Ray Peat's Newsletter

As low temperature rises with thyroid treatment, the symptoms associated with hypothyroidism will disappear. Broda Barnes, PhD, MD

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Body temperature, inflammation and aging

From the time Carl Fahrenheit made the first mercury thermometers in 1714 until the early 1900s, the average normal adult temperature was 98.6. At present, the temperature of young men averages 1.06 degrees F lower, and that of young women, 0.58 degree F lower (Protsiv, et al., 2020). Another study (Waalen and Buxbaum, 2011) in 18,630 people found even lower temperatures—1.4 degrees lower in men, 1.1 degrees lower in women. Between 1930 and the recent studies, the only other large study involved data from 1971 to 1975, so it's possible that nearly all of the change has occurred in the last 50 years. During this time, the prevalence of many serious diseases has increased, but there is very little curiosity about the possibility that these trends are meaningfully related.

I think there are clear cultural reasons for the lack of interest in lower body temperatures. The old saying, "the brighter the candle burns, the sooner it goes out," is often quoted to people who seem excessively energetic and enthusiastic. A variation of that idea is still common, and taken very seriously—the idea that everyone has only a certain number of heart beats, and that they will live longer if their heart beats slowly. Closer to the candle metaphor, some people argue that we can process only a certain number of calories in a lifetime, and so a slower rate of metabolism leads to a longer life, illustrated by the different metabolic rates and life-spans of mice and elephants.

In 1928, a book (*The Rate of Living*) by Raymond Pearl, a genetic determinist and Johns Hopkins University professor, gave this popular idea the appearance of science, claiming that the maximum life span is inversely proportional to the basal metabolic rate. One of his famous examples was that, when seeds are sprouted in a saucer, the one that grows fastest dies the soonest. In the absence of the nutrients of soil, it's obvious that the seed's stored nutrients will limit the extent and duration of its growth, but that has nothing to do with aging—it's just an extension of the candle metaphor, with the seed endosperm playing the role of candle wax.

This simple technique of measuring basal body temperature as a guide to determining thyroid function and permitting proper treatment when necessary did not appeal to the medical profession. Apparently some physicians had reservations about a test which might permit patients to arrive at their own diagnoses. Perhaps some had reservations because the test involved no fee.

This idea resonated through the science culture as well as the popular culture for decades, and in 1956 Denham Harman's theory that free radicals produced by mitochondrial respiration

were the cause of aging was just what the "rate of aging hypothesis" needed for another 50 years of acceptance. In the last 20 years, an abundance of data has accumulated showing that the theory is radically mistaken. For example, John Speakman and Martin Brand have published various examples in which basal metabolic rate is proportional to life span (e.g., Speakman, et al., 2004). They showed that a higher rate of oxidative metabolism reduced the formation of harmful random oxidation, as well as being associated with longer life.

A high rate of mitochondrial oxygen consumption produces heat that allows the organism to maintain an optimal body temperature. When the body temperature is lowered, reactive oxygen species such as superoxide increase; mitochondrial production of superoxide increases slightly, elimination decreases greatly (Camara, et al., 2004). The slower oxygen consumption at lower temperatures shifts the redox of the system toward an excess of NADH, while HIF and cytokines are increased in hypothermia (Toriuchi, et al., 2020; Lee, et al., 2019; Albrecht, et al., 2012; Peyssonnaus, et al., 2007.)

The doctrine that the organism is a machine defined by a blueprint in the genes has been associated with a "wear and tear" theory of aging since August Weismann's time. He argued that the "germ line" is immortal, and the soma, the body, is mortal in the sense that it lacks the ability to renew itself. He was thinking of extrinsic causes of damage, such as infections, rather than intrinsic causes such as free radicals, but the idea of immortal genes producing a machine-like mortal body necessarily leads to the belief that damage to the machine will inevitably accumulate.

However, when the organism is seen as a constant process of adaptation, rather than as a machine that has to get along with the parts that were formed in early youth, metabolic energy is recognized to be a constructive thing, and things that reduce our energy—such as a decrease of body temperature—are seen as threats to life and successful adaptation.

Our body temperature is maintained by the rate of energy production, and that's mainly the result of the oxidation of fuels by mitochondria. The depth of the burning candle metaphor in our culture, and the belief that free radicals produced by mitochondrial respiration are the main cause of the changes occurring in aging, have led to a fear of things that increase our oxygen consumption and raise our body temperature, such as caffeine, and to a reverent attitude toward antioxidants such as vitamin C, and things that lower our oxygen consumption and body temperature such as serotonin, nitric oxide, and estrogen.

In the 1930s, it was known that thyroid hormone increases the metabolic rate and raises the body temperature. Since serum cholesterol decreased in proportion to the increase of metabolic rate by thyroid supplementation, it was suggested that measuring cholesterol could be used to diagnose hypothyroidism. In the early 1930s Broda Barnes went to eastern Europe where hypothyroidism was endemic, and found that the three outstanding health problems in the area were infectious disease, heart disease, and breast cancer. When he later became a physician, he incorporated this knowledge into his practice, and through his career demonstrated that supplemental thyroid cleared up chronic or repeated infections and prevented death from heart disease. He also observed that anemia was often remedied by raising the body temperature. His work showed the value of keeping the body temperature close to the normal 98.6 F or 37 C .

When the pure substance thyroxin became available and displaced the use of powdered thyroid gland to treat hypothyroidism, it led to two very important misconceptions that were incorporated deeply into the practice of medicine. It was decided that no more than 5% of the population was deficient in thyroid hormone, and experiments were used to argue that thermogenesis and increased metabolic rate and oxygen consumption weren't important effects of the hormone, because the liver was the only organ that increased its oxygen consumption when thyroxin was added, and because added thyroxin *decreased* the brain's oxygen consumption.

The error was in defining thyroxin as the thyroid hormone. The liver is the main organ that converts thyroxin into the active thyroid hormone, triiodothyronine, T3, so it was able to respond metabolically to thyroxin. In the brain, with a limited ability to activate thyroxin, an excess

interfered with the T3 already present before the brain tissue was isolated. The current, and strongly enforced, "official" medical standards instruct doctors to disregard temperature, metabolic rate, and symptoms when evaluating thyroid status.

The reaction against Broda Barnes' use of temperature to diagnose hypothyroidism was partly motivated by the belief that a subnormal temperature is protective. This deep belief has probably contributed to the official preference for use of the relatively inactive thyroxin rather than the thermogenically active thyroid, USP, and T3, and to the lack of interest in the association between hypothermia and chronic infections, heart and circulatory problems, kidney disease, chronic inflammatory disease and other problems that increase with aging.

The higher rate of oxygen consumption that occurs at higher body temperature corresponds to a high rate of carbon dioxide production, and an inhibition of lactate formation, with maintenance of a more oxidized balance that reduces inflammation. The beneficial effects of high altitude on health and longevity (Zubieta-Calleja, 2017; Simeonov and Himmelstein, 2015; Ghahramani, et al. 2011) have been known for a long time, and it's now known that high altitude increases the metabolic rate (tending to prevent obesity) and the level of thyroid hormone in the blood, especially the active T3. In one study (Alhazmi, et al., 2018), T3 was four and a half times higher in people living at a high altitude, T4 was about three times higher, and TSH (a promoter of inflammation) was reduced by more than 25%. The high altitude studies show very convincingly that a high metabolic rate is strongly associated with greater longevity and better health.

Besides the misinterpretation of thyroid physiology, probably the biggest muddle in biological doctrine is the interpretation of the decline in temperature at menopause. Younger, cycling, women have slightly higher average temperatures than men and postmenopausal women. Because of advertising, menopause has been defined as the failure of the ovaries to produce estrogen; the definition created an enormous market for estrogen replacement treatments.

When women cycle, their ovaries produce very large amounts of progesterone, and progesterone causes a sharp increase in temperature. Estrogen antagonizes progesterone's functions, including its thermogenic effect. In rat studies, within a week of removing their ovaries, their serum estrogen level has returned to normal, because all parts of the body produce estrogen. When the menstrual cycles stop, the ovaries stop producing progesterone (while all parts of the body keep producing estrogen), with the result that the body temperature falls, becoming similar to that of men of the same age. Estrogen independently causes vasodilation and increased heat loss (Charkoudian, et al., 2017). Estrogen, in a variety of ways, lowers body temperature (for example, Laudenslager, et al., 1982; Baker, et al., 1994).

Starting suddenly around the time of menopause, cortisol is higher, probably as compensation for the lost stabilizing effects of progesterone, and the increased inflammatory processes resulting from lower body temperature. Aromatase, the enzyme that produces estrogen, is present in muscles, fat, blood vessels, and many other tissues, and its activity is increased by cortisol, and decreased by progesterone. The changed activity of these two steroids at menopause can account for the sudden increase in the degenerative diseases, inflammation, depression, etc. Atherosclerotic blood vessels and osteoporotic bones contain increased amounts of aromatase; the increased aromatase corresponds to increased extracellular matrix and the development of fibrosis. Bright light, which is thermogenic Danilenko, et al., 2013), suppresses the level of cortisol (Jung, et al., 2020).

Thousands of publications have tried to explain all the unpleasant effects of aging in women as the result of a deficiency of estrogen, trying to justify the sale of estrogen supplementation to treat the degenerative processes that are closely associated with the increased aromatase and local production of estrogen.

Respiratory and circulatory problems increase with menopause, corresponding to increases in inflammatory cytokines and cortisol, and decreases in progesterone and thyroid hormone. Both thyroid and progesterone are thermogenic, and lower estrogen levels. Atrial fibrillation incidence doubles after menopause, and produces increasing mortality with aging. It has been

described as an epidemic (Lábrová, 2008; Ball, et al., 2013). It can be predicted by a prolonged QT interval on an electrocardiogram, which indicates a retarded restoration of cell energy after a contraction, and involves slowed conduction of the signals that are necessary for coordination of an organized heart rhythm. A similar effect of hypothermia is seen in the brain, with the ability to remember and to reason varying with temperature. The QT interval is prolonged by hypothermia, hypothyroidism, and by estrogen, and normalized by progesterone and thyroid function. The standard treatment for atrial fibrillation is destruction of part of the conduction system of the heart, called ablation, which costs more than $25,000 in the U.S., and results in a very high percentage of heart failure. Correction of the problematic prolonged QT interval with thermogenic agents such as progesterone, thyroid, and aspirin (Korkmaz-Icöz, et al., 2016) isn't of interest to the profession.

Asthma, allergies and anaphylaxis increase after menopause, with a shift of cytokines toward increased inflammation. These inflammation promoting effects of estrogen have been recognized, but the knowledge hasn't had much effect on the medical use of estrogen. The dogmatic insistence that menopause is a state of estrogen deficiency, and the general lack of interest in body temperature, have made it impossible to publish more than warnings that estrogen supplementation can make menopausal asthma worse. A lower body temperature increases asthma symptoms (Horton and Chen, 1979; Chen and Chen, 1982).

The extent of hot flashes in menopause corresponds to the presence of inflammation and later, to the development of heart disease. Body temperature has been measured before, during and after menopausal hot flushes. Sweating and reddening of the skin are mechanisms for dissipating heat, so it isn't surprising that the body temperature decreases quickly during the hot flush. Nitric oxide is involved in skin vasodilation, and estrogen increases nitric oxide in blood vessels of the skin. In the skin, progesterone's thermogenic effect involves vasoconstriction (Charkoudian and Stachenfeld, 2016).

To avoid thinking about estrogen's possible role in the hot flash, many doctors prefer to insist that the episodes are the result of an increase in core temperature activating an unstable temperature regulating system.

Probably because of aspirin's anti-fever effect, the medical culture tends to think of it as antithermogenic, despite its known stimulation of mitochondrial oxygen consumption. Like thyroid hormone, aspirin prevents stress-induced loss of sodium, which is an important part of our temperature and energy regulating system. Physicians usually prescribe acetaminophen (also called paracetamol and Tylenol), which is hypothermic, instead of aspirin. Nutritional thermogenic factors include sodium, calcium, vitamin D, carbohydrates, especially sugar, and protein, which interact with our endogenous energy regulating factors, especially thyroid and progesterone.

Things that decrease energy and body temperature increase some essential mediators of inflammation, and those changes are deeply associated with the processes of aging. A diet high in polyunsaturated fatty acids creates hypothermia and promotes torpor in animals before hibernation (Ruf and Arnold, 2008), and a high ratio of PUFA to saturated fats in the diet is associated with a shorter lifespan. For example, in mice on a calorie restricted diet, those receiving the more saturated lard lived longer than those receiving fish oil or soybean oil (López-Domínguez, et al., 2015).

Inflammation is a kind of adaptive response, but it leaves behind some fibrotic changes and atrophy of functional cells, along with an increased tendency to resort to the inflammatory response. Part of this cumulative inflammatory tendency can be seen in the increase with aging of inflammatory cytokines, especially IL-1, IL-6, TNF, and a decrease of antiinflammatory cytokines such as IL-10, and increases of other inflammation promoting peptides such as angiotensin, parathyroid hormone, and CRP.

Many of the changes caused by daily stresses are reversed during deep slow wave sleep. The amount of slow wave sleep is decreased with aging. A few animal studies have found that artificially extended sleep reversed some of the major problems of old age. Progesterone is able to increase the amount of slow wave sleep, probably because of its effect on body temperature—warm baths, warm climate, and exercise as well as

endogenous thermogenesis all increase slow wave sleep (Caufriez, et al., 2011; Raymann, et al., 2008; Fronczek, et al., 2008; Jordan, et al., 1990).

A combination of energy-promoting factors that increase body temperature and increase deep sleep seems like a reasonable approach to extending the healthy life span.

Although carbon dioxide causes vasodilation in the skin, increasing heat loss, it raises body temperature, by increasing heat production more than the amount lost (Schaeffer, et al. 1975). Like progesterone, increased CO2 increased slow wave sleep (Wang, et al., 2011).

If longevity is shortened as a result of the accumulation of changes resulting from inflammatory adaptations, then living in different environments, requiring different kinds of adaptation, will cause major changes in lifespan. The genetic determinists have insisted that there is an intrinsic maximum human lifespan of 100 to 110 years, and that although caloric restriction can extend the average lifespan, by slowing the "burning of the candle," it doesn't change the maximum lifespan, and that claims of greater longevity (especially without caloric restriction) are necessarily false.

One of the best documented long lives was Old Tom Parr in England, who was taken to London at the age of 152 in 1635 to meet the king. All his major life events were recorded by the church. His normal diet was said to be old bread and cheese rinds. More recently, several areas with a high proportion of very old people have been noticed; these were in areas where the church kept accurate records of births, marriages, and deaths. In 1922, a professor of physical chemistry from the University of Kiev, Dr. Sadowein, reported that in the village of Derbent in the Caucasus, 20 people, in a population of 120, were over 100 years old. Their diet consisted almost exclusively of bread and fermented cow's milk, with some sheep cheese. In other high altitude areas, such as the Andes, the use of sheep's milk is very common, along with a high percentage of old people. Milk, calcium, and vitamin D are important thermogenic factors (Melanson, et al., 2003; Zemel, 2005). Exposure to bright sunlight, besides producing vitamin D, is thermogenic, increasing oxygen consumption.

Calcium itself has powerful anti-inflammatory effects, but milk also contains a variety of protective anti-inflammatory peptides, and there is some evidence that fermentation produces additional anti-inflammatory peptides. Although a milk based diet could account for much of the health benefit of high altitude, even in the U.S. where the diet doesn't differ much in higher altitude cities, there is a significant improvement of health and longevity at higher altitudes. In two large cities in Bolivia, each with a population of about 2.7 million (Santa Cruz, altitude 416 meters, La Paz, about 3800 meters), the city at moderate altitude has 6 people of at least 100 years, while the higher city has 48 (Zubieta-Calleja, 2017).

Altitude and a milk based diet are obviously two important thermogenic factors that slow the accumulation of harmful adaptations, but there are many other controllable factors that could extend longevity even more. Reducing inflammatory factors is important, and personal choices can make a big difference, for example choosing easily digestible foods to reduce endotoxin, avoiding the polyunsaturated fatty acids that interfere with cell respiration and form inflammatory prostaglandins, avoiding antioxidant supplements that create a reductive excess, and choosing foods that contain antiinflammatory-thermogenic compounds, such as citrus fruits with their high content of flavonoids that support cell respiratory functions.

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