Cancer: Disorder and Energy

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> "For every thing that lives is holy, life delights in life...."
> — W. Blake

> "Life is a condition alternating between excitation, destruction and unbalance, and reorganization, equilibrium and rest."
> — Kurt Goldstein

Oncological pathologists, looking at slices of a tumor, believe they can guess when the cells have an evil intention. However, biologists studying living cells find that cells can do only what they are allowed to do by their environment.

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According to the World Health Organization, cancer is now the leading cause of death in the world. Although many "causes" are known, and despite the "War on Cancer," nothing practical has been done to reduce the incidence of cancer. Since Nixon started that war, the number of people dying annually in the US has increased faster than the population. In ancient Rome and Egypt, cancer was rare; cancer has been identified in only one Egyptian mummy. In the US and several other countries, between 2002 and 2005 there was an unprecedented decline (7% in the US) in the incidence of breast cancer, when the medical use of estrogen decreased following the Women's Health Initiative report showing that estrogen caused cancer, dementia, strokes and heart attacks. However, when the public was reassured about estrogen's safety, breast cancer incidence began increasing again each year.

The cancer industry has been flexible and imaginative in ways of presenting "age standardized" death rates to show that they are making progress against cancer, but there are philosophical and scientific problems in "oncology" (i.e., the study or treatment of lumps) that should be considered by anyone who plans to do business with that profession.

In the 19th century (in Johannes Muller's lab), cancers, like other animal tissues, were found to be made up of cells, and by 1858, all diseases were said to be caused by disturbances in cells (Rudolph Virchow). The atomic and molecular theory of matter was becoming accepted at the time that animals were found to be made up of cells, and in both cases the "elementary particles" seemed to have a special power to explain things. This idea of a cellular basis of disease gradually displaced the old idea that diseases were caused by an imbalance of the body fluids, or humors. In 1863, Virchow recognized that inflammation, involving leukocytes, was a common feature of cancer, but that aspect of his work was neglected for a long time.

Recent medical textbooks reveal no major change in the understanding of cancer since Virchow's time, except that "genes" (which weren't known during Virchow's life) gradually became the most important aspect of cells. The typical modern textbook describes the cellular disturbance of cancer as the result of an "initiating" mutation in a gene, which gives it the potential to develop into a cancer, if it subsequently is exposed to a "promoter," which causes it to multiply. In some versions of the theory, a promoter is a second mutation that causes proliferation, but in other versions the promotion is caused by chemicals binding to receptors the way hormones do, to stimulate proliferation. Typically, textbooks (and reports of continuing research) describe subsequent changes in the genes that cause a cancer to progress from a simple excess of cells through stages of increasing malignancy: hyperplasia, dysplasia, carcinoma in situ, invasive cancer.

One of the reasons that the medical understanding of cancer hasn't changed significantly since Virchow's time is that blaming misbehaving cells for causing a tumor fits into the older medical tradition, that has existed at least since the time of Hippocrates, 400 BC, which treated tumors either by cutting them out, or by burning them off with caustics. Virchow's identification of misbehaving cells provided a clear mental image of exactly what the physician must try to destroy. And it's probably hard to get interested in something which could seriously limit your professional activities if it turned out to be true.

The "cellular basis of cancer" was developed simultaneously with the germ theory of disease, and in the case of cancer, the deviant cells came to be considered an alien substance, "not-self," analogous to infective germs. Paul Ehrlich's search for poisons that were specific for bacterial pathogens was quickly extended to the idea of finding poisons that would distinguish between cancer cells and the patient's cells.

Hippocrates' therapeutic approach to cancer may have survived for 2400 years, but the ideas of his younger contemporary, Plato, about order and causation have probably had a greater effect on medicine. Plato believed that the world of experience is inferior and accidental, and that there are timeless "Forms" that are the real substances. In the atomic theory of matter, eternal, unchanging atoms took the place of platonic forms, and there are still molecular biologists who insist that life can only be explained in terms of its constituent atoms ("What else is there but atoms?"). This philosophy of timeless forms was a deep commitment of people like Gregor Mendel and August Weismann, whose ideas dominated the thinking of early 20th century geneticists. Genes were the immutable essence of organisms, and the cells, tissues, and organs that form the organism are merely temporal and accidental. Weismann's "germ plasm" or germ line contained the immortal genes, the rest of the body lacked them, and was essentially mortal.

For most of the 20th century, the official doctrine was that most of the cells of the adult body became stationary once the body reached its adult size, and that aging consisted of the "wearing out" of those mortal cells. When a tumor, containing new cells, would appear and grow, these cells were called "immortal," because they didn't follow the rule for normal, stationary, mortal cells. Their "immortality" is often demonstrated by growing them endlessly in culture dishes. Normal cells, if they can be made to survive in a culture dish, are likely to be "transformed" into cancer, demonstrated by their ability to replicate in

dishes.

This is an important ideological point, that developed as biologists were experiencing the extreme difficulty of getting cells to replicate, or even to survive, in culture dishes. It has only recently been realized that cells need more than nutritional and hormonal signals to survive in culture; they require certain textural, structural, even rhythmically repeating conditions that mimic their surroundings in the living body.

Applied to cancer, the gene theory made it seem clear that the changes occurring in tumor cells were irrevocable, and it has seemed self-evident to oncologists that the only hope the cancer patient has is for the physician to destroy every bit of the alien substance. The recurrence of a cancer that has been removed has been evidence to them that fragments had remained, or that the cancer had distributed its seeds into other parts of the body. This seems to be the necessary conclusion if cancer is "caused" by defective genes.

New ideas of causality have grown up in science beside, or within, the science culture that is committed to platonism, reductionism, and genetic determinism. A few biologists, including Ana Soto and Carlos Sonnenschein, are applying more realistic ideas of causality to ecological, developmental, and cancer research. They have said (Soto, et al., 2009) "The ecological developmental biology (eco-devo) movement rejects the notion that development is merely the unfolding of a genetic program." If events such as cancer aren't "caused by genes," understanding the causes of cancer and the appropriate ways to treat it will require more holistic ways of looking at the tumor's relation to the organism, and the organism's relation to the environment.

It has been more than 40 years since experimenters demonstrated that cancer cells could be caused to revert to normal, by changing their environment. Harry Rubin (2006) has observed that cells can accumulate hundreds of mutations, and still function normally in the organism, but when separated and grown in a culture dish their differences become obvious. The surrounding cells in the body are causing the defective cells to remain normal in appearance, function, and growth behavior, instead of acting like cancer cells, and can also cause "stem-like" cells to differentiate appropriately.. He says "Intimate contact between the interacting cells is required to induce these changes." When stem cells enter a tumor, they don't find that regulatory, normalizing interaction with normal cells.

Work like Rubin's shows that even "myriad" mutations don't necessarily cause cancer, and another line of research shows that things which don't cause mutations can cause cancer--the "non-mutagenic carcinogens." The presence of mutations is neither sufficient nor necessary for causing cancer, but tumors do eventually accumulate serious damage, which causes most of the tumor cells to die quickly. Biological stress, or excitotoxic energy deprivation, destabilizes the genome; genetic changes develop as a result of prolonged destructive influences. The "non-genotoxic" carcinogens first cause inflammation, excitation, and energy impairment, leading to fibrosis, and atrophy. Cycles of cell injury, death, and repair cause chromosomes to deteriorate as the tissue loses its organization.

When a cell is stimulated, it responds, and the response requires energy. The stronger and more continuous the stimulus, the more energy the cell needs to continue responding. In some conditions, cells can desensitize themselves, to survive in the presence of continuous stimulation or irritation, but otherwise they are killed when they don't have enough energy to keep responding.

When a nerve is stimulated and responds, a wave of negative electrical charge passes through it; the electrical field accompanies a structural change in the cytoplasm of the nerve; similar changes occur in other types of cell. Stimulation of a nerve with negative (cathodal) polarity causes swelling, stimulation with the opposite polarity causes the opposite behavior; when nerve cells are inhibited, they shrink (Tasaki and Byrne, 1980; Tasaki, et al., 1988; Tasaki, 1999).

Swelling, an increase of the water content of an area of tissue, is a general feature of inflammation (Weiss, et al., 1951), whether it's in a lump caused by a bee sting, a bruise, or hives, or a cancer. Besides the instantaneous uptake of water described by Tasaki, there are increases that continue because of metabolic and chemical changes in the irritated cell. Tasaki has used gels of synthetic polymers to demonstrate that an electrical field can cause these changes, without the need for the "chemical osmotic" changes that are customarily assumed to account for the swelling changes caused by stress (Tasaki, 2002). When the pH of a protein gel becomes more alkaline, it swells. The electrical activation of a nerve causes a quick shift towards internal alkalinity (Endres, et al., 1986), followed by a sudden increase in lactic acid production. Although increased lactic acid causes acidity of an irritated or inflamed region, the conversion of pyruvic acid to lactic acid causes the interior of the stressed cell to become more alkaline, causing it to swell. This is the same process that causes the familiar swelling of tired muscles.

If blood vessels swell, the delivery of oxygen may be restricted, and hypoxia causes more intense swelling, because more lactic acid is produced, and less oxidized. This swelling pressure resembles an increase of osmolarity. For over 100 years, it has been customary to treat shock with "isotonic" fluids, which are in balance with well oxygenated tissues, with approximately 290 milliosmoles per liter, but this usually causes edema, swelling, and weight gain. Stressed tissues have been found to be in balance with fluids of much higher osmolarity, for example 372 mOsm/L (Tranum- Jensen, et al., 1981), and sometimes much higher.

Apart from its acidity, lactic acid acts as an excitatory signal. A very slight increase above the normal amount of lactic acid in the body fluids excites sensitive cells, and the amounts reached in inflamed tissues and in cancers will excite even stable cells such as myelinated nerves (Uchida and Murao, 1975).

Cancer cells show all the signs of being intensely stimulated, and this includes a high rate of oxygen consumption (deGroof, et al., 2009). The stimulation increases the energy requirements beyond the ability of the mitochondria's capacity to meet them, leading to the production of lactate even when a normal amount of oxygen is present. Even when both glucose and oxygen are supplied (which they usually aren't), the tumor cells will consume amino acids as fuel, as well as using them as

material for growth. Tumors have been called "nitrogen traps" or "glutamine traps," but this has meaning beyond the use of the nitrogen for growth; it is involved in the energetic inefficiency of this process, and the reorganizing effects this wasteful flow of energy has on the tissue structure (Medina, 2001). When glutamine enters the Krebs cycle to be used as fuel, this interferes with the ability to oxidize glucose, causing more lactic acid to be formed, contributing to the excitation and increased energy requirement.

Lactic acid activates the other major mediators of inflammation, including prostaglandins (made from PUFA), free fatty acids (including arachidonate, that forms prostaglandins; Schoonderwoerd, et al., 1989), nitric oxide, carbon monoxide, proteolytic enzymes that degrade the extracellular matrix, TNF (Jensen, et al., 1990), hypoxia inducible factor (Lu, et al., 2002; McFate, et al., 2008), interferon, and interleukins. Arachidonic acid itself can increase lactate production (Meroni, et al., 2003). TNFalpha and interferon gamma activate lactic acid production by increasing prostaglandins (Taylor, et al., 1992).

Most of the present information about cancer cells' behavior, such as reactions to radiation and chemical toxins, has been based on the study of cells in culture dishes. For more than 70 years, it was generally believed that radiation caused mutations and cancer by directly modifying the cells' genetic material. Then, it was discovered that fresh cells that were added to a dish of irradiated cells also developed mutations. The radiation causes cells to emit excitatory, inflammatory, substances such as serotonin and nitric oxide, which injure the cells that are later put near them.

Applying this information to the existing knowledge that radiation induces cancer in animals, the doctrine of genetic determinism inferred that the radiation "bystander effect" is just another mechanism by which radiation produces the "mutant cancer cell" or clone of cancer cells. But the difference between events in vitro and in vivo is that cells which are injured in the organism immediately initiate a process of healing, and in that situation each of the substances emitted by injured cells is acting both locally and systemically to activate repair or regeneration of the damaged tissue. Cells isolated in a culture dish can't call on the organism for the necessary materials, so the responses of the "bystander" cells, leading to mutations and death, seem meaningless. The injured cells are merely toxic, rather than potentially being a stimulus to healing.

When any part of a living organism is injured, for example by x-rays or surgery, the emitted substances affect the endocrine and nervous systems, activating processes that change metabolism and behavior. The injured tissue takes on new functions, for example by locally synthesizing estrogen, cortisol (Vukelic, et al., 2011), and other hormones, as well as stimulating the normal endocrine glands to secrete them. These interactions have been generally disregarded in cancer treatment, because of the gene centered theory of cancer, but they are essential for understanding the "malignancy" of tumors, that property that makes them likely to return after the tumor has been destroyed, and to spread to other tissues. Has anyone ever heard of a radiologist or surgeon who measured estrogen or the various mediators of inflammation before, during, and after their treatments? Long range survival after breast cancer surgery is affected by the time in the menstrual cycle when the surgery is done (Lemon, et al., 1996).

All sorts of stress, inflammation, and tissue injury increase the concentration of estrogen, both locally and systemically. Estrogen in turn produces hypoxia, swelling, lactic acid formation, and stimulates cell multiplication. Even a brief period of hypoxia will cause the secretion of lactate and other chemoattractants (Neumann, et al., 1993), which will cause cells to move into the hypoxic area from the blood stream. Although lactic acid attracts immune cells, it probably reduces their anticancer functions, and it stimulates the formation of new blood vessels, supporting continued growth and expansion of the multiplying cells (Hirschhaeuer, et al., 2011). When a tissue is being repaired normally, the new cells sense a quorum, and stop multiplying. The return of nerves to the damaged area is part of the regenerative process; nerves have inductive and stabilizing effects on differentiating cells.

These complex interactions between tumor cells and the rest of the organism are not considered by the ideology of medical oncologists. The ruling belief is that the malignancy of cells can be determined by examining them microscopically, and that their rate of growth can be determined, and that the tumor's approximate time of origin can be estimated. After surgically removing a tumor, the administration of chemotherapy and/or radiation is governed by mathematical descriptions of the expected behavior of cancer cells.

The mathematical relation of mortality to aging was described by Benjamin Gompertz, an actuary, in 1825, based on the understanding that people become less able to resist dying as they get older. This Gompertzian growth curve, which is realistic when applied to a population of people, flies, or rabbits, was applied to tumor growth (A.K. Laird, in 1964). Gompertz' reasoning that the probability of a person's dying increases with age has nothing to do with cancer cells, and there is very little evidence that his law of growth is useful for describing tumors. Laird's evidence consisted of 19 tumor samples, taken from 10 mice, 8 rats, and a rabbit. Her suggestion that the continuing deceleration of the growth rate might represent a natural growth regulating process wasn't influential, but her use of an actuarial formula, suggesting certain properties of cancer cells, has been extremely influential. It seems to be the profession's great need for justification that has made a Law of Tumor Growth so important to them.

At the time Laird did the tumor growth study, there was considerable interest in the idea that the immune system could be induced to prevent tumor growth. In 1951, Chester Southam, of the Sloan-Kettering Institute, tested his theory of cancer immunity on hundreds of patients and prisoners, and his results were widely reported. He found that pieces of tumor implanted in healthy people caused a local intense inflammation, which healed completely after two or three weeks. In sick people, the rejection of the cancer implant took about twice as long, and in people who already had cancer, the implant was very slow to be destroyed, and sometimes it was still present when they died.

In 1889, Stephen Paget had noticed that cancers metastasize only into certain organs, and compared the cancer cells to seeds that "can only live and grow if they fall on congenial soil." While many people, like Southam, saw a failing "immune system" as part of the congenial soil, and suggested vaccination to activate an immune rejection of the tumor, others have suggested "reducing the soil to dust," making growth impossible in a more general way. Recently, this attitude has taken the form of

different ways of "starving" cancer, by reducing sugar in the diet, or by blocking cells' ability to use sugar. The idea of making the "soil" inhospitable to cancer is a variation on the theme of killing the unwanted tissue.

As long as the lump is defined as an alien material, killing it by any means seems reasonable, but if it is seen as the body's attempt to repair itself, then killing it is no more reasonable than it would be to cut the spots out of someone with smallpox. When a cell is dying, it emits growth stimulating signals (Huang, et al., 2011). That's a normal part of tissue renewal. Some of its substance guides the differentiation of new cells, as demonstrated long ago by Polezhaev (discussed in my previous article, "Stem cells, cell culture, and culture: Issues in regeneration"). Anything that injures a tissue enough to require cells to be replaced causes the activation of a regulatory protein, hypoxia-inducible factor, HIF, which inhibits mitochondrial respiration, causing a shift toward glycolytic metabolism, increasing substances needed for growth. HIF is essential to the healing of any wound. Even glucose deprivation can cause the induction of HIF.

Prostaglandins, made from polyunsaturated fatty acids released by stimulation, can cause HIF to increase, but HIF also causes prostaglandins to increase. Lactic acid increases the expression of HIF, while HIF causes cells to shift metabolically to depend on converting glucose to lactic acid, that is, to adopt the "cancer metabolism." HIF is recognized as a fundamental problem in "cancer therapy," since HIF allows the cancer to resist the treatment, but the treatment increases HIF.

Radiation, chemotherapy, and surgery all activate these processes of cell replacement, and unless something has changed to improve the organism's recuperative ability, it isn't clear why the cells which replace the missing part should be more able to satisfactorily complete the recovery process than the original cells were. Even the amount of radiation in a single dental x-ray is enough to activate the excitatory-inflammatory processes, and a "therapeutic" x-ray to any part of the body excites similar, but much greater, processes throughout the body. But the ideology of "the cancer cell," and the Gompertz Growth Law, guide the practice of cancer treatment.

Many years ago, Harry Rubin was impressed by hearing from a pathologist that he had been able to find diagnosable cancer somewhere in the body of every person over the age of 50 that he had autopsied. If everyone has cancer by the age of 50, that means that cancer is harmless for most people, and that small cancers might frequently appear, and be spontaneously removed as part of the body's regular house-cleaning. One of the reasons that spontaneous regression of tumors seems so rare is undoubtedly that most tumors are quickly cut out by surgeons.

Preventing injury should be a basic consideration, but the medical slogan, "first do no harm," just doesn't apply to the cancer treatment industry, and this results from the doctrine of "the cancer cell," which is something to be destroyed or kept from multiplying. In the process of diagnosing a cancer, and during the course of treating it, the patient is usually subjected to multiple x-ray examinations, sometimes given radioactive drugs that supposedly concentrate in hidden tumors to emit positrons, and often has toxic contrast agents injected even for MRI examinations. These procedures, even before the destructive "therapies" begin, are adding to the body's inflammatory burden, interfering with the body's ability to complete a healing process. Decisions about pain control usually disregard the effects of the drugs on tumor growth and general vitality--for example, the opiates stimulate histamine release, which increases inflammation and tumor growth.

In 1927, Bernstein and Elias found that rats eating a fat free diet had almost no spontaneous cancer, and many studies since then in animals and people have shown a close association between polyunsaturated fatty acids and cancer. The polyunsaturated fatty acids in themselves, and their breakdown products, are excitatory and destabilizing to normal cells, but by modifying the sensitivity and energy production of cells, they limit cells' ability to respond to stimulation and destabilizing influences. Although they aren't essential for wound healing (Porras-Reyes, et al., 1992), they and their metabolites, the prostaglandins, are very conspicuous in wounds and tumors, and their proportion generally increases with aging. The prostaglandins are involved in several vicious cycles, including that with HIF mentioned above. This makes the PUFA and prostaglandins important to consider in relation to optimizing wound healing, and decreasing cancerization. Aspirin's protective and therapeutic effects in cancer are starting to be recognized, but there are several other things that can synergize with aspirin to reduce the circulation of free fatty acids and their conversion to prostaglandins. Niacinamide, progesterone, sugar, carbon dioxide, and red light protect against both free fatty acids and prostaglandins.

Since excitation leads to intracellular alkalinity and swelling, reducing the excitation seems reasonable, and many things which protect cells against excitation also have demonstrated anticancer effects. Local anesthetics, antihistamines, and antiinflammatory substances and some anesthetics such as xenon (Weigt, et al., 2009) are safe. Inhibitory substances related to GABA are being investigated for their ability to stop tumor growth. Simply stopping excessive excitation tends to restore the dominance of oxidative respiration over glycolysis.

To restore the supply of oxygen, sugar, and nutrients, swelling must be stopped. Hyperosmotic fluids act directly on swollen cells, removing water. Stopping excitation allows a return to efficient metabolism and reduces the injury potential, allowing the pH to decrease; with lower pH, the cell releases some of its water.

Increasing carbon dioxide lowers the intracellular pH, as well as inhibiting lactic acid formation, and restoring the oxidation of glucose increases CO_2. Inhibiting carbonic anhydrase, to allow more CO_2 to stay in the cell, contributes to intracellular acidification, and by systemically increasing carbon dioxide this inhibition has a broad range of protective anti-excitatory effects. The drug industry is now looking for chemicals that will specifically inhibit the carbonic anhydrase enzymes that are active in tumors. Existing carbonic anhydrase inhibitors, such as acetazolamide, will inhibit those enzymes, without harming other tissues. Aspirin has some effect as an inhibitor of carbonic anhydrase (Bayram, et al., 2008). Since histamine, serotonin (Vullo, et al., 2007), and estrogen (Barnett, et al., 2008; Garg, 1975) are carbonic anhydrase activators, their antagonists would help to acidify the hypoxic cells. Testosterone (Suzuki, et al., 1996) and progesterone are estrogen antagonists that inhibit carbonic anhydrase.

With aging, cells have less ability to produce energy, and are often more easily stimulated. The accumulation of polyunsaturated fats is one of the factors that reduce the ability of mitochondria to produce energy (Zhang, et al., 2006,

2009; Yazbeck, et al., 1989). Increased estrogen exposure, decreased thyroid hormone, an increased ratio of iron to copper, and lack of light, are other factors that impair the cytochrome oxidase enzyme.

The increased intracellular alkalinity and intracellular calcium that result from the combination of those factors increase the tendency of cells to be overstimulated, leading to aerobic glycolysis, the cancer metabolism. Improving any part of the system tends to increase carbon dioxide and decrease lactate, permitting differentiated functioning.

There are many people currently recommending fish oil (or other highly unsaturated oils) for preventing or treating cancer, and it has become almost as common to recommend a sugar free diet, "because sugar feeds cancer." This is often, incorrectly, said to be the meaning of Warburg's demonstration that cancer cells have a respiratory defect that causes them to produce lactic acid from glucose even in the presence of oxygen. Cancer cells use glucose and the amino acid glutamine primarily for synthetic purposes, and use fats as their energy source;the growth stimulating effect of the "essential fatty acids" (Sueyoshi and Nagao, 1962a; Holley, et al., 1974) shows that depriving a tumor of those fats retards its growth. The great energetic inefficiency of the cancer metabolism, which causes it to produce a large amount of heat and to cause systemic stress, failure of immunity, and weight loss, is because it synthesizes fat from glucose and amino acids, and then oxidizes the fat as if it were diabetic.

Estrogen, which is responsible for the fact that women burn fatty acids more easily than men, is centrally involved in this metabolic inefficiency. When a tissue is exposed to estrogen, within minutes it takes up water, and begins to synthesize fat, with a tendency to produce lactic acid at the same time. The alkalizing effect of lactic acid production is apparently what accounts for the uptake of water. Since it takes longer, at least 30 minutes, to produce a significant amount of new enzymes, these early changes are explained by the activation of existing enzymes by estrogen.

The transhydrogenases, or the transhydrogenase function of the steroid dehydrogenases, which shift metabolic energy between glycolytic and oxidative systems, have been shown to explain these effects of estrogen, but the transhydrogenases can be activated by many stressors. The biological function of the transhydrogenases seems to be to allow cells to continue growth and repair processes in a hypoxic environment. Estrogen can start the process by creating new pathways for electrons, and will promote processes that are started by something else, and progesterone is estrogen's natural antagonist, terminating the process.

Recently, a group at Johns Hopkins University (Le, et al., 2012) has been working out the implications of this ability to change the metabolism under hypoxia: Using an isotope-labeled amino acid, ". . . glutamine import and metabolism through the TCA cycle persisted under hypoxia, and glutamine contributed significantly to citrate carbons. Under glucose deprivation, glutamine-derived fumarate, malate, and citrate were significantly increased." The implication of this is that if the tumor isn't supplied with sugar, it will increase the rate at which it consumes the host's proteins. Forty years ago the work of Shapot and Blinov was showing the same effect, except that they demonstrated the involvement of the whole organism, especially the liver, in interaction with the tumor (Blinov and Shapot, 1975).

The alkaline cancer cell surrounds itself by the acid that it emits, and this extracellular acidity increases the ability of fatty acids to enter the cell (Spector, 1969); cancer cells, although they are synthesizing fat, also avidly take it up from their environment (Sueyoshi and Nagao, 1962b). This fat avidity is so extreme that cancer cells in vitro will eat enough polyunsaturated fat to kill themselves. This has been offered as proof that fish oil kills cancer. Saturated fats, however, have a calming effect on cancer cells, inhibiting their aerobic glycolysis (Marchut, et al., 1986) while permitting them to resume the respiratory production of energy.

The foods that nourish the patient well enough to support healing while permitting energy reserves to be built up are also the foods that don't interfere with the hormones, that don't cause spurious excitation of the tissues. The polyunsaturated fats directly stimulate the stress hormones, activate the excitatory amino acid signals, and directly excite cells, while the saturated fats have opposite effects, and are anti-inflammatory, and also don't interfere with mitochondrial function. When we eat more carbohydrate than can be oxidized, some of it will be turned into saturated fats and omega-9 fats, and these will support mitochondrial energy production. Carbohydrates in the diet also help to decrease the mobilization of fatty acids from storage; niacinamide and aspirin support that effect. Sugars are probably more favorable than starches for the immune system (Harris, et al., 1999), and failure of the immune system is a common feature of cancer. Polyunsaturated fats are generally known to suppress the immune system. Foods that provide generous amounts of sodium, calcium, magnesium, and potassium, help to minimize stress. Trace minerals and vitamins are important, but can be harmful if used excessively--iron excess is important to avoid.

Emodin, an anti-inflammatory substance found in cascara sagrada bark and other plants, is similar to other molecules that have been used for treating cancer, and one of its effects is to lower HIF: "Consistently, emodin attenuated the expression of cyclooxygenase 2 (COX-2), VEGF, hypoxia inducible factor 1 alpha (HIF-1!), MMP-1 and MMP-13 at mRNA level in IL-1"and LPS-treated synoviocytes under hypoxia" (Ha, et al., 2011). MMP-1 and MMP-13 are collagenase enzymes involved in metastasis. When cells are fully nourished, supplied with protective hormones, and properly illuminated, their ability to communicate should be able to govern their movements, preventing--and possibly reversing--metastatic migration.

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