the brain restores itself, and it's the phase that is decreased in aging. Prostaglandins, produced from polyunsaturated fats, produce increased wakefulness (Takemiya, 2011).

When the amount of DHA in women's blood was compared to their babies' sleep behavior in their first two days, the "infants in the high-DHA group had significantly less sleep-wake transition and more wakefulness than did infants in the low-DHA group," and this was interpreted to mean that "more wakefulness in the infants in the high-DHA group also reflects greater maturity" (Cheruku, et al., 2002). In newborns, a mature sleep pattern is probably not a good sign. Several studies have reported an association between higher maternal DHA and increased allergies in the children (Gonzalez-Gil, 2016).

Another ubiquitous stressor is bacterial endotoxin, and young organisms have multiple protective adaptations to it; with advancing age, its effects become more dangerous. As the polyunsaturated fats accumulate, the activation of cyclooxygenase (prostaglandin synthase) by endotoxin produces progressively larger inflammatory effects. Endotoxin, amplified by the prostaglandins, promotes the degenerative processes (for example, Griffin, et al., 2013) in cancer, stroke, dementia, heart and kidney failure, and sarcopenia, the age-related loss of muscle. Inhibiting the conversion of polyunsaturated fats to prostaglandins, for example by aspirin, protects against those degenerative processes (for example, Trappe, et al., 2001).

The success of an organism's adaptive interactions can be seen in the maintenance of a stable balance of reductive and oxidative processes. Mere size is a stabilizing factor; a quickly responsive nervous system is another factor. From birth to old age, our rate of metabolism decreases progressively. Up to about the age of 12, the rate of mortality decreases, as our mass increases along with the maturation of structures. After puberty, the mortality rate increases as our metabolism, nerve function, and other adaptive

processes slow. A decrease of the rate of oxidative metabolism leads to increased lipid peroxidation (Brand, 2000; Salin, et al., 2015; Schaar, et al., 2013; Sanz, 2016).

There is now an abundance of knowledge about the factors that retard metabolism and adaptation, but biomedical research has been directed away from an integral understanding of the nature of life, and from holistic metabolic interpretations of cancer and the other diseases of aging, by powerful interests with ulterior motives.

At the time that Denham Harman shifted his interest from insecticides to medicine, the idea that polyunsaturated fats were nutritionally essential and beneficial was being widely advertised. If they were essential for life, then their oxidative instability, leading to the production of toxic lipid peroxidation products, was an unavoidable fact of life, seeming to confirm the rate of living theory of aging. The ideology of the seed oil industry was designed to mesh with the needs of other industries.

It's now well established that the tissue content of polyunsaturated fatty acids is strongly influenced by diet, and that reducing their intake, or increasing the intake of saturated fats (Nanji, et al., 2001; Bronnikov, et al., 2010), can have beneficial effects in the degenerative and inflammatory diseases. Unfortunately, there's no trillion dollar industry, or even a single government agency, devoted to building on that information.

REFERENCES

Nat Rev Cancer. 2016 Jul 29. **From Krebs to clinic: glutamine metabolism to cancer therapy.** Altman BJ, Stine ZE, Dang CV.

Am J Physiol Gastrointest Liver Physiol. 2008 Jan;294(1):G27-38. **A new model for nonalcoholic steatohepatitis in the rat utilizing total enteral nutrition to overfeed a high-polyunsaturated fat diet.** Baumgardner JN(1), Shankar K, Hennings L, Badger TM, Ronis MJ.

Exp Gerontol. 2000 Sep;35(6-7):811-20. **Uncoupling to survive? The role of mitochondrial inefficiency in ageing.** Brand MD.

Biochemistry (Mosc). 2010 Dec; 75(12):1491-7. **Dietary supplementation of old rats with hydrogenated peanut oil restores activities of mitochondrial respiratory complexes in skeletal muscles.** Bronnikov GE, Kulagina TP, Aripovsky AV.

Am J Physiol Endocrinol Metab 298: E354–E361, 2010. **Effect of a cyclooxygenase-2 inhibitor on postexercise muscle protein synthesis in humans.** Burd NA, Dickinson JM, Lemoine JK, Carroll CC, Sullivan BE, Haus JM, Jemiolo B, Trappe SW, Hughes GM, Sanders CE, Jr, Trappe TA.

Am J Clin Nutr. 2002 Sep;76(3):608-13. **Higher maternal plasma docosahexaenoic acid during pregnancy is associated with more mature neonatal sleep-state patterning.** Cheruku SR, Montgomery-Downs HE, Farkas SL, Thoman EB, Lammi-Keefe CJ.

Genes Dev. 2012 May 1;26(9):877-90. **Links between metabolism and cancer.** Dang CV.

Prostaglandins. 1978 Feb;15(2):317-24. **Prostaglandins and sleep. Awaking effect of prostaglandins and sleep pattern of essential fatty acids deficient (EFAD) rats.** Dzoljic MR.

Eur J Clin Nutr. 2016 Jul;70(7):819-23. **Whole-blood fatty acids and inflammation in European children: the IDEFICS Study.** González-Gil EM, Santabárbara J, Siani A, Ahrens W, Sioen I, Eiben G, Günther K, Iacoviello L, Molnar D, Risé P, Russo P, Tornaritis M, Veidebaum T, Galli C, Moreno LA.

J Gerontol A Biol Sci Med Sci. 2015 Nov; 70(11):1334-42. **Reconsidering the Role of Mitochondria in Aging.** Gonzalez-Freire M, de Cabo R, Bernier M, Sollott SJ, Fabbri E, Navas P, Ferrucci L.

J Neurosci. 2013 Sep 18;33(38):15248-58. **Cyclooxygenase-1-dependent prostaglandins mediate susceptibility to systemic inflammation-induced acute cognitive dysfunction.** Griffin ÉW, Skelly DT, Murray CL, Cunningham C.

J Gerontol. 1956 Jul;11(3):298-300. **Aging: a theory based on free radical and radiation chemistry.** Harman D.

J Gerontol. 1957 Apr;12(2):199-202. **Atherosclerosis: a hypothesis concerning the initiating steps in pathogenesis.** Harman D.

Lancet. 1961 Jan 28;1(7170):200-1. **Mutation, cancer, and ageing.** Harman D.

Radiation Research: May 1962, Vol. 16, No. 5, pp. 753-763. **Role of Free Radicals in Mutation, Cancer, Aging, and the Maintenance of Life.** Harman D.

J Gerontol. 1961 Jul;16:247-54. **Prolongation of the normal lifespan and inhibition of spontaneous cancer by antioxidants.** Harman D.

J Gerontol. 1971 Oct;26(4):451-7. **Free radical theory of aging: effect of the amount and degree of unsaturation of dietary fat on mortality rate.** Harman D.

J Am Geriatr Soc. 1972 Apr;20(4):145-7. **The biologic clock: the mitochondria?** Harman D.

J Gerontol. 1975 Nov;30(6):647-54. **Rat brain fatty acid composition: effect of dietary fat and age.** Eddy DE, Harman D.

J Am Geriatr Soc. 1976 Jul;24(7):301-7. **Free radical theory of aging: effect of dietary fat on central nervous system function.** Harman D, Hendricks S, Eddy DE, Seibold J.

J Am Geriatr Soc. 1977 May;25(5):220-9. **Free radical theory of aging: effect of age, sex and dietary precursors on rat-brain docosahexanoic acid.** Eddy DE, Harman D. "Increasing the peroxidizability of dietary fat has an adverse effect on the function of the central nervous system (CNS) in the rat."

Adv Exp Med Biol. 1989;266:3-15. **Lipofuscin and ceroid formation: the cellular recycling system.** Harman D

Biochim Biophys Acta. 2015 Jun-Jul; 1847(6-7):514-25. **Increased reactive oxygen species production during reductive stress: The roles of mitochondrial glutathione and thioredoxin reductases.** Korge P, Calmettes G, Weiss JN.

J Pharmacol Exp Ther. 2001 Nov;299(2):638-44. **Dietary saturated fatty acids reverse inflammatory and fibrotic changes in rat liver despite continued ethanol administration.** Nanji AA, Jokelainen K, Tipoe GL, Rahemtulla A, Dannenberg AJ.

Biol Lett. 2015 Sep;11(9):20150538. **Individuals with higher metabolic rates have lower levels of reactive oxygen species in vivo.** Salin K, Auer SK, Rudolf AM, Anderson GJ, Cairns AG, Mullen W, Hartley RC, Selman C, Metcalfe NB.

Biochim Biophys Acta. 2016 Aug; 1857(8):1116-26. **Mitochondrial reactive oxygen species: Do they extend or shorten animal lifespan?** Sanz A.

PLoS Genet. 2015 Feb 11;11(2):e1004972. **Mitochondrial and cytoplasmic ROS have opposing effects on lifespan.** Schaar CE, Dues DJ, Spielbauer KK, Machiela E, Cooper JF, Senchuk M, Hekimi S, Van Raamsdonk JM.

Neuroscience. 2012 Jan 27;202:326-33. **Effects of diet and behavioral enrichment on free fatty acids in the aged canine brain.** Snigdha S, Astarita G, Piomelli D, Cotman CW.

J Exp Biol. 2005 May;208(Pt 9):1717-30. **Body size, energy metabolism and lifespan.** Speakman JR.

Aging Cell. 2004 Jun;3(3):87-95. **Uncoupled and surviving: individual mice with high metabolism have greater mitochondrial uncoupling and live longer.** Speakman JR, Talbot DA, Selman C, Snart S, McLaren JS, Redman P, Krol E, Jackson DM, Johnson MS, Brand MD.

Crit Rev Biochem Mol Biol. 2013 Nov-Dec;48(6):609-19. **Stress eating and tuning out: cancer cells re-wire metabolism to counter stress.** Stine ZE, Dang CV.

Neurochem Int. 2011 Nov;59(6):922-4. **Prostaglandin E2 produced by microsomal prostaglandin E synthase-1 regulates the onset and the maintenance of wakefulness.** Takemiya T

Am J Physiol Regul Integr Comp Physiol 300: R655–R662, 2011. **Influence of acetaminophen and ibuprofen on skeletal muscle adaptations to resistance exercise in older adults.** Trappe TA, Carroll CC, Dickinson JM, LeMoine JK, Haus JM, Sullivan BE, Lee JD, Jemiolo B, Weinheimer EM, Hollon CJ.

Am J Physiol Regul Integr Comp Physiol 304: R198–R205, 2013. **Prostaglandin and myokine involvement in the cyclooxygenase-inhibiting drug enhancement of skeletal muscle adaptations to resistance exercise in older adults.** Trappe TA, Standley RA, Jemiolo B, Carroll CC, Trappe SW.

Front Physiol. 2013 Jul 17;4:185. **Membrane potential and cancer progression.** Yang M, Brackenbury WJ.

Mech Ageing Dev 16: 345–353, 1981. **Aging: effects on the prostaglandin production by skeletal muscle of male rhesus monkeys (Macaca mulatta).** Young MK, Bocek RM, Herrington PT, Beatty CH.

****