Age Pigment: Cause and Effect of Aging and Stress

From the original article. Author: Ray Peat.

I have written about the many toxic effects of unsaturated oils, estrogen, and excess iron, and how each of these contributes to certain features of aging and age-related degenerative diseases. Now I am going to discuss *some of the ways those toxic effects converge,* creating a new, "terminal toxin," and how some of the features of aging can result from the presence of this toxin. Rather than using the vague idea of "free radical damage," I think I can show a simple mechanism by which the terminal toxin, lipofuscin, produces the essential features of aging. I suspect that familiarity with this mechanism will be a necessary step in understanding how the high-energy cellular state of youth can be restored.

The word, "lipofuscin," is coming into common usage, so it is worth knowing that its root meaning is "dark fat." The root, *fuscus,* occurs in the word obfuscate, to obscure. Biologists, who know about the dye called fuchsin, which has nothing to do with lipofuscin, often confuse the words and mispronounce lipofuscin.

In pointing out how oils, estrogens, and iron contribute to aging, I don't mean to distract from their *specific* toxic effects **;** rather, those specific effects become more harmful as the organism is weakened by aging.

Lipofuscin, ceroid pigment, age pigment, and liver spots all describe approximately the same thing, though each researcher tends to insist on certain idiosyncratic distinctions, because there is still hardly a "scientific culture" of averaged-out terms and concepts. This is a strange situation, since the substance has been studied occasionally since the first report in 1842, making it scientifically about as old as organic chemistry itself. In 1954, I asked my biology professor (who was in his sixties) what he thought the cause of aging was, and he said some people believed that it was the result of the accumulation in cells of insoluble metabolic by-products, called "metaplasm." His remark was in my mind later when I watched an amoeba dividing under the microscope **;** it seemed to have become sludgy, viscous, and lethargic, and then as it divided, the new cells appeared to be moister and more elastic, as if they had diluted some kind of ballast that produced internal friction.

In 1954 there was a report of a girl whose skin turned black from using an ointment containing estrogen. Later, in the 1960s, I noticed that many women using birth control pills developed patchy brown spots on their faces. As I read more about pigmentation, I saw that estrogen, like a variety of irritants, promoted the development of ordinary dark pigment, melanin, in the skin, and that this was different from the liver spots or age pigment that often begin to appear in middle age, and that become so noticeable on the hands, arms, and faces of most old people. As it turns out, both types of pigment are produced by oxidation of smaller molecules which causes them to coalesce into complex masses, but at that point the difference becomes total. Melanin protects against further oxidative injury, but lipofuscin tends to promote further injury. Later, I learned that estrogen was implicated in the production of age pigment, at least in the uterus. (Atkinson, et al., 1949; Kaunitz, et al., 1948.)

Another kind of pigmentation, that is sometimes seen in the skin around the eyes, has been found to contain substances derived from hemoglobin. The heme/porphyrin pigments are interesting in relation to aging, not just because estrogen is known to be involved in the overproduction of the porphyrins, but because lipofuscin has been reported (Bjorkerud, 1963, 1964) to contain the heme group, and because the metabolites of heme (the bile pigments, With, 1968 **;** pyrroles, Figge, 1945) have been associated with cancer. (As I have mentioned elsewhere, the metabolism of heme produces carbon monoxide, which could produce a self-sustaining respiratory defect.)

That estrogen should have a role in three different types of pigmentation is interesting. What common feature is there in the physiology of these pigments that relates to estrogen?

(Some sources describe a syndrome--Sprinz- Nelson/Dubin-Johnson syndrome, or maverohepatic icterus--that supposedly involves the accumulation of all three pigments--melanin, porphyrin, and lipofuscin--in the liver. The simultaneous formation of different types of pigment might account for some of the disagreements in the study of lipofuscin.)

Melanin is produced in the skin under the influence of ultraviolet light, and in the brain's substantia nigra, it is believed to be produced in relation to a free-radical-generating cycle of dopamine metabolism. Since melanin is an effective antioxidant, it is assumed that its formation represents a defense against free radicals. In the skin, ultraviolet light's primary "target" appears to be the polyunsaturated fats, in which it produces free radicals. *Estrogen--especially when it has been changed into the catecholestrogen form--is known to participate in futile cycles of oxidation-reduction, with the production of free radicals.* In 1972, I demonstrated that estrogen powerfully promoted the reduction of the dye, TTC, possibly by such a free-radical mechanism.

Lipofuscin is produced by the over-feeding of unsaturated fats (such as fish oils, B. G. de Gritz and T. Rahko, Gerontology 42, 1995) and the underfeeding of vitamin E, relative to the amount of unsaturated oils (Hartroft and Porta, 1967). Ultraviolet light, iron, and aluminum promote its formation, apparently by the production of free radicals. The free radicals generated by estrogen, and by estrogen's promotion of iron absorption, would contribute to the lipid peroxidation. Stress, which is known to intensify free radical production, also accelerates the production of lipofuscin. (Chaudary, 1995.) I have found that *estrogen* (Peat, 1972) *induces cellular conditions that resemble those produced by x-rays and carcinogens* (Devik, 1963), *and which probably reflect the production of superoxide or other radicals.*

Porphyrins are known to be produced under the influence of estrogen, but anything which interferes with cellular respiration appears to stimulate their production, as part of a mechanism of adaptation to oxygen deficiency that leads to the production of more hemoglobin. Lipofuscin itself contains the heme group, and wastes oxygen in a sort of short-circuit between NADH and oxygen (NADH-oxidase, Bjorkerud, 1963; Strehler, 1967). *This is also one of estrogen's important effects.*

While the formation of melanin seems to be one of the healthy responses to free radicals, and is governed by an enzyme

system, lipofuscin seems to be produced nonenzymically, directly by the damaging free radical process itself, and the porphyrins are apparently an adaptive response to oxygen deprivation, rather than to an excess of free radicals.

There would seem to be a sequence of events. If the antioxidant defenses, including melanin formation, are inadequate, then lipofuscin would be formed. If the consumption of oxygen by lipofuscin is sufficient, the heme-synthetic pathway would be activated.

One of the reasons for the lack of interest in lipofuscin has been the doctrine that it is nothing but a little harmless "extra baggage" the cells have to carry, that couldn't account for all of the changes that occur in aging. "Somatic mutations" have been offered as an explanation for the age-related increase of cancer, atherosclerosis, diabetes, arthritis, autoimmunity, and even for the metabolic slowing that is characteristic of aging. The basic doctrine of aging, held by those in power, has been that, since it involves a generalized slowing of most biological processes and loss of precise regulation, and since the "genes" are held to control all cell processes, the essential changes must happen in the nucleus. Lipofuscin occurs in the cytoplasm, and sometimes is found outside of cells, so its role "must be passive," according to that mainline doctrine.

But exactly the opposite view--that the crucial changes that accompany aging occur in the cytoplasm--fits the evidence more accurately.

For example, there is a steady **dehydration** of tissues with aging, and a **slowing** of metabolism. The ability to tolerate stress decreases with age, and chromosomes seem to be easier to damage, and slower to be repaired. According to S.J. Webb, the cell's "bound water" protects against radiation-induced mutations. Since DNA repair is a process that consumes energy, the lower metabolism and low energy production which result from dehydration could lead to an accumulation of mutations. But no one has ever proposed that mutations cause the steady dehydration that occurs with aging. (The dehydration, I think, is most likely a defensive reaction of cells, maybe involving the heat-shock/stress proteins, to preserve the cells' domain of control over their metabolic water, under conditions of limited energy production. I think this resistance against the uptake of water helps to maintain the differentiated state, and to prevent uncontrolled growth.)

If the cell's ability to *retain* water is partly dependent on ATP, as Gilbert Ling has shown, then interference with energy production could cause the dehydration, in a vicious circle. If lipofuscin interferes with the cell's energy production, or ability to retain water, then it is in a position to create some of the characteristic features of aging. In S. J. Webb's studies of bound water, he found that inositol protected cells by helping them to retain water. His studies are especially interesting, considering Lehninger's observation that "mannitol, or other polyhydroxylic solutes" cause mitochondrial swelling, or inhibit their contraction. [Mannitol is a straight-chain analog of inositol.] (Pages 188-191, *The Mitochondrion,* 1964.) Thyroxin also causes mitochondrial swelling.

In Ling's view, ATP causes cells to retain water in a tightly organized form, and when ATP is seriously depleted, adsorbed potassium is released to become osmotically active, and sodium and chloride enter along with water, which is then in the "loosely held" state of normal bulk water, lacking the special properties of water that had been dominated by polymer surfaces. This swelling has been called "depolarization swelling," and is partly responsible for the swelling of injured or dying cells. Presumably, less drastic energy changes will cause physiological changes in the amount of *organized water* , in which water is usefully retained in proportion to the energy level.

While rodents live a year or two--and die in a much more hydrated state than people or animals that live approximately a century--at the end of a rodent's normal life span its cells (e.g., brain and heart) contain as much lipofuscin as the cells of century-old people do. Dogs accumulate lipofuscin about 5.5 times as fast as people do, and people live about 5.5 times as long as dogs. **This is just what we might expect if lipofuscin is the "terminal toxin."** Loss of cell water would have an influence, but wouldn't be the decisive factor. (The total amount of water in a cell doesn't matter so much, if the energy-producing and functional parts of the cell are deenergized and dehydrated, impairing the cell's responsiveness and adaptability.)

Besides energy production, probably the cell's most basic mechanism of adaptation is the alteration of its structure, which is going on constantly, with the production of new proteins and the destruction of old proteins. This "protein turnover" slows with aging, and the change is mainly on the side of decreased ability to break down old proteins. **Lipofuscin directly inhibits the proteolytic enzymes which break down proteins.** Unsaturated fats have a similar action, even when they aren't noticeably converted into lipofuscin **.** They inhibit mitochondrial energy production, which obviously could affect synthetic processes, but it has been known for many years that they also inhibit proteolytic enzymes, although this information tends to be familiar only within certain contexts, such as food chemistry, clot chemistry, immunology, thyroidology, etc.

The mitochondria are continually being repaired and replaced. Inhibition of proteolytic enzymes will cause their repair and replacement to lag, with the result that these crucial energy-producing organelles will "age."

There is evidence indicating that lipofuscin forms in lysosomes and as degenerate mitochondria. With a mitochondrial origin, heme would be present because there are heme-containing enzymes in the mitochondria, but any lipofuscin forming primarily within lysosomes could also absorb heme-like groups from other sources.

It is the heme group which gives the lipofuscin particle the NADH-oxidase function, described by Bjorkerud. **Measured in a respirometer, lipofuscin granules respire similarly to mitochondria, except that they do not produce any ATP.** As a result, a large amount of lipofuscin will compete with mitochondria for the oxygen which is available to the cell, and will also consume the energy that is available as NADH, and will lower the cell's ability to produce ATP and to function.

When mitochondria are activated, they swell. The swelling-contraction cycle of normal activity is relatively slight. Another kind of swelling, associated with lipid peroxidation, is more extreme, and leads to the destruction of the mitochondria. (Iron, excess unsaturated fats, and many other substances that react with sulfhydryl groups--incuding glutathione--can cause this

kind of swelling.) For every molecule of oxygen consumed by cytochrome oxidase, two molecules of water are produced. If lipofuscin is consuming the oxygen, it will produce the water, and the underfunctioning mitochondrion will produce neither ATP nor water, as a consequence of inadequate oxygen. Lipofuscin, therefore, will tend to dehydrate the mitochondria. Anything that inhibits respiration seems to inhibit the physiological swelling. Besides the small contribution of metabolic water, there are probably physical processes associated with respiration that govern mitochondrial water content.

Mitochondrial activation is associated with swelling, and extreme mitochondrial dehydration very likely represents a failure to produce energy effectively, and I suspect tends to cause the destructive collapse of the organelle. But elsewhere in the cell, the vicinity of the lipofuscin will tend to become hydrated, and this wouldn't be subject to the regulating effect of ATP.

Estrogen's early effects include activation of dehydrogenases and peroxidase (Jellinck and Lyttle, 1971 **;** Talalay and Williams-Ashman, 1958; Temple, et al., 1960), and it participates in the interaction of NADH and NADPH as well as in the oxidation of NADH (Beard and Hollander, 1962, Hollander and Stephens, 1959; Yokota and Yamazaki, 1965; Lucas, et al., 1955; Villee, et al., 1965). The oxidation of NADH is involved in many harmful free radical processes. (McCay, 1971, an early study, but recently others have been published.) The most visible early effect of estrogen is to stimulate water-uptake by the cell. How it causes this immediate swelling isn't known, but it probably involves this consumption of oxygen, since simply cutting off the cell's supply of oxygen also causes water-uptake and edema. (Maybe ATP is needed to "extrude" water from the cell generally, as it is in the mitochondria.) The oxidation of NADH tends to raise the pH of the cell, and by increasing the electrical charge of the proteins this would be likely to cause swelling. I suspect that the normal (respiratory) function of oxygen is to adjust the electrical charge of the cell proteins, in a way that favors ATP synthesis and controls hydration. ATP (which is an acid, and is strongly adsorbed to proteins, influencing their charge) is known to cause swollen mitochondria to extrude water.

Although the exact meaning of the NADH-oxidase NADH-peroxidase activities isn't known, it is interesting that they are so strongly affected both by estrogen and by lipofuscin. **Whatever else these enzyme-functions do, they waste oxygen and consume the cell's energy, producing free radicals in the process.**

Unsaturated fatty acids have a higher affinity for water than saturated fats do. In the presence of water, they swell. To isolate functional mitochondria, it was discovered that hypertonic sucrose stabilized the mitochondria, apparently by opposing a strong tendency to swell. But when animals are fed a diet rich in unsaturated fats, the mitochondria have a lower swelling tendency than do those of animals that are "deficient" in polyunsaturated fats. This is the opposite of what might be expected from the physical behavior of the unsaturated fats, so the difference probably involves the metabolic activity of the mitochondria, rather than their physical chemistry. (**"...the active swelling stimulated by respiration has a high temperature coefficient, which is consistent with a chemical or enzymatic process...."** Lehninger, pages 184-185.) **For one thing, the unsaturated fats simply block respiration by blocking the electron transport chain, and by inhibiting cytochrome oxidase.** In fetuses and young animals up to the time of weaning, one site of the cardiolipin molecule, which is essential for cytochrome oxidase function, contains the saturated fat, palmitic acid. After that, as the animal's respiratory activity declines, the palmitic acid is replaced by linoleic acid. At the same time that respiration is being inhibited by the unsaturated fats, lipofuscin begins to accumulate, further interfering with respiration, by consuming oxygen outside the mitochondria.

When fed a diet high in unsaturated fat and low in vitamin E, lipofuscin forms rapidly, and the incidence of cancer and other diseases of aging--including diabetes--increases greatly. (Regarding glucose metabolism, Barnard, et al., 1995 **;** many more references are given in my article on diabetes, scleroderma, and oils.)

It is interesting that the first publication identifying dietary fat as an essential cause of cancer (1927) appeared almost at the same time as the demonstration (Pinkerton, 1928, cited by E. A. Porta, et al., 1987) that a substance resembling lipofuscin could be produced by bubbling oxygen through unsaturated fat (fish oil). Various types of unsaturated fish or seed oils have since then been used to produce lipofuscin *in vivo* and *in vitro*.

Hartroft and Porta (1967) demonstrated that the pro-oxidant metals, especially iron, accelerate the formation of age pigment, and recent experiments confirm those observations. (Zs.-Nagy, et al., 1995.) Aluminum and silicon, which have a role in brain and blood vessel aging, also have a role in the formation of age pigment. (Tokutake and Oyanagi, 1995.)

My observations of extracts of aged tissue, soaked in ether or pyridine, showed an absorption spectrum in the ultraviolet frequencies that indicated the pigment was a complex mixture with unsaturated fats, but with the specific absorption indicating the presence of heme or related material.

When artificial lipofuscin, made by ultraviolet irradiation of mitochondrial preparations, is added to cell cultures, the cells act as if they had aged suddenly, and then die. (von Zglinicki, et al., 1995.)

Similarly, when mitochondria are extracted from old cells, and injected into young cells, the young cells behave as if they had aged.

One of the remarkable things about the NADH-oxidase described by Bjorkerud is that it is cold-inactivated. I have argued (Peat and Soderwall, 1971, 1972) that estrogen activates enzymes of this type, but a mere excess of water could have a similar function, and if these granules produce their own water, **they will tend to support the condition which activates themselves, while also tending to decrease the metabolic activity of mitochondria.** Where the water is being produced, there is a lack of ATP, and where the ATP is being produced, there is a limiting lack of oxygen. While estrogen causes cells to take up water immediately, before any other cellular change is seen, my argument has been that it makes the cellular water more "bulk-phase" like, with less of the structure (vicinal water) evident in water near surfaces **;** this argument is based on NMR studies of water in tissue treated with estrogen (Peat, 1972). The damaging effects of estrogen on mitochondria (Gonzales-Angulo, et al., 1970), in this view, might be the result of changing enzyme activities by

affecting water structure, as well as of causing a redistribution of water between cellular organelles.

Estrogen causes changes in collagen synthesis that resemble changes occurring in aging (Loeb, et al., 1939 **;** Henneman, 1968) and in oxygen deprivation (Chvapil, et al., 1970). The theory that cross-linking (hardening) of collagen causes aging is popular (e.g., Kohn, 1971), but it seems odd that the idea of interactive factors in hypoxia--estrogen, collagen, and lipofuscin--hasn't been of greater interest. ***Hypoxia*** (Goldfischer and Bernstein, 1969), ***radiation, and stress*** (lipofuscin accumulation with restraint stress **:** Chaudhary, et al., 1995) ***like estrogen, cause accumulation of collagen and lipofuscin,*** and lipofuscin contributes to hypoxia and stress. The fact that puberty in girls is accelerated by unsaturated fats, and delayed by their deficiency, is just one of the many indications of the close connection between estrogen and the unsaturated fatty acids.

The doctrine that radiation causes cancer simply by causing mutations has grown up in the scientific culture that has paid essentially no attention to lipofuscin. All sorts of ionizing radiation produce free radicals in unsaturated oils, and so naturally radiation will contribute to the formation of the age pigment. In the depleted, low energy state that develops when a large amount of lipofuscin has accumulated, chromosome damage will occur, and will not be repaired as it is in the youthful high energy state. *Mutations in themselves don't cause aging* (Curtis, 1963 **;** Kohn, 1971,* see quotation at end), *but aging creates a disposition for mutations to accumulate*. (It was found that men who exercised before breakfast produced large numbers of chromosome breaks. The energy provided by breakfast made a visible difference in the amount of chromosome damage produced by exercise. The chronic low energy state that results from being full of rancid fat must amplify the damage done by ordinary stress.)

Minimizing radiation, of course, is important, and if we aren't primarily worried about radiation as a direct mutagen, the comforting thought of a "threshold of safety" disappears. The same principle applies to the avoidance of environmental toxins (so many of which are estrogenic), since the factors that promote age pigment all seem to be additive. **The age pigment is a final common pathway in which many types of damage converge,** in the way many different factors converge in the drying of paint. By depleting the cell's energy, lipofuscin accumulation causes trivial challenges to become increasingly harmful, in a vicious circle that tends to accelerate the production of lipofuscin.

Some of the factors that significantly accelerate the formation of lipofuscin--dietary polyunsaturated fats, deficiency of vitamin E and selenium, and excess iron--are things that can be manipulated without great effort. Some of the proven factors that retard its formation, such as a low calorie diet, are not so easy to sustain, and require some study.

If a "program in the genes" controlled the rate of aging, dietary modification should make no difference at all, but calorie restriction slows the rate of aging, as it slows the rate of lipofuscin formation. (C. M. McCay's experiments in the 1930s, 1952 **;** W. A. L. Moore, et al., 1995.)

The doctrine of "programmed aging," and the Hayflick doctrine, maintain that cells have an innate capacity to undergo about 50 divisions, and that "aging" consists of having used up their limited capacity for division. It is clear that the medium in which the cells are cultured affects their ability to multiply, and that serum from old animals slows their growth. The experimental data from human cells cited by Hayflick oddly fail to support his theory. For example, cells from a sick 87 year old person underwent 29 divisions in culture, and those from a 26 year old person killed in a car accident were able to divide only 20 times in culture. Cells from a single individual, in different (repeated) cultures show very different "limits." (Williams, et al., 1987.) The appropriateness of the culture medium for the particular needs of the cells seems to be the issue, and all cells do have a "memory" or "program," reflecting their developmental state and function. Because of this cellular memory or inertia, a damaged condition might be passed on to daughter cells, and even to a subsequent generation or two, before full vigor can be restored. Historically, these "lingering effects" of the environment have been called "dauer-modifikationen." I believe our present level of pollution, by this sort of lingering effect on development, is going to produce an increasing incidence of birth defects, immunodeficiency, accelerated aging, and cancer, if biological remedies aren't found to neutralize its effects. The harmful effects of estrogen--DES, for example--persist for generations. Besides the hundreds of estrogenic chemicals accumulating in the environment, medical estrogen has been prescribed for approximately 200 stupid purposes. Harvard Medical School lent its prestige to the deadliest and most anti-scientific of these promotions, and government agencies have endorsed the fools and colluded with the criminals. Similar medical/industrial/governmental conspiracies have operated in many other areas, notably in the use of iron and seed oils.

The Possibility of Remedies

There is evidence that cells can clear themselves of lipofuscin, but the mechanism isn't understood. As a result of low oxygen tension in the fetus, lipofuscin appears, but then disappears after birth. The composition of this material could be different from the material that develops later, but the greater metabolic activity of the newborn is probably related to the ability of cells to destroy it or to excrete it. Recently, it has been proposed that a variety of psychotropic drugs promote its excretion (Riga and Riga, 1995), but most of those drugs have serious side effects. In cultured brain cells, it was found that vitamin E and ethyl alcohol promote its disappearance. Since alcohol's toxic effects largely derive from its interactions with unsaturated oils and iron, a small amound of alcohol might be useful in clearing lipofuscin. I have often seen topically applied vitamin E with progesterone remove age spots from the skin. In younger (age 45 to 55) women who have developed the spots while using estrogen, the spots sometimes disappear when they stop using estrogen. In much older people, the use of vitamin E and progesterone has sometimes only caused the spots to slowly become lighter, during several months.

Since lipofuscin contains proteins and metals as well as fats, it has been suggested that activation of proteolytic enzymes would facilitate its removal, but it is partly the inhibition of proteolytic enzymes by lipofuscin that makes it a difficult problem. The low calorie diet which delays the formation of lipofuscin is known to increase the activity of proteolytic enzymes, and I think this is largely the result of reduced exposure to unsaturated fats. According to the Shutes' research, vitamin E facilitates the clearing of blood clots by activating proteolytic enzymes. At the time they were doing their research, it was recognized that estrogen and unsaturated fats inhibit proteolytic enzymes. While the heart-disease industry has done a lot of pharmaceutical research on the regulation of the clotting process, there is much less research on the proteolytic

enzymes which *remove* clots. The Shutes introduced the issue more than 50 years ago, and I suspect that their observations showing that vitamin E, thyroid, and progesterone protect against heart disease by opposing the clotting effects of estrogen (and unsaturated fats) came too close to saying that the problem can be solved without the help of the great drug industry. A solution for degenerative diseases which shows estrogen and polyunsaturated oils to be essential parts of the *problem* is not one that will find many research grants.

To me, the chemistry of lipofuscin indicates that we should minimize our exposure to unsaturated fats, iron and other metals, and estrogen, while cautiously exploring the ways to prevent their cumulative damage. Since many things promote oxidation in one context and inhibit it in another, caution is important in exploratory research. Copper, for example, can cause harmful oxidation, but it is required for melanin synthesis, superoxide dismutase, cytochrome oxidase, and other enzymes, and its deficiency leads to intense oxidative damage from iron. When there is clear evidence that a particular form of copper is safely assimilated, it might be a desirable food supplement. At present, I think mollusks and crustaceans are the safest sources of copper.

Many "antioxidants" that are being promoted for medical/nutritional use are seriously toxic, even mutagenic or carcinogenic. The "adaptogen," mildronate, protects mitochondrial ATP production by restricting the oxidation of long-chain fatty acids. This type of antioxidant seems to reinforce natural protective processes (Meerson, 1991), and is not likely to have the toxicity of the phenolic, or polyphenolic, antioxidants. Other particular therapies for aging might include direct restoration of ATP and hypoxic (high altitude) adaptation to stimulate the regeneration of mitochondria.

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Currently, I think the most important issue is to find foods that are practically free of the polyunsaturated fats. Low fat milk and cheese are suitable, and are desirable because of their low iron content, but are not ideal for an exclusive diet. A supplement of vitamin E and coconut oil should have a significant effect on the rate of aging **:** the effect of coconut oil is to reduce the need for vitamin E, to act as a dilutional chain-breaker in free radical propagatioin, and to provide energy at a high level to repair cell damage. While unsaturated oils contribute to the inlammatory process (and there is serious question as to why evolution would produce the mechanism of inflammation, since its effects on balance seem harmful), coconut oil doesn't, and the inflammatory "eicosanoids" made from the "essential" fatty acids probably contribute to the formation of age pigment in certain situations, such as in atherosclerosis. Since free radicals are produced in the formation of prostaglandins, aspirin and other antiinflammatory drugs have a sort of antioxidant effect, which might explain their apparent role in the prevention of Alzheimer's disease.

The thyroid hormone itself has been found to be protective against lipid peroxidation, and even against radiation damage, and thyroid function is promoted by coconut oil. Proper thyroid function minimizes the production of adrenaline, and adrenaline--like estrogen--increases our exposure to fatty acids. Potatoes and many fruits are fairly low in the unsaturated fats and iron. The ketoacid equivalents of the essential amino acids are found in some plant materials that are very low in unsaturated fats and iron. When the right combination can be found, it would be possible to have varied foods that provided calories, minerals and vitamins, with either protein or a protein equivalent, which wouldn't lead to the accumulation of unmetabolizable fats and metals.

An important, but neglected, aspect of respiration, resulting from proper thyroid function, is the production of carbon dioxide. Carbon dioxide has some remarkable properties, including the regulation of circulation and mineral balance. I believe it probably has a direct role in the production of ATP, and by its physical-chemical effects, it might be an essential factor for activating the enzymes of the lysosomes, which have the capacity to clear age pigment from cells. The effects of diet, hormones, and oxygen deprivation on aging and lipofuscin could be mediated importantly by their effects on the production of carbon dioxide.

An outstanding feature of the "false respiration" of lipofuscin is that it produces no carbon dioxide.

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