

## **BASIC SCIENCE ASPECTS OF THE MITOCHONDRIA SECTION X**

### **CANCER**

Cancer is the second largest cause of death and disability in the United States. The trend has been a geometric progression in the incidence of cancer for the past half Century, which parallels several factors: the increase in environmental pollution, the decrease in the nutritional content of processed foods, the replacement of natural foods by such processed foods in the American diet, and the increase in the use of pharmaceuticals which block and inhibit natural bodily processes.

Mitochondria are pivotal in the causation and cure of cancer. The transformation of a normal cell to a malignant cell, the reversal of that process, and the destruction of transformed malignant cells are mitochondrial events, all mediated by changes in the form and function of mitochondria.

Cancer cannot be understood without some understanding of the mitochondria, their role in the life and death of the cell, the various functions they perform and how the breakdown of these functions can lead to malignant transformation of the cell.

Cancer can be and, for a long time, has been successfully treated and cured by people who have never heard of mitochondria, by using empirical treatments which affect mitochondria.

Life and health are dependent on a successful symbiotic relationship between our nucleated cells and the mitochondria which carry out a host of functions necessary for the processes of life.

### **HISTORY LESSONS**

Otto Warburg first described the cancer cell as an essentially anaerobic cell, living by

glycolysis. Albert Szent-Gyorgi gave us a very lucid explanation of what happens to a cell when it divides and cannot find its way back to the oxidative state.

From these two insights, it is now possible to understand the mechanism by which a normal cell becomes malignant, through the loss of its symbiotic relationship with its mitochondria and reverts to its pre-symbiotic state of primordial function.

Dr. Warburg states it thusly:

" There are prime and secondary causes of diseases. For example, the prime cause of the plaque is the plaque bacillus, but secondary causes of the plaque are filth, rats, and the fleas that transfer the plaque bacillus from rats to man. By a prime cause of a disease I mean one that is found in every case of the disease.

Cancer, above all other diseases, has countless secondary causes. But, even for cancer, there is only one prime cause. Summarized in a few words, the prime cause of cancer is the replacement of the respiration of oxygen in normal body cells by a fermentation of sugar. All normal body cells meet their energy needs by respiration of oxygen, whereas cancer cells meet their energy needs in great part by fermentation. All normal body cells are thus obligate aerobes, whereas all cancer cells are partial anaerobes. From the standpoint of the physics and chemistry of life this difference between normal and cancer cells is so great that one can scarcely picture a greater difference. Oxygen gas, the donor of energy in plants and animals is dethroned in the cancer cells and replaced by an energy yielding reaction of the lowest living forms, namely, a fermentation of glucose. - - -

If a lowered oxygen pressure during cell growth may cause cancer, or, more generally, if any inhibition of respiration during growth may cause cancer, then a next problem is to show why reduced respiration induces cancer. Since we already know that with a lowering of respiration fermentation results, we can re-express our question: Why does cancer result if oxygen-respiration is replaced by fermentation?

The reverse process, the dedifferentiation of life, takes place today in greatest amount before our eyes in cancer development, which is another expression for dedifferentiation. To be sure, cancer development takes place even in the presence of free oxygen gas in the atmosphere, but this oxygen may not penetrate in sufficient quantity into the growing body cells, or the respiratory apo-enzymes of the growing body cells may not be saturated with the active groups. In any case, during the cancer development the oxygen-respiration always falls, fermentation appears, and the highly differentiated cells are transformed to fermenting anaerobes, which have lost all their body functions and retain only the now useless property of growth. Thus, when respiration disappears, life does not disappear, but the meaning of life disappears, and what remains are growing machines that destroy the body in which

they grow. - - -

Since the Lindau lecture of June 1966 many physicians have examined - not unsuccessfully - the practical consequences of the anaerobiosis of cancer cells. The more who participate in these examinations, the sooner will we know what can be achieved. It is a unique aspect of these examinations that they can be carried out on human patients, on the largest scale, without risk, whereas experiments on animals have been misleading many times. The cure of human cancer will be the resultant of biochemistry of cancer and of biochemistry of man. A list of selected active groups of respiratory enzymes will soon be published, to which we recently added cytohemim and d-amino-Levulinic acid, the precursor of oxygen-transferring hemins. In the meantime commercial vitamin preparations may be used that contain, besides other substances, many active groups of the respiratory enzymes. Most of these may be added to the food. Cytohemim and vitamin B 12 may be given subcutaneously. (A synonym of "active group" is prosthetic" group of an enzyme.)

There exists no alternative today to the prevention of cancer as proposed at Lindau. It is the way that attacks the prime cause of cancer most directly and that is experimentally most developed. Indeed millions of experiments in man, through the effectiveness of some vitamins, have shown, that cell respiration is impaired if the active groups of the respiratory enzymes are removed from the food; and that cell respiration is repaired at once, if these groups are added again to the food. No way can be imagined that is scientifically better founded to prevent and cure a disease, the prime cause of which is an impaired respiration. Neither genetic codes of anaerobiosis nor cancer viruses are alternatives today, *because no such codes and no such viruses in man have been discovered so far*<sup>1</sup>; but anaerobiosis has been discovered.)

What can be achieved by the active groups, when tumors have already developed? The answer is doubtful, because tumors live in the body almost anaerobically, that is under conditions that the active groups cannot act. On the other hand, because young metastases live in the body almost aerobically, inhibition by the active groups should be possible. Therefore we propose first to remove all compact tumors, which are the anaerobic foci of the metastasis. Then the active group should be added to the food, in the greatest possible amount, for many years, even forever. This is a promising task. If it succeeds, then cancer will be a harmless disease.

Moreover, we discovered recently a) in experiments with growing cancer cells in vitro that very low concentrations of some selected active groups inhibit fermentation and the growth of cancer cells completely, in the course of a few days. From these experiments it may be concluded that de-differentiated cells die if one tries to normalize their metabolism. It is a result that is unexpected and that encourages the task of inhibiting the growth of metastases with active enzyme

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<sup>1</sup>These have now been discovered and are discussed below.

groups.

a) In press in Hoppe-Seylers Zeitschrift für Physiologische Chemie 1967. 10 g riboflavin per ccm or 10 g d-Aminolevulinic acid inhibit in vitro growth and fermentation completely but inhibit respiration less. As expected, ascites cancer in vivo is not cured.

As emphasized, it is the first precondition of the proposed treatment that all growing body cells be saturated with oxygen. It is a second precondition that exogenous carcinogens be kept away, at least during the treatment. All carcinogens impair respiration directly or indirectly by deranging capillary circulation, a statement that is proved by the fact that no cancer cell exists, the respiration of which is not impaired. Of course, respiration cannot be repaired if it is impaired at the same time by carcinogens.

A few years later, another Nobel Laureate, Albert Szent Gyorgi, in his treatise *Electronic Biology and Cancer* restated the problem thusly:

## ORIGIN OF LIFE<sup>2</sup>

When life originated some three billion years ago, our globe must have been a very unpleasant place, hot and pitch dark, being surrounded by a heavy layer of water vapor. There was no light and no oxygen. We can only philosophize that under those conditions life could have built only the simplest forms, which, to make life continuous, had to proliferate as fast as conditions permitted. The protein molecules formed must have been rather stable, with no loose ends or unbalanced forces. They had to be "closed-shell molecules" with their electrons arranged in pairs. There must have been a strongly reducing atmosphere containing chiefly electron donors, but no electron acceptors. Among the donating groups the strongly reducing SH must have played an important role, involved in the process of proliferation. We can expect that under those conditions the electronic energy bands were saturated, nonconductant, and the protein dielectric.

As our globe cooled and the surrounding water vapor condensed, eventually, red light of long wavelength could reach the surface of the earth, whereupon life developed a green dyestuff which could capture the red photons, and still makes our meadows green. With the energy of the captured photons the living systems separated the elements of water, fixing the H to carbon, creating foodstuffs, while releasing the oxygen as O<sub>2</sub> into the atmosphere. Oxygen is an oxidizing agent, an electron acceptor, which could induce profound changes in the nature of the protein by separating its electron pairs, making highly reactive free radicals out of its inert

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<sup>2</sup>Szent-Gyorgyi, Albert, *Electronic Biology and Cancer*, Marcel Dekker, NY (1976)

closed-shell molecules. It could desaturate the energy bands, thus making semiconductors out of dielectrics, creating unbalanced forces which could link protein molecules together to increasing complex structures which performed increasingly complex and subtle reactions, leading to differentiation and to a new state of the living systems which I called the " $\beta$  state" to distinguish it from the  $\alpha$  state which preceded the appearance of oxygen.

The unbridled proliferation of the  $\alpha$  period was incompatible with the development of complex structures. To maintain the harmony of the whole it had to be arrested and regulated. But even without regulation the semisolid structures must have interfered with cell division, which involves a complete rearrangement of the cellular interior, and demands a more liquid state. To be able to divide, the cell has to dismount its structures to a great extent, dismounting first the most bulky structure, the nucleus, the membrane of which is dissolved and the chromatin condensed into a small number of mobile chromosomes. Also the oxidative mitochondria have to be disassembled, making the cell more dependent on fermentation for energy. All this means that the dividing cell has to dedifferentiate and return, to an extent, to the  $\alpha$  state. After completed division the cell has to find its way back to the oxidative-resting  $\beta$  state, building up again its structures and electron transport chains. Should the cell find its road of return to the  $\beta$  state deranged, or should the  $\beta$  state be made unstable by some extraneous factor, then the cell would have to persist in the proliferative  $\alpha$  state and tumor would result.

When nature creates new mechanisms she does not throw the old ones away but builds the new ones on top. So the building of solid structures in the  $\beta$  period did not mean that the system of soluble molecules was eliminated. It became the basis of metabolism and served as a matrix into which the new insoluble structures were embedded, and continued to perform its simple "vegetative function," fermentation, catering for the embedded structures which released the total energy of food, opening the way to the differentiation, the end product of which is us.

It should be remembered that at the time these writings were published, endosymbiont nature and origin of mitochondria had not yet been established and most biologists believed that mitochondria were synthesized from other membrane systems of the cell. In Albert Lehninger's classic treatise *The Mitochondrion, molecular basis of Structure and Function*, New York, W.A. Benjamin, 1965, the biogenesis of mitochondrion from other membrane systems is set forth completely and in passing, there is a suggestion that some scientists are beginning to contend that mitochondria may be of bacterial origin.

This latter concept was not fully accepted until 1981, after the demonstration of a mitochondrial genome and the publication by Margulis of *Symbiosis and Cell Evolution*, San Francisco, W. H. Freeman, 1981. Dr. Warburg and Szent-Gyorgi had arrived at their conclusions based entirely on chemical analysis without the benefit of electron microscopy and other techniques developed after their theories were published.

Actually, Dr. Warburg had made some of the pivotal discoveries about mitochondria much earlier. In 1913, he had found cellular respiration to be associated with granules, in soluble elements of cell structure, a finding he reported in Warburg, O., *Arch Ges Physiol* 154:599 (1913) and had made important contributions, the understanding of cytochromes in his book Warburg, O., *Schwermetalle als Wirkungsgruppen von Fermentation*, Verlag W. Saenger, Berlin, 1948, pp. 212 ff. and Szent-Gyorgi, S., *Discovery of a catalytic effect of the four-carbon dicarboxylic acids* had been the information that permitted Dr. Hans Krebs to elucidate the citric acid or Krebs cycle.

According to Lehninger's book:

"These were the major events just preceding the confluence of the biochemical and cytological research on mitochondria. Actually, very few biochemists concerned themselves with the possible importance of the fact that respiratory enzymes were found to be associated with particulate matter of cells and tissues. It was a part of the biochemical *Zeitgeist* that particles were a nuisance and stood in the way of purification of the respiratory enzymes. Yet it almost seems paradoxical that it was two biochemists who had many years earlier made important discoveries on the occurrence of biological oxidation-reduction mechanisms in granular elements of the cell"

Drs. Warburg and Szent-Gyorgi were biochemists, not cytologists, and left the details of mitochondrial structure to others. Nevertheless, in principle, they were quite correct and this has been borne out by a large amount of research since that time.

Bradford and Allen in their *Primordial Thesis of Cancer* Med Hypoth 1992; 37:20-3, brought these concepts into harmony and later developments. So that while the details continue to be worked out, the principle that malignant transformation in cells results from a break down in mitochondrial structure and function remains not only viable but also essential to an understanding of the process.

#### REJECTION OF WARBURG HYPOTHESIS BY ESTABLISHMENT

Dr. Robert A. Weinberg is a founding member of the Whitehead Institute of Biomedical Research and Professor of Biology at the Massachusetts Institute of Technology, where he is head of the Oncology Lab and, as such, is a respected and preeminent establishment cancer researcher. In his book, *Racing to the Beginning of the Road: The Search for the Origin of Cancer*, NY Harmony Books 1996, he explains why Dr. Warburg's cancer thesis was ignored by the establishment thusly:

" - - - So the problem of cancer, we agreed, needed to be understood in terms of the cells that invent their own, self-directed manifesto of growth and destruction. In fact, the problem could be reduced even further. The ultimate answer to the cancer problem would come from looking at the single ancestral cell that founds the colony of cancer cells by transforming itself from a normal, well-behaved member of a community into a renegade.

How did the single ancestral cell, the renegade, make all this happen? What caused it to decide to strike out on its own—or, conversely, how did a normal cell know when to grow and when to hold back and remain quiet?

The first big answer came long before my friends and I began our work. One of the most brilliant scientific minds of twentieth century science had a clear vision of the solution to the cancer problem, crafted with precision and powerful logic. He knew how the cancer problem would be solved. And he knew it with great—even total—certainty. He started this all. - - -

'Rubbish!' With a single word, the old man swept away a whole field of competitors. 'Forget everything they say. All you need to remember is what I have just told you.' He and he alone had uncovered the origin of cancer. The engine that drove normal cells to divide uncontrollably had now been revealed. Other ideas had been lying around on the workbench of science. But those ideas were, without

exception, inspired by ignorance and cobbled together by second-class minds.

'Rubbish' was the kindest word he could find. The verdict was clear-cut. So, too, was his own success. Already one of the greatest biochemists of the twentieth century—maybe the greatest—Otto Warburg had moved on from his early successes to conquer yet another important field of scientific research.

Many of those in his audience already knew Warburg. As the acknowledged leader of German biochemistry, he had come to visit them here in Stockholm a quarter of a century earlier. In December of 1931, he had come at the invitation of the Nobel Committee to collect the Prize. The award recognized his research on energy metabolism.

Warburg had figured out how cells harvest energy by burning sugars. His work was, by any standards, an extraordinary piece of research. Having conquered one major problem, he had gone on in the 1930s to attack two more: cancer and photosynthesis. Both had been waiting for unambiguous resolution. And both had yielded to the powerful tools that he had developed earlier to solve the problem of energy metabolism. It was 1955, and Warburg was seventy-two and back in town, still active, lecturing the cream of the Swedish scientific community on his advances, which had uncovered the deepest roots of cancer. The evening visit proved to be memorable. A full forty years later my Swedish friends would still be talking about it.

The researchers and physicians who came to hear Warburg that evening knew full well that the mystery of cancer would not be solved by studying tumors with the naked eye. Even the analysis of individual cancer cells under the microscope promised few satisfying explanations. The real answers seemed to lie far deeper, in the submicroscopic world of the molecules inside cancer cells. Few were as well equipped as Warburg to study the molecules of life that held the key to the cancer puzzle.

The German researchers who had preceded Warburg—his teachers and his teachers' teachers—had worked with the total certainty that their microscopes would lead them straight to the root cause of cancer. When their work began, in the first third of the nineteenth century, many of them believed that tumors arose from mucus and plasma that somehow aggregated into large masses. Only later did their microscopes show that tumors, like normal tissues, were assembled from the individual building blocks they now were calling cells. By mid-century their mindset was further shaped by Rudolf Virchow, one of the leaders of nineteenth-century German medical research. His dictum, *omnis cellula e cellula*—all cells arise from yet other cells—was applied at first to understand how a complex embryo arises from a fertilized egg. Subsequently they applied Virchow's law to the cells in a tumor, which seemed also to descend from cell-like ancestors.

Later they moved on to solve the question of where cancer cells originate. By about 1850 they had reached a definitive conclusion: cancer cells arose directly from the normal cells of the organ in which they were first discovered. Normal liver cells spawned hepatomas, stomach cells produced gastric carcinomas, brain cells

engendered glioblastomas. Some of the cells present in a normal tissue apparently decided to grow abnormally. Their descendants then formed huge cell populations, resulting in tumors large enough to be visible to the naked eye. *Omnis cellula e cellula* seemed to explain everything.

Then they hit a stone wall. Having reduced cancer to a disease of misbehaving cells, they could move no farther. No one knew what made cells grow normally or abnormally. No one knew how cells decided their own fates. Half a century passed.

In the 1920s, Warburg and a small group of other organic chemists appeared on the scene. They had an entirely new way of posing the cancer question. The real solution, they argued, lay in the chemistry of the cell, beyond the world visible through the microscope. The answers would come from analyzing the complex chemical machinery operating within the living cell. They meant the machinery of cellular metabolism: the hundreds—likely thousands—of chemical reactions that allowed cells to synthesize chemical building blocks and generate energy. Beyond or behind these biochemical reactions lay no further subtlety, no more hidden forces.

If the metabolism of a normal cell provided a complete explanation of its normal behavior, it followed that the life of the cancer cell could be explained by some type of abnormal metabolism. In effect, the cancer problem could really be reduced to something very simple: a key biochemical reaction governing cell proliferation. When this reaction fired properly, the cell around it would grow normally; when it misfired, runaway cell growth would ensue, and with that would come cancer—a straightforward story of cause and effect.

By 1955, the year of Warburg's Stockholm lecture, hundreds of biochemists had begun comparing the metabolism of cancer cells with that of normal cells, looking for the elusive malfunctioning reaction, the Holy Grail of cancer research. But Warburg had already found it, as he made abundantly clear during his memorable talk.

“The single ultimate root cause, from which all of cancer's aberrations can be traced, is anaerobiosis—life without oxygen. All normal cells have an absolute requirement for oxygen, but cancer cells can live without oxygen—a rule without any exceptions. “Cancer was ultimately a problem of how cells used or misused oxygen to burn sugars.

Warburg had succeeded in reducing the cancer problem to its primal cause. Those who proposed alternative explanations of cancer's origins were, as he said on frequent occasion, either incompetent or—worse—outright frauds. Their theories would fall by the wayside, as had a thousand other ideas that pretended to explain the origins of malignancy.

Warburg's explanation was based on a simple yet compelling proof: Cancer cells, unlike normal cells, could grow and divide without oxygen. More to the point, when he took normal cells from an embryo and forced them to grow in a Petri dish in the absence of oxygen, those oxygen-starved cells took on the traits of cancer cells. In itself, the observation of this transformation represented a milestone in

cancer research, since usually such conversions took place deep within the recesses of living tissues.

If a normal cell could be converted into a cancer cell at will, as he had now succeeded in doing, all the answers would fall quickly in place. The rest of cancer research that followed would, at best, be only a minor commentary on what he already accomplished.

Warburg's insight into the cause of cancer also led him to propose a powerful preventive treatment: By exposing animals or humans to the same biochemical compounds that cells normally use to catalyze oxygen-driven combustion, any tendency for cancerous outgrowths to appear could be blocked.

His own preliminary experiments gave indications that this trick would work. "How long cancer prevention will be avoided depends on how long the prophets of agnosticism will succeed in inhibiting the application of scientific knowledge in the cancer field. In the meantime, millions of men must die of cancer unnecessarily." Though the syntax was awkward, the message was, as always, crystal clear: Provide cells with oxygen and they will grow normally; deprive them and cancer will ensue. Rigorous science had finally broken open the age-old problem.

Warburg's Stockholm appearance was in all respects an extraordinary performance—a lecture given in a style that brooked no opposition. The answers to the major questions posed by him were arrayed on large charts that he had mounted in the front of the lecture hall. Warburg's faithful assistant and manservant of thirty years paced back and forth in front of the charts with a long wooden staff, pointing out key pieces of data and important conclusions as the lecture progressed.

When it was over, polite questions were ventured by several of the older Swedish professors. After all, a lecture by the most prominent biochemist of the century demanded some perfunctory follow-up. None of the questions were particularly probing. Warburg knew more about the subject than did anyone in his audience. Also, those who had come to hear him risked ridicule by provoking him with even mildly critical questions. No one had the stomach to take on the attack dog who happened to be their honored guest.

Rarely had any researcher working on the origins of cancer spoken with such certainty. And yet, in spite of the passion, the conviction, the voice of absolute authority, many leaving the lecture hall that evening did not want to believe Warburg. The skepticism of some had little to do with the details of Warburg's science; their motives centered on Warburg himself. They very much wanted him to be wrong, for whatever reason they or anyone else could find.

At the time of his Stockholm lecture, Otto Warburg had been a practicing biochemist for more than half a century. During his career, he had attracted a long list of enemies. Most anyone he encountered in the world of science had either failed to measure up to his own standards of scientific quality or had been unable to appreciate his ideas. His martinet style was learned in no small part in the Prussian military, where, as he said, he had learned "how to command and how to obey."

Warburg was a half-Jew who continued to work in the Third Reich while many of his relatives and colleagues fled for their lives or were shipped off in boxcars to the camps. He had only one item on his personal agenda: his own career.

His formula for survival was shrewd: he lived off Hitler's morbid fear of cancer. More than any man alive, he provided the Fuehrer with the hope of prevention and cure, so Hitler reclassified him as a quarter-Jew. That slight adjustment of his pedigree allowed him to pass under the wire and continue his research while the war raged around him. The Nazis even set him up with his own research institute.

Warburg's detractors knew all this history. Beyond that, they detested his style, his authoritarian voice, his imperial German certainty. Long before the 1955 performance, his style had become passé. Science was more democratic now, and for the first time in almost a century, there were many centers of power and influence outside the prestigious German research institutes. After two world wars, German science was a shell of its former self. The long rows of German scientists queuing up for their Nobel Prizes were no more than faint memories. That gave many in his Swedish audience great satisfaction. Hence, many who walked out of his 1955 lecture had come to view him as a relic, a detested one at that.

But there were also some who questioned the substance of his science. Was cancer actually triggered by the absence of oxygen in cells? His overall strategy of trying to understand cancer by puzzling out the biochemistry of the cancer cell seemed to represent the correct tack. The issue was whether the particular reaction that Warburg had identified lay at the heart of the cancer puzzle or represented a distracting side issue.

A few of his listeners were also troubled by the unusual coincidence that tied the different phases of his career together. First came his Nobel Prize work on oxygen and sugar combustion. Now, exactly the same thinking and techniques had been transferred directly to another, ostensibly unrelated problem, that of cancer. It seemed an unusual stroke of good luck that his monumental work on energy metabolism early in life would lead so directly and effortlessly to the solution of a second, equally monumental problem later on.

Maybe Warburg, by picking his favorite biochemical reaction, had bet on the wrong horse. Maybe, in his drive to find the root cause of cancer, he had chosen the wrong molecules among the thousands inside the cell. Maybe his credentials as the world's best biochemist did not guarantee him a sure ticket to solve the cancer problem.

There was yet another unspoken factor that influenced the skeptics in Warburg's audience: their increasing distaste for cancer research. Though greatly respected by the general public, this kind of science appeared to be attracting researchers whose credentials and credibility were less than impressive. Perhaps Warburg had been sucked into the swamp of cancer research together with a host of scientific mediocrities. Maybe he had even sunk in over his head.

Many scientists working on other medical problems had come to see the

cancer research field as a large garage filled with dozens of highly specialized mechanics. Each was expert in one or another automotive system, and had his own strongly held point of view on how to solve any problem brought before him. When a poorly running car was brought into this garage, the carburetor specialist would look it over and insist on a fault in its carburetor; the machinist knew that the cylinder bores needed to be remachined; the exhaust-system man would demand that a new muffler be installed. Each would assert that the large problem they all confronted was, by a stroke of good fortune, solvable through the particular expertise that he happened to possess.

Warburg, some feared, had become the mechanic specializing in energy metabolism, seeing all the problems of the biological world through the eyes of an energy specialist. They knew of another biochemist, an expert in RNA molecules, who insisted on defects in his favorite molecule as the explanation of cancer. A third, who studied damage to DNA molecules, was persuaded that this process provided the answer. A fourth, who looked at chromosomes, saw abnormal numbers of chromosomes in cancer cells. A fifth, who studied the breakdown of proteins in cancer cells, was convinced that this process provided a clear and unassailable explanation of runaway growth. There were as many explanations for cancer as there were subspecialties in the field of biochemistry.

Warburg remained aloof from the noisy crowd of cancer researchers. Why argue with them, when the answer was perfectly clear? Anyone having only a bit of insight into science could understand the essential difference between a cancer cell and a normal cell, “without knowing what life really is.” “Imagine,” he wrote, “two engines, the one being driven by complete, the other by incomplete, combustion of coal. A man who knows nothing at all about engines, their structure, and their purpose, may discover the difference. He may, for example, smell it.” The smell of the engine inside the cancer cell seemed to suffice to explain all of its bizarre properties.

Still, Warburg lived with another problem that somehow, though quietly ignored, would not go away. There was no obvious reason why the abnormal combustion he described should lead directly to runaway cell growth. The connection seemed arbitrary. It made no more sense than a defective windshield wiper providing the underlying explanation of why an engine stalls or a brake fails. So Warburg’s theory eventually fell short. The others fared no better. Their proponents had spent time looking around familiar lampposts for the answer. None of them could come up with a convincing reason why the patch around his particular lamppost held the key. They were all looking where they knew to look.

Their forays into cancer research, in which they tried to fit the disease into familiar molds, were not working. Cancer needed to be studied on its own terms. That made them very uncomfortable. In the early 1950s, some began to look at cancer in a totally different way. The newcomers turned their backs on sophisticated Nobel Prize research. Indeed, their approach was rather simpleminded: They looked at how often cancer struck different sub- populations of humanity. They soon found

that common tumors appeared in different groups at dramatically different rates. That clue was far removed from the inner workings of cells, but unlike Warburg's smoking engines, it represented a solid start.

Their finding that cancer struck in predictable ways was the springboard for all that followed, the foundation that ultimately allowed my friends and me to move the problem forward." - - -

The next forty-five years of rejection of these observations in favor of spending Billions of Dollars in diverse research instead of following these indisputable leads has produced the fiasco of the last "War on Cancer" by the Allopathic research establishment. During this time the mortality rate from cancer has risen steadily, despite 70 Billion Dollars spent on this research.

It is not likely that either Warburg or Szent-Gyorgi were aware of the pivotal role of free radical damage in mitochondria.

The free radical theory of aging was first described by Dr. Denham Harman, in 1954. He stated that a "single common process, modifiable by genetic and environmental factors, was responsible for aging and death of all living things", and identified this process saying, "Aging is caused by free radical reactions, which may be caused by the environment, from disease and intrinsic reactions within the aging process." Dr. Harman's conclusion, written more than forty years ago, sums up much of what is finally agreed upon today by scientists:

The free radical theory of aging is supported by studies on the effect of ionized radiation on living things, the dietary manipulations of endogenous free radicals, the reasonable explanation that the free radical theory provides for aging, and finally the increasing number of studies which show that free radical reactions are involved in the pathogenesis of specific diseases.

Dr. Harman's theory was largely ignored and rejected; as late as 1977, authorities in the chemical field were still not convinced that superoxide could "Act as a deleterious or cytotoxic species in living cells". The idea that dangerous free radicals were present in the human biological

system was considered untenable by most biologists until 1969. They were convinced that disease must come from outside of man, not as a by-product of normal biological functions. At that time, a copper-containing protein had been isolated from red blood cells that had no known function. It was then discovered that this copper protein also contained zinc. It was an enzyme uniting two superoxide molecules to form one molecule of hydrogen peroxide and one molecule of oxygen. The protein was renamed superoxide dismutase (SOD) because of its ability to combine two molecules of superoxide.

Since the subunit for SOD was superoxide, a free radical, it became apparent that at least one free radical is normally found in biological systems. With this realization, research in this area of biology began opening a new avenue of research in which other free radicals were subsequently discovered. Their scavengers were discovered shortly thereafter.

It was recognized that superoxide and the hydroxyl radical were instrumental as causative factors not only in many degenerative diseases but in the aging process as well. In general, knowledge of the free radicals wasn't widespread in the scientific community until the 1980's and research in that era didn't really get started until the late 1980's.

Dr. Harman anticipated the present interest in antioxidant prevention and treatment of cancer by 30 years with the publication of his paper "*Prolongation of the Normal Life Span and Inhibition of Spontaneous Cancer by Antioxidants*", in the *Journal of Gerontology* 16:274 in 1961.

Warburg suggested feeding patients the chemicals which support the Krebs Cycle as a means of treating cancer, feeling that a deficiency of these might be the cause of the failure of oxidative phosphorylation in cancer cells. This helps where there are deficiencies, but at that time, detailed information about mitochondrial function was lacking.

If Warburg's and Harman's insights had been followed up on by research of the intensity and liberal funding done by the people described in Dr. Weinberg's book, by now the cancer plague would probably have been a thing of the past.

It may also be noted that Warburg's work all took place before the explosive growth of industrial and chemical production of the 1960's to 1990's, and that the world he lived in was not particularly polluted. The medical therapeutics of his day were, by and large, the synthetic petrochemicals which were developed after the end of World War II and were, to a large extent, still fairly natural. The antibiotic age has just dawned.

A current medical text of that time recommended the herb Condurango as a cancer treatment.<sup>3</sup> Antimitotic chemotherapy was still off in the future at that time and the incidence of cancer was still fairly low. The Materia Medica listed in that treatise contains over 50% herbal remedies.

Food was still generally locally produced without chemicals or artificial fertilizer, pesticides or herbicides, many of which were first produced during and immediately after World War II. While motor vehicles had been around for half a century, there were only about 25% as many as are operated today and rail transportation was very much in use for passengers as well as freight. There was far less particulate air pollution and smog. Many city water supplies were still potable and relatively unpolluted, not filled with toxic chemicals and the other toxins we add to mask them. Not surprisingly, there was far less cancer and far less of the factors known to produce oxidative damage than there is today.

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<sup>3</sup>Mullen, Edward, Handbook of Medical Treatment, Philadelphia, F. A Davis Company (1942)

For most of the 20th Century, at least until well into the 1970's, there was a social stigma attached to cancer and it was not openly discussed. Its increasing incidence in the population over the past twenty-five years seems to have overcome the stigma and open discussion brought the incidence to public attention.

The public attention resulted in the government's ill-fated "War on Cancer", which was waged in its entirety by the Allopathic cancer research establishment and ended in a humiliating defeat after years of astronomical expenditure of research funds.

Fortunately, not all scientists chose to join the cancer establishment and quite a few did follow up on Warburg and Szent-Gyorgi's leads. Most of these were not cancer researchers; they were biologists, biochemists, and other basic science researchers who soon discovered the missing link, which has been so studiously ignored by the cancer research establishment- mitochondria. They also discovered the genetic codes of anerobesis and the cancer viruses, which Dr. Warburg noted had not been discovered at the time he announced his hypothesis.

1. Woods MW, DuBuy HG. Cytoplasmic diseases and cancer. *Science* 1945; 102:591-593.
2. Weinhouse S. Oxidative metabolism of neoplastic tissues. *Adv Cancer Research* 1955; 3:269-325.
3. Warburg O. On the origin of cancer cells. *Science* 1956; 123:309-314.
4. Graffi A. 1st die URSACHE DER MALIGNEN Entartung eine Mutation der Mitochondrien? [Is mutation of mitochondria the cause of malignant degeneration?]. *Zentralblatt fur Gynakologie* 1968; 90:945-8.
5. Gause GF. Cancer and mitochondrial DNA. *Brit Med J* 1969; 3:413-4.

6. Anderson TJ. Cancer and mitochondrial DNA. *British Med J* 1969; 3:593.
7. Hadler HI, Daniel BG, Pratt RD. The induction of ATP energized mitochondrial volume changes by carcinogenic N-hydroxy-N-acetyl-aminofluorenes when combined with showdomycin. A unitary hypothesis for carcinogenesis. *J Antibiot* 1971; 24:405-17.
8. Kara J, Mach O, Cerna H. Replication of Rous Sarcoma Virus and the biosynthesis of the oncogenic subviral ribonucleoprotein particles (“viroosomes”) in the mitochondria isolated from Rous sarcoma tissue. *Biochem Biophys Res Comm* 1971; 44:162-170.
9. Schumacher HR, Szekely IE, Fisher DR. Letter: Mitochondria in oncogenesis revisited. *Lancet* 1973; 2:1207-8.
10. Hadler HI, Daniel BG, A correlation between the carcinogenicity of isomeric N-hydroxy-N-acetylaminofluorenes and their in vitro effect on mitochondria. *Cancer Res* 1973; 33:117-22.
11. Hoberman HD. Is there a role for mitochondrial genes in carcinogenesis? *Cancer Res* 1975; 35:3332-5.
12. Wilkie D, Egilsson V, Evans IH. Letter: Mitochondria in oncogenesis. *Lancet* 1975; 1:697-8.
13. Duchesne J. A unifying biochemical theory of cancer, senescence and maximal life span. *J Theor Biol* 1977; 66:137-145.
14. Pedersen PL. Tumor mitochondria and the bioenergetics of cancer cells. *Prog Exp Tumor Res* 1978; 22:190-274.
15. Oberley LW, Oberley TD, Buettner GR. Cell differentiation, aging and cancer: the possible roles of superoxide and superoxide dismutases. *Med Hypoth* 1980; 6:249-68.
16. Hartung J. Might cancer be a failed response to renegade mitochondria? *J Theor Biol* 1982; 94:173-8.
17. Reid RA. Can migratory mitochondrial DNA activate oncogenesis? *TIBS* 1983; 8:190-191.
18. Wilkie D, Evans IH, Egilsson V, Diala ES, Collier D. Mitochondria,

- cell surface, and carcinogenesis. *Internat Rev Cytol* 1983; 15(Suppl):157-89.
19. John P. Mitochondrial regulation of cell surface components in relation to carcinogenesis. *J Theor Biol* 1984; 110:377-381.
  20. Oberley LW, Oberley TD. The role of superoxide dismutase and gene amplification in carcinogenesis. *J Theor Biol* 1984; 106:403-22.
  21. Glaichenhaus N, Leopold P, Cuzin F. Increased levels of mitochondrial gene expression in rat fibroblast cells immortalized or transformed by viral and cellular oncogenes. *EMBO J* 1986; 5:1261-1265.
  22. Shay JW, Werbin H. Are mitochondrial DNA mutations involved in the carcinogenic process? *Mutation Res* 1987; 186:149-60.
  23. Oberley LW, Oberley TD. Role of antioxidant enzymes in cell immortalization and transformation. *Mol Cell Biochem* 1988; 84:147-53.
  24. Richter C. Do mitochondrial-DNA fragments promote cancer and aging? *FEBS Lett* 1988; 241:1-5.
  25. Ames BN. Endogenous DNA damage as related to cancer and aging. *Mutation Res* 1989; 214:41-46.
  26. Trounce I, Byrne E, Marzuki S. Decline in skeletal muscle mitochondrial respiratory chain function: Possible factor in aging. *Lancet* 1989; i:637-639.
  27. Bandy B, Davison AJ. Mitochondrial mutations may increase oxidative stress: Implications for carcinogenesis and aging? *Free Radical Biol Med* 1990;8:523-539.
  28. Ames BN, Gold LS. Endogenous mutagens and the causes of aging and cancer. *Mutation Res* 1991; 250:3-16.
  29. Zotin AI. Mitokhondrial'naia teoriia kantserogeneza. (The mitochondrial theory of carcinogenesis.) *Izvestiia Akademii Nauk SSSR Serii Biologicheskaja* 1991; Nov-Dec(6):805-15.

30. Baggetto LG. Role of mitochondria in carcinogenesis. *Europ J Cancer* 1992; 29A:156-9.
31. Bradford RW, Allen HW. The primordial thesis of cancer. *Med Hypoth* 1992; 37:20-3.
32. Arora KK, Parry DM, Pedersen PL. Hexokinase receptors: preferential enzyme binding in normal cells to nonmitochondrial sites and in transformed cells to mitochondrial sites. *J Bioenerg Biomemb* 1992; 24:47-53.
33. Nagley P, Mackay IR, Baumer A et al. Mitochondrial DNA mutations associated with aging and degenerative disease. *Ann NY Acad Sci* 1992; 673:92-102.
34. McCabe ER. Role of mitochondria in oncogenesis. *Biochem Med Metab Biol* 1992; 47:105-7.
35. Richter C. Pro-oxidants and mitochondrial Ca<sup>2+</sup>: Their relationship to apoptosis and oncogenesis. *FEBS Lett* 1993; 325:104-7.
36. Cotton DW, Rogers S. Aging, cancer, and mitochondrial deterioration. *Lancet* 1993; 341:281-2.
37. Wolvetang EJ, Johnson KL, Krauer K et al. Mitochondrial respiratory chain inhibitors induce apoptosis. *FEBS Lett* 1994; 339:40-44.
38. Ozawa T. Mechanism of somatic mitochondrial DNA mutations associated with age and diseases. *Biochim Biophys Acta* 1995; 1271:177-189.
39. Vaillant F, Nagley P. Human cell mutants with very low mitochondrial DNA copy number ( $\_d$ ). *Hum Mol Genet* 1995; 4:903-914.

Building upon this research, Dongchon Kang, Koichiro Takeshige, Mutsuo Sekiguchi and Keshav K. Singh in their introduction to *Mitochondrial DNA Mutations in Aging, Disease and Cancer*, Springer-Verlag, Berlin Heidelberg New York (1998) can state authoritatively:

"Studies described as early as 1930 by Warburg and most recently, by Kroemer's group, suggest mitochondrial involvement in cancer, perhaps through its central role in energy production and programmed cell death (apoptosis). Several other lines of evidence suggest a role of mitochondria in carcinogenesis. These include presence of mtDNA fragments into nuclear genomes, transmission of oncogenic viral DNA, mitochondrial activation of chemical carcinogens and altered affects of mitochondrial Ca<sup>2+</sup> homeostasis. In addition, mitochondria, being the primary site of ROS, contribute to spontaneous mutagenesis which may lead to neoplastic transformation and human cancer. A role for mitochondria in cancer is further supported by the presence of a tumor suppressor protein in mitochondria. The exact biochemical function of this tumor suppressor protein is not clear. However, it is believed to be involved in breast cancer and aging.

A mitochondrial role in carcinogenesis may also involve the Bcl-2 protein. Anti-apoptotic Bcl-2 protein is localized to the mitochondrial membrane, and it possesses anti-oxidative activity. Two mitochondrial proteins involved in the induction of apoptosis have been identified with the use of cell-free systems, proving a critical role for mitochondria in apoptosis. Cytochrome c and apoptosis-inducing factor (AIF) are located in the intermembranous space and are released upon initiation of apoptosis, coinciding with the permeability transition of mitochondria. Bcl-2 protein inhibits the release of the factors as well as transition in membrane permeability. Dysfunctional mitochondria alter the sensitivity of cells to apoptotic stimuli. A block in apoptosis is thought to be a major determinant of cellular transformation, thus aberrant mitochondria may contribute to carcinogenesis. The role of Bcl-2 in apoptosis is also evident in neurodegenerative diseases. - - - "

In this regard, see:

1. *Prevention of Apoptosis by Bcl-2: Release of Cytochrome c from Mitochondria Blocked*", Yang, et al, Science, (1997)Vol 275 (5303):1129-1132.
2. *The Bcl-2 Protein Family: Arbiters of Cell Survival*, Adams and Cory, Science, (1998) 281(5381):1322-1326
3. *Mitochondria and Apoptosis*, Green DR, Reed JC, Science, 1998;281(5381):1309-1312
4. *A Matter of Life and Cell Death*, Evan G, Littlewood T., Science, 1998;281(5381):1317-1322.
5. *Mitochondrial events in the life and death of animal cells: a brief overview*. J. Bioenerg Biomembr 1999;31(4):291-304

6. *Mitochondrial dysfunction in the pathogenesis of necrotic and apoptotic cell death.* Lemasters JJ, Qian T, et al. *J. Bioenerg Biomembr* 1999;31(4):305-19
7. *Mitochondria at the crossroad of apoptotic cell death.* Thress K, Kornbluth S, Smith JJ, *J. Bioenerg Biomembr* 1999;31(4):321-6
8. *Mitochondrial redox signaling during apoptosis.* Cai J, Jones DP, *J. Bioenerg Biomembr* 1999;31(4):327-34
9. *Progress on the mitochondrial permeability transition pore: regulation by complex I and ubiquinone analogs.* Fontaine E, Bernardi P, *J. Bioenerg Biomembr* 1999;31(4):335-45
10. *Mitochondrial oxygen radical generation and leak: sites of production in states 4 and 3, organ specificity, and relation to aging and longevity.* Barja G., *J. Bioenerg Biomembr* 1999;31(4):347-66
11. *Mitochondrial genome mutation in cell death and aging.* Ozawa T., *J. Bioenerg Biomembr* 1999; 31(4):377-90
12. *The Release of Cytochrome c from Mitochondria: A Primary Site for Bcl-2 Regulation of Apoptosis.* Kluck, RM, et al., *Science*, 1997, 275(5303):1132-1136
13. *Mutations in SDHD, a Mitochondrial Complex II Gene, in Hereditary Paraganglioma,* Baysal, BE, et al., *Science* 2000, 287(5454):848-851
14. *Mitochondrial respiratory chain disorders I: mitochondrial DNA defects,* Leonard JV, Schapira AHV, *Lancet* 2000, 355:299-304

### **The Development of the Concept:**

A healthy cell is a cell which possesses sufficient energy to carry out its functions and perform its work. Sickness is simply a lack of sufficient energy to carry out the functions of life. While many different kinds of insults and injuries can destroy cells. They do so by depleting its energy or by depleting its ability to utilize energy resources. A cell becomes sick when it does not

have enough energy to carry out its normal functions or is unable to meet the increased energy requirements influenced by various stresses; such a cell can be rejuvenated if its energy is somehow restored, regardless of the initial causes of its problems - cells die simply because they have no energy or life.

The main source of energy in cells comes from a molecule called ATP or Adenosine Triphosphate. Cells convert nutrients and products of metabolism to energy by manufacturing ATP, whose energy resides in high-energy phosphate bonds. As each phosphate is broken off, the bond connecting it to the rest of the molecule provides energy the cell can use for growth, reproduction, muscle contraction or anything it needs to do.

The process of making ATP is carried out in small organisms contained in each cell which are called mitochondria. They are found in every cell in the human body with the notable exception of red blood cells. The more work a cell has to perform, the more mitochondria it has. Mitochondria are generally felt by biologists to be symbionts since they do not share the DNA of the cells they inhabit but have their own DNA.

These endosymbionts, possessing their own DNA, reproduce independently of the cells reproduction and do not participate in the genetic inheritance which characterizes the cells; mitochondrial inheritance is solely by maternal inheritance, being passed to the offspring as a part of the ovum, as the sperm contain no mitochondria.

All aerobic life forms, plant, animal and fungal, contain mitochondria which are very similar.

The mitochondrial DNA of human mitochondria is said to have around 8 distinctive haplotypes which are believed to correspond to 8 human metabolic types.

Recently, Majid Ali shed light thusly:

### **Oxidative Injury to Mitochondrial Ecology<sup>4</sup>**

"Mitochondria play a major role in human energy dynamics (ATP synthesis and related reactions), and a functional deficit may be expected to result in diminished supply of high energy phosphate bonds. In mitochondria, electron transfer is *coupled* to oxidative phosphorylation via a proton gradient, and the energy *released* from oxidation is transferred to the ATP synthase *trapping* system. A class of compounds called *uncouplers* can block electron-transfer-linked phosphorylation at any of the three stages (energy production, transfer, or trapping). Redox reactions may release free energy ( $\Delta G$  negative). Such energy may be dissipated as heat, as indicated earlier, or be trapped as a proton gradient. Whether energy is dissipated or trapped depends on the characteristics of biologic membranes rather than on the reaction itself. Any substance that allows protons to leak across membranes will play an uncoupling role, since it will block the transfer of energy between electron flow and ATP synthesis.

More than 90% of the oxygen used in the human body is utilized by mitochondrial cytochrome oxidase, which transfers four electrons into an oxygen molecule to produce two molecules of water. Under ordinary circumstances, reduction of oxygen by cytochrome oxidases in the above reaction does not release active oxygen radicals. This is assured by transitional metal ions such as iron, copper, vanadium, and titanium, which are carried in the active sites of cytochrome oxidases. Such metal ions occur in variable states of oxidation, and changes in such states facilitate transfer of single electrons in an orderly fashion in which various partially reduced forms of oxygen are held bound to the metal ions. These ions also play essential roles in spontaneous oxidation (autoxidation) of several nonradical compounds including ascorbic acid; thiols such as cysteine, homocysteine, and reduced glutathione; catecholamines such as epinephrine and norepinephrine; and a host of amines such as 3,4-dihydroxyphenylalanine (DOPA) and 6-hydroxydopamine.

Deficits in mitochondrial function arise by two mechanisms: (1) a block in electron flow or ATP synthesis which results in lactic acidosis; and (2) uncoupling electron flow from ATP synthesis (Luft's syndrome) in which oxidation occurs at a rapid rate but without a concomitant increase in ATP synthesis (energy released is dissipated as heat). In both conditions, mitochondria increase in numbers and are often deformed, and the muscle cells show ragged red fibers. Surprisingly, ATP measured in muscle tissue in such cases is often near normal; however, there is a marked reduction in creatine phosphate  $P_i$  ratio--from a normal value of 9:1 to 1:1 in some affected individuals.

Human mitochondrial DNA (mtDNA) is about 16,000 bases long. Of the 13 polypeptides that it encodes, six are for NADH dehydrogenase, three for cytochrome oxidase, two for ATP

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<sup>4</sup>Ali, Majid, Oxidative Regression To Primordial Cellular Ecology, J. Integrative Medicine, 1998, 2:4-55

synthase, and one for cytochrome bc<sub>1</sub> complex. Point mutations in mtDNA of various degrees occur with predictably variable results, so that some cells may be produced with normal and others with defective mitochondria. For example, in one such mutation a defect in NADH dehydrogenase results in a block in electron flow from flavin to quinone and leads to fatal infantile myopathy. Other variants of mitochondrial malformations and malfunctions lead to certain types of cardiomyopathy, ophthalmoplegia, and encephalopathy. In Kearns-Sayre syndrome and related disorders, many body organs are clinically affected; however, in some cases, clinical symptomatology is limited to the skeletal muscle (fatal infantile myopathy) and brain (Leigh syndrome).

Oxidative mitochondrial injury leads to disturbance of cellular energy metabolism. Persistently elevated lactic acidosis levels indicate accelerated mitochondrial injury. Direct and indirect evidence that such injury is oxidative in nature may be drawn from the following: Reduction of mtDNA content, increased lactic acid production, and loss of mitochondrial cristae (indicating oxidatively-induced mitochondrial dysfunction) occurs when mitochondria are exposed to oxidizing influence of a variety of drugs. Bryostatin, a novel antineoplastic agent and protein kinase activator, causes myalgia by two mechanisms: 1) oxidative impairment of energy metabolism and 2) delayed proton washout from muscle indicating vasoconstrictive action. Norepinephrine and ADP stimulate Mg<sup>2+</sup> efflux from intact cardiac myocytes and mitochondrial respectively. It has been proposed that direct hormonal regulation of myocardial Mg<sup>2+</sup> plays a regulatory role in homeostasis. However, evidence for that remains inconclusive.

In McArdle's disease (myophosphorylase deficiency), impairment of glycogenolysis leads to exercise intolerance and exercise-induced myalgia--exercise related changes that are similar to CFS and fibromyalgia. The half-time for intracellular ADP recovery, an indication of maximal mitochondrial oxidative phosphorylation, is abnormally low in McArdle's disease and, predictably, will be shown to be low in CFS and fibromyalgia. Activities of respiratory-chain enzymes containing mitochondrial DNA (mtDNA)-encoded subunits are impaired in a patient with progressive weakness of extremities. In another 16-year-old with cytochrome c oxidase deficiency, high lactic acid levels indicated mitochondrial enzyme dysfunction.

In the past, the histologic and metabolic studies of mitochondrial function in CFS have been deemed inconclusive. However, recent studies show clear evidence of structural and functional derangements of mitochondria in the ORPEC state. Recently, Eisenger and colleagues reported glycolysis abnormalities in fibromyalgia. Plioplys and Plioplys described electron microscopic observations of muscle mitochondria in CFS patients. Vecchiet et al reported reduction of some mitochondrial enzyme activities, inversion of cytochrome oxidase/succinate dehydrogenase ration, increments of common deletion of 4977bp, mitochondrial pleio/polymorphism, and "monstrosity" of mitochondria in CFS. Other lines of evidence for mitochondrial injury include damage observed with laser scanning confocal microscopy. It seems highly likely that further investigations into this matter will disclose additional evidence of mitochondrial dysfunction in clinical syndromes associated with the ORPEC state."

In 1997, Douglas C. Wallace of Emory University noted:<sup>5</sup>

"Increasingly, mitochondrial diseases are recognized as a relatively common cause of degenerative diseases in both children and adults. While the role of mitochondria as the power plants of the cell has been understood at the biochemical level for decades, the role of mitochondrial defects in human disease has only recently been recognized. The delay in recognizing the importance of mitochondrial disease is the result of their variable and complex signs and symptoms as well as the novel genetics and atypical inheritance of mitochondrial defects.

The mitochondria generate energy by breaking down carbohydrates and fats through a chain of chemical reactions. Since each organ in the body relies on mitochondrial energy to a different extent, the nature and severity of symptoms vary widely in patients, depending on the specific mutations in their nuclear and mitochondrial genes. Indeed, since the percentage of mutant mitochondrial DNAs ...can differ among individuals in the same family and even among tissues of the same individual, the same mitochondrial DNA mutation can cause different symptoms even in members of the same family.

Though all tissues make and need mitochondrial energy, the areas of the body that are most reliant on mitochondrial energy are the central nervous system (brain and spinal cord), heart, skeletal muscle, endocrine systems (glands like the thyroid and pancreas) and kidneys. By their effects on these areas, mitochondrial diseases can cause certain forms of blindness, deafness, dementia, movement disorders, epilepsies, seizures, heart disease, muscle disease, diabetes and kidney problems.

Moreover, depending on the gene involved and the severity of the mutation, mitochondrial diseases can affect people of all ages, from newborns through adulthood. Well-known mitochondrial diseases of children are Leigh's syndrome, cardiomyopathy, and medium-chain acyl CoA dehydrogenase (MCAD) deficiency. Typical mitochondrial diseases of young adults include Leber's hereditary optic neuropathy and Kearns-Sayre syndrome. Mitochondrial defects have also been implicated in more common diseases such as diabetes, dystonia, and Alzheimer's disease ...In fact, it has been suggested that mitochondrial DNA mutations accumulate with age in the different tissues of our bodies, progressively eroding energy production, and playing an important role in the progression of degenerative diseases and in aging.

Mitochondrial diseases, while only lately identified, are not rare. They may be an important component of some of the most common degenerative problems which plague our society. It is vital that this important new mechanism for disease be actively investigated and understood so that mitochondrial disorders can be routinely considered when diagnosing acute diseases of the newborn as well as the progressive disorders of aging."

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<sup>5</sup> Wallace, Douglas C. of Emory University, *Exceptional Parent*, Vol. 27, No. 6, June 1997:

Dr. Wallace recently expanded these remarks, as follows:<sup>6</sup>

### **Somatic mtDNA Mutations in Aging and Cancer**

"The delayed onset and progressive course of mitochondrial diseases suggests that mitochondria function may decline with age. This hypothesis is supported by multiple reports of age-related declines in primate mitochondrial oxidative phosphorylation enzyme activities in skeletal muscle, liver and brain, and the associated accumulation of somatic mtDNA rearrangements in these same postmitotic tissues. For example, polymerase chain reaction (PCR) experiments have shown that skeletal muscle from human subjects under the age of 40 contains primarily intact mtDNAs, whereas skeletal muscle from subjects over the age of 50 shows an accumulation of a wide array of mtDNA rearrangements. In addition, the skeletal muscle of elderly subjects has been found to have RRFs, with each COX<sup>-</sup> and SHD<sup>+</sup> fiber containing a different mtDNA mutation. This confirms that each of the mutations arose de novo and was selectively amplified within the cell to create the regional respiratory defects.

Somatic mtDNA mutations also occur in the brain. Quantitation of the common 5-kb mtDNA deletion has shown that mtDNA deletions accumulate markedly in the basal ganglia and various cortical regions in humans after age 75. An analogous age-related accumulation of somatic mtDNA rearrangements also occurs in mouse tissues, the extent of which is proportional to life-span rather than absolute time.

The cause of the somatic mtDNA mutations is likely to be oxidative damage, which increases with age in the mtDNA of both man and mouse. Patients with chronic ischemic heart disease, which is associated with cyclic bursts of mitochondrial ROS during ischemia and reperfusion, have been found to harbor 8 to 2000 times more mtDNA deletions in the heart than age-matched controls. Similarly, cortical mtDNA deletion levels are elevated in patients with Alzheimer's and Huntington's disease, and mtDNA from the former group shows increased oxidative damage.

These observations have led to the hypothesis that somatic mtDNA mutations accumulate in postmitotic tissues with age as a result of mitochondrial ROS damage. The resulting age-related decline in oxidative phosphorylation would ultimately degrade the tissue's bioenergetic capacity until it falls below a certain threshold, resulting in symptoms and senescence. This same age-related decline in oxidative phosphorylation could interact with inherited mitochondrial defects, which would account for the delayed onset and progression of mitochondrial diseases.

Somatic mtDNA mutations have also been identified in various tumors and tumor cell lines. These mutations include intragenic deletions, missense and chain-termination point mutations, and

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<sup>6</sup>Wallace, Douglas C., Mitochondrial Disease in Man and Mouse, Science, Vol. 283, pp 1482-1488, 5 March, 1999

alterations of homopolymeric sequences that result in frameshift mutations. In principle, these mutations could contribute to neoplastic transformation by changing cellular energy capacities, increasing mitochondrial oxidative stress, and/or modulating apoptosis.<sup>7</sup>

As can be seen from a review of the rapidly growing literature on Mitochondrial Diseases, quite a few diseases which are due to mtDNA deletions are manifest in infancy and early childhood, as syndromes, some of which are rapidly fatal, some of which can be treated. These distinct syndromes can be and should be treated in centers where this is diagnosed and treated. On the other hand, there is a growing awareness of much later onset of mitochondrial diseases which are due to decline in mitochondrial function with age due to mutations or to toxic influences with mitochondrial processes, or deficiencies in oxygenation due to repeated episodes of ischemia and reperfusion which lead to generation of Reactive Oxygen Species and other free radicals which can lead to mitochondrial damage and decline in mitochondrial function.

To distinguish these from the infant and early childhood diseases, we call these acquired mitochondrial diseases and disorders.

These acquired mitochondrial dysfunctions which lead to degeneration of tissues and organs can be treated, reversed and prevented by regenerative therapies on an outpatient basis.

The relatively slow onset of some of these disorders, due to a gradual diminution of tissue oxygenation rather than the abrupt onset of ischemic disorders, leads to damaging of tissues rather than the apoptosis seen after ischemia and reflow. The affected cells become dormant; their metabolic fires banked and slowly smoldering rather than amply oxygenated. Such dormant cells

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<sup>7</sup>This is also addressed in another paper by Dr. Wallace and others in 1995 - Wallace, D.C., Shoffner, J.M., Trouce, I. et al 1995. Mitochondrial DNA mutations in human degenerative diseases and aging. *Biochem. Biophys. Acta* 1271:141-151.

can be brought back to normal or near normal function by appropriate measures.

Examples of such dormant cells are found in macular degeneration which can be reversed by electro-magnetic therapies; the penumbra surrounding infarcts in strokes which can be and are restored to function by hyperbaric oxygen therapy which avoids the excitotoxin induced apoptosis of reflow by supplying oxygen to the tissues, and the reversal of cardiac myopathy by pulsed electromagnetic therapy.

Antibiotics which attack bacteria and arrest their growth can have a profound effect on the structure and function of some of the mitochondria of the cells. Oral antibiotics affect not only mitochondria but also the gut flora adversely. This causes a dysfunctional gut ecology which in its turn allows toxins to reach the cells of various systems and interfere with mitochondria function.

Mitochondrial DNA encodes for the production of a number of proteins which are essential for carrying out oxidative phosphorylation. The production of these proteins is being studied by genetic biochemists who routinely utilize common antibiotics to block such protein processing. Some of the antibiotics used are chloramphenicol, tetracycline, and erythromycin. Other chemicals are capable of acting as uncouplers of phosphorylation, i.e., sodium fluoride, which in many places is routinely added to the drinking water.

Synthetic compounds such as drugs, herbicides, pesticides, fertilizers or industrial pollutants are capable of interfering with or interrupting the life processes of mitochondria. These are routinely dumped into the aquifer from which they find their way into the human digestive system and eventually reach the mitochondria to disrupt mitochondrial function.

Antibiotics are singled out here along with fluoride as examples but there are thousands of synthetic compounds used therapeutically and industrially which are capable of affecting the

structure and function of mitochondria by interfering with the production of energy (ATP) as well as causing the generation of Reactive Oxygen Species and other free radicals.

Many food additives used to extend the shelf life of processed foods may be capable of producing such damage to the mitochondria as well.

Meats frequently contain the residues of antibiotics which are included in the feed. Some of these antibiotics' residues remain in the meat along with hormones used for promoting growth. When these reach the human digestive system, where bowel dysbiosis exists, they may easily reach the blood and then are carried to organs to the mitochondria of the cells.

The healthy cell is in what Szent-Gyorgi termed the  $\beta$  or oxidative resting state, producing abundant energy for its work through oxidative phosphorylation, and the electron transport chain of the mitochondria; when something interferes with this oxidative function to decrease energy production significantly, the cell begins to revert towards the  $\alpha$  state, an anaerobic state. When it does so, it loses its functions and is barely able to maintain its structure. It may revert completely to the primordial state and resume the incessant mitosis characteristic of malignancy, or it may not reach that state and simply become dormant.

There is always the possibility that it can be returned to the healthy oxidative state and sometimes this occurs spontaneously.

#### THE NATURE OF CANCER AS A MITOCHONDRIAL DISEASE

Mitochondria have a large number of complex functions in the body, far beyond their role of producing energy. We also know that these endosymbionts possess their own genome, which is far less protected than is the genome contained in the nucleus and far more vulnerable to environmental toxins and pollutants than is the nuclear genome. We now know that when the

mitochondria become unable to adequately perform their functions, the cells will either die, become dormant, or undergo malignant transformation. The possibility exists to cause such cells to revert to normal aerobic cells, capable of normal function. This can be accomplished in a number of ways.

The allopathic approach has been to kill such cells rather than attempt to reconvert them to normal function. This has been consistently unsuccessful and, quite often, kills the patient rather than the tumor.

Anything which inhibits the production of antioxidants will eventually cause cancer or some other degenerative disease. Anything which promotes the production of antioxidants will help to prevent cancer and other degenerative diseases. Because of this realization, the use of antioxidants is becoming the medicine of the 21st Century.

Many of the traditional non-allopathic cancer therapies can now be understood in light of their activity as antioxidants and ability to promote antioxidant activity. The anticancer effects of a large number of herbs can be understood because of their activity as antioxidants.

The key to interruption of the function of mitochondria is through free radical damage to the mtDNA or other structures in the mitochondria. The proper antioxidants or combination of antioxidants and methylation enhancing factors would logically be therapeutic.

Most of the potent antioxidants are plant derived, and these make up an important part of the total antioxidant defense system. The antioxidant properties may be from vitamins, minerals, or compounds which possess the free radical scavenging property or promote the metabolic pathways of compounds which do have antioxidant properties.

For a supply of such antioxidants and the constituents which make them up, humans are

dependent on the foods they consume, which increasingly do not contain all the nutrients they should. Foods are processed by adding chemicals which have very deleterious effects on the body. It is generally necessary for all Americans to supplement their food intake with the vitamins, minerals and other non-nutritive components of foods in order to ensure that they have an adequate supply of antioxidants and the components which make up antioxidants. People should avoid some modern processed foods which contain deleterious substances.

Mitochondria age due to pollution-caused deletions and other mutations to their DNA or to the Nuclear DNA which encodes mitochondrial proteins. These mutations are due to free radicals produced in the mitochondria as a result of interference with the function of the complexes which transport electrons to produce ATP and, ultimately, combine with oxygen to produce water.

The high rate of cancer and coronary heart disease in the United States and other wealthy nations is largely due to industrial pollution and extremely high intake of pharmaceuticals, both prescribed and over-the-counter. All of these elements have the property of blocking or inhibiting some natural biochemical process in the body. In poorer nations with much less access to such drugs, the cancer rate is much lower.

The extremely high death rate from cancer is due to the toxic and ineffectual use of chemotherapy agents to aggressively treat cancers.

Cancer is one disease which manifests itself in different organs and tissues. It invariably results because of a breakdown of antioxidant defenses and free radical damage to the mitochondria of the cells making up the affected organ or system. Clumps of malignant cells may develop daily but are reversed by the body's immune system. Such small foci of malignancy may be routinely detected in CSCT scanning, and their spontaneous appearance and disappearance seems to be a

normal part of the body's functions. Those which occur and are not reversed become clinical cancers.

Since the appearance and spontaneous disappearance of small clumps of malignant cells produces no symptoms, and is generally unnoticed unless the individual undergoes some sort of electromagnetic scan, the precise incidence and rate of this is not known. There are thousands of recorded and reliably reported instances of the spontaneous remission of larger tumors which regressed without treatment. Many malignancies for years have been detected first at autopsies of individuals whose deaths were from unrelated causes.

Hundreds of thousands of individuals have been successfully cured of cancer at unorthodox cancer clinics, both in the United States and offshore. These cancers were reversed and their reversal resulted in return of the affected tissues to normal function.

Unorthodox cancer clinics rarely publish statistics concerning the cure rate. When they do, these are not published in the peer reviewed periodic literature. The only statistics available are those of clinics utilizing orthodox cancer therapies and these increasingly are dismal for most cancers.

The single most productive result of cancer research was the publication of the National Research Council's report on *Diet, Nutrition and Cancer*. This shed some light on the problem, and led to a considerable line of research into the role of nutrition and nutrients in both the causes and means of curing cancer.

The information that many foods, i.e., the cruciferous vegetables such as cabbage, broccoli, Brussels sprouts, all of which contain substances known as Beta Isothiocyanates, have a profound preventive effect on the development of cancer in those who regularly consume them. These

compounds are also highly effective antioxidants.

Ongoing research has discovered many other foods and food components which also have considerable antioxidant properties, such as Alpha Lipoic Acid, Cysteine, Glutamine, Methionine, N-Acetylcysteine, Pectin, Quercetin, Hesperidin, Diosmin, Resveratrol, Elegendic acid, Curcumin, Cinnamic acid, Lutein and Zeaxanthin, Lycopene, Coenzyme Q-10 and DHEA.

There are different species of free radicals, and each of these requires different types of antioxidants to scavenge and control them. The body has an integrated system of antioxidant defenses, to suppress the various free radicals and this system is dependent on a variety of antioxidants and the nutritional precursors to antioxidants. This system can generally function adequately, but its operation can be interfered with by the buildup of toxins from environmental pollutants, food additives and therapy with pharmaceuticals. All of these may have an inhibitory and blocking effect on the processes responsible for mounting the antioxidant defense.

Prevention of cancer depends on two elements: the intake of the proper nutrients to act as a build-up of antioxidant defenses and the avoidance of chemicals and substances which can interfere with the antioxidant defense and lead to the excessive generation of free radicals capable of damaging and interfering with energy production in the mitochondria.

There is a form of liver cancer which at first seems to be connected to the virus which causes Hepatitis C. This disease produces cirrhosis in 50% of its sufferers and 10% of the sufferers go on to develop liver cancer. It is apparent that the cancer is not the direct result of the virus but of the disturbed liver metabolism resulting from the viral infection.

The immune system is believed by the Allopathic research establishment to consist of cells which destroy malignant cells by ingesting them. These cells contain a large amount of NADH

oxidase, an enzyme which promotes the antioxidant system. It may be that these cells, rather than destroying cancer cells, may be energizing them with their antioxidants, to help them return to normal function. Worn out cells are, phagocytized in the body by macrophages.

In 1997, Drs. L.C. Clark, O.F. Combs, Jr., B.W. Turnbull and others for the Nutritional Prevention of Cancer Group, published a Study in the Journal of the American Medical Association (227:1957-1963) reporting the results of a study of over a thousand people who consumed 200mcg Selenium in a high selenium yeast tablet daily for ten years. This was a controlled study, in which a comparable group of people who did not consume the selenium supplement was studied as well.

In the group taking the daily selenium supplement, there was a 37% drop in all cancers, and a 50% drop in cancer deaths, 46% fewer cases of lung cancer, 67% fewer cases of esophageal cancer, 62% fewer colon cancers and a 72% reduction in prostate cancer, as compared to the control group during that 10 years.

The primary antioxidant effect of Selenium is that it is a precursor to Glutathione Peroxidase. Selenium supplementation produces a 33% increase in glutathione activity. Whether or not this property was responsible for the reduction in cancer incidence observed in these studies, it certainly played a significant role in it.

This takes us back to the original Warburg Hypothesis of the 1950's in which Dr. Warburg and his co-workers first elucidated the cancer cell as an anaerobic throwback and to Albert Szent-Gyorgi's elucidation of malignancy as a reversion to the primordial state (Alpha State) from the oxidative or Beta State of normal function and validates these concepts by providing the information about the nature, etiology and function of mitochondria.

Antioxidant therapies will not, of course, cure every cancer patient; there are other factors in

the causation of cancer which cannot be addressed at the cellular level.

Most people with cancer, who genuinely want to be cured of the disease, can be cured with antioxidant therapy and the avoidance of the exposure to chemicals which interfere with the antioxidant defense system if the disease has not progressed to the point of incurability.

Patients who have undergone unsuccessful allopathic radiation and chemotherapy will be more difficult to treat and cure than those who have not undergone such assaults. Many of these people can be cured in unorthodox cancer clinics which employ one species or another of detox and antioxidant treatments.

There is absolutely no validity to the allopathic approach of using toxins to cure what is a toxic disease. Two toxins generate toxicity in a geometric progression. The only way to cure cancer is to rid the body of its toxic load and this simply cannot be accomplished by adding more toxins to the mix.

The human body has a very effective set of defenses against toxins. For millennia, it was fairly effective in a natural world where the toxins it encountered were themselves natural. The human body was not designed to deal with a world as loaded with artificial and synthetic toxins as the world has become over the past fifty years.

Dr. Allen J. Leibermann of Charleston S.C., in his Foreward to Krohn, et als "The Whole Way to Natural Detoxification", Pt. Roberts Washington, Hentley & Marks (1966) remarks:

"Everyone realizes that our planet is increasingly polluted, but few recognize that humans are the final resting place for many of the toxic substances and materials to which we are exposed. Even fewer know what can be done to reduce the body's burden of toxins or xenobiotics, through a process known as detoxification. The population of the earth is faced with an increasing risk from toxic chemicals and physical forces, and now more than ever, humans may be facing a race between knowledge and extinction".

The rise in the incidence of cancer and deaths from cancer not only parallels the rise in the development and use of toxic chemicals and materials in the environment, but also toxins in our food and water supplies and pharmaceuticals ingested by the ton. The rise in cancer incidence and deaths is directly caused by such toxic ingestion and the body's increasing inability to cope with this toxic overload of xenobiotics. Not only has allopathic medicine failed to realize this, but its very therapeutic system is the source of the ingestion of a large part of this toxic load. Therefore, allopathic medicine is not only unable to cure cancer, but responsible for the cause of much cancer.

The comments of Dr. James F. Balch in his recent treatise "The Super Antioxidants", New York, M. Evans & Co. (1998), state the problems succinctly:

"Normally, enzyme free radical-scavenging activity occurs in every cell, but there are specific factors that may enhance or subdue this activity. The first of these factors to consider is the *total burden* of free radicals the body confronts. General Custer's troops lost the battle at Little Big Horn for a simple reason: too many Indians. In the same way, the limited number of antioxidants in your body can be overrun by too many oxidants. Free radicals are generated continuously, so it is essential to provide the cells with the best possible conditions for dealing with them. For each cellular component there is a specific concentration that must be reached before cellular damage occurs. Given the right circumstances, the activity of free radical-scavenging enzymes maintain free radical concentrations below this minimum toxic concentration (MTC). The safety margin between free radical concentration and the MTC is wide, but that safety margin decreases as the total free radical burden increases. The more oxidation occurring in a cell, the less efficiently the body is able to control it.

Genetic regulation is another factor that controls both the absolute quantity and the efficiency of each free radical-scavenging enzyme. Each individual has a different capacity and rate of scavenging free radicals. Patients with genetically low absolute concentrations of free radical-scavenging enzymes are more susceptible to free radical damage at the cellular level. Consequently, they are more susceptible to free radical induced or mediated disease. This is one reason why longevity, certain diseases, and a specific rate of aging can be seen in families. Often it is equally evident that one family member ages more rapidly or has more disease and breaks the pattern because of tobacco and/or alcohol use. In such a case, that individual's

ability to deal with oxidation was the same as the other family members, but his or her intake of oxidants and antioxidant inhibitors was greater.

Nutritional status can decrease free radical-enzyme scavenging activity. Your body needs what it needs. You can't expect to be deficient in some vitamin or mineral and not be affected by it. Marginal vitamin deficiencies, particularly of vitamins C and E, can decrease the cell's ability to scavenge free radicals. Even cellular depletion of certain trace elements leads to decreased free radical-enzyme scavenging activity. Conversely, adequate amounts of these elements lead to efficient antioxidant functioning. These trace elements are essential cofactors for the synthesis and proper functioning of the free radical-scavenging enzymes. We have already mentioned selenium as a cofactor necessary for the production of glutathione peroxidase. Organic iron is needed for catalase to do its job. Inappropriate nutrition can lead to marginal deficiencies in some of the cofactors necessary for maximum free radical-scavenging activity. But even marginal deficiencies can lead to devastating effects if oxidation is not controlled.

Drug therapy affects enzymatic antioxidant systems in two ways. First, drugs, prescription or otherwise, can produce marginal deficiencies of trace elements by depleting cellular trace element concentrations. Also, drug metabolism can increase the total burden of free radicals. Increases in the total burden of free radicals often occur during drug administration. Most drugs are intended to shock the system into fighting certain symptoms, but this shock tends to pull trace elements away from their normal function and increase oxidation. Free radicals then are produced by almost all drugs as they are metabolized into less toxic compounds. For example, Adriamycin is an anticancer drug that is highly toxic to the heart because of the oxidative stress it creates. But Dr. Horie has found that the antioxidant properties of aged garlic extract nullifies its threat to the heart without interfering with its intended cancer-fighting properties. Therefore, drug metabolism places an excessive free radical load on the capacity of an individual's system of free radical-scavenging enzymes and depletes its ability to deal with that load.

Environmental factors can also increase the total burden of free radicals. Pollution, secondhand smoke, emotional stress, and many other factors may increase cellular oxidation. Any sudden excessive increase in the total burden of free radicals that is secondary to therapeutic, dietary, or environmental factors can lead to free radical cell membrane damage. Radiation, in the form of electromagnetic fields, is unavoidable in our culture ruled by computers, microwaves, and high-tension power lines. Even the radiation from sunlight increases oxidation. Pesticides and other contaminants in our food sources and water significantly affect the diseases prevalent here as compared to countries with simpler farming methods. Many of these environmental factors can be controlled if we are aware and take appropriate measures, like drinking purified water. Other factors cannot be

controlled, and the oxidation they cause must be accounted for in our supplementation.

All of the factors listed above can alter the efficiency of the free radical-scavenging systems. Regardless of the underlying cause, when the minimum toxic concentration (MTC) is exceeded, cellular damage occurs and the patient will ultimately exhibit clinical symptoms of the disease process. Which disease shows up will be determined by which enzyme system within which organs have failed and where the toxic concentration is. This means it is absolutely necessary to see to it that the system has everything it needs to function properly.

These enzyme-scavenging systems are designed as a fail-safe system to prevent the formation of hydroxyl radicals. Since there is no enzyme to scavenge the hydroxyl radical, failure of the free radical-scavenging system places more of a burden on other systems to rid the body of this toxin. The success of the enzyme system is dependent on a number of factors, including the presence of adequate amounts of selenium, glutathione, and glutathione reductase. When these factors are absent in a given patient, the probability that the patient will develop free radical-mediated disease increases significantly."

The average American is always gulping pills which control his or her muscle aches and pains, mask fatigue and depression. The average American has been brainwashed into believing that not only are pharmaceuticals generally harmless, but they are good for what ails you. A person cannot watch two hours of network TV without exposure to a half-dozen pharmaceutical ads. No one wants to believe that the family doctor is misguidedly prescribing poisons which can cause and contribute to the development of degenerative diseases.

There is the thought that surely the FDA wouldn't approve these drugs if they can cause or contribute to cancer - after all we have the DeLaney laws about carcinogenesis.

No one at the FDA has ever given the slightest thought to what effect the pharmaceuticals they regulate have on free radical production or whether or not they promote or inhibit antioxidant activity. Their purpose is the regulation of allopathic drugs. This is the same agency which routinely approves the addition of toxins to the food supply as preservatives.

Nevertheless, the person with cancer who will not stop ingesting synthetic pharmaceuticals will probably not be successfully cured with antioxidant therapy. There are natural alternatives for all pharmaceuticals.

People with cancer who feel they must consume alcoholic beverages should switch to moderate intake of red wines which have potent antioxidant properties.

Most foods containing antioxidants can be eaten raw. There are a few exceptions such as cooked tomatoes which are a rich source of Lycopenes, but raw tomatoes yield only a small fraction of the Lycopenes; Brussels sprouts have very decided antioxidant contents but this is obtainable only from cooked Brussels sprouts and not from those which are raw.

While fresh fruits and vegetables are important and have formed the basis for several successful cancer treatment diets, some considerations should also be given to the important nutritional and antioxidant aspects of soy and whey protein concentrates in anti-cancer diets. Soy products contain the isoflavonoids genisten and diadzen which have been shown to prevent prostate cancer, whey proteins are rich in glutathione and other amino acids which promote antioxidant metabolism.

The treatment program of Dr. Donald J. Kelley and later of Dr. Nick Gonzales for the treatment of pancreatic cancer was based upon the prescription of diets tailored to the patient's metabolic type. 100% of the patients who followed this program were cured of pancreatic cancer which is usually considered a fatal and untreatable condition.

There are reports from anthropologists who use mitochondrial DNA typology to trace the development and migration of humans throughout the world. There are 6 to 8 different DNA haplotypes in mitochondrial DNA, and these may have a lot to do with the individual's metabolic

type.

Diet, for people with cancer, should be prescribed by the treating physician based upon the individual's metabolic type as determined by trace mineral hair analysis.

The body's natural means of detoxification are through the liver, the bowels, the kidneys, the skin, and the respiratory system.

One of these which does not appear to have received much attention in cancer therapy is the kidney - recent reports from Nephrologists and Urologists indicate that one of the consequences of end-stage renal failure is the development of widely disseminated cancers in such patients, which may be caused by the accumulation of toxins ordinarily removed from the body by the kidneys.

Some herbs and hot water baths have the effect of promoting renal output. Since kidney cells are dependent on mitochondrial function, decreasing the total toxic load could conceivably influence renal function. Synthetic diuretics such as Lasix should be avoided but natural diuretics might well be helpful. Increasing water intake is helpful because many of the elderly are dehydrated. Non-steroidal Anti-Inflammatory Drugs, particularly Tylenol, should be strictly avoided by cancer patients because of its damaging effects on the kidney.

Cancer, as a disease, has a large spiritual and psychological component which is extremely difficult to address on an outpatient basis. Since socialization of cancer patients with each other has a profound effect on the outcome of treatment. This as well as the dietary component of cancer therapy are difficult to achieve on an outpatient basis for a large number of patients. Diet therapy should consist of more than handing a patient a list of foods they should or should not eat as a part of their treatment.

This problem is solved in a number of cancer clinics where the patients are fed three meals

per day at the clinic which insures that the patients get the proper diet as well as some occasions for socialization during meals.

These patients undergo an intensive course of treatments of 6 weeks to 3 months duration, during which they are treated on a daily basis, and spend 8 to 10 hours of the day at the clinic.

As in all mitochondrial diseases, the first step is detoxification. The second step is nutritional supplementation along with herbal and homeopathic support. Energy treatments, such as the Sodi Pallares protocol, as well as chiropractic, acupuncture and massage are all helpful. The next step is oxidative therapy with ozonized water baths.

In cancer treatment, metabolic typing and classification should be the beginning point for the initial workup and appraisal of every patient. The metabolic type can be determined accurately by hair analysis and such tests are routinely done during the first visit, along with a dietary history.

Mitochondrial DNA genotyping is a new technology which is proving to be important in understanding the individual's metabolic inheritance and capabilities, nutritional needs and is an important adjunct to hair analysis in detecting the diseases to which the individual may be prone to develop as well as preventive means to avoid these.

Energy medicine has been around for many decades. Oriental Medicine, Acupuncture, and Homeopathy are current forms of energy medicine.

Magnets have been used for centuries as treatments. Electricity was widely used from 1880 until about 1910, when "medical science" declared it to be quackery.

In the past two decades, Acupuncture and Homeopathy have been merged by the development of electroacupuncture, sometimes known as electrodermal testing, now commonly used by physicians, Chiropractors and Acupuncture practitioners.

Electromagnetic devices such as EAV are able to read signals from the acupuncture meridians. These signals originate from the ATP polarized cells of each organ and travel to the surface of the skin along well-defined meridians or pathways in the form of electrons. The strength of the signal can be determined by the operator who is able to test the response of the body to certain substances placed in the circuit of the device. In this way, problems in the body's energetic fields can be diagnosed and treated by Homeopathy, Herbs and Acupuncture techniques.

Very small electromagnetic vibrations can be very effective in treating problems which have a decreased energetic component. The art and science of such energy medicine is beyond the scope of understanding of "medical science" but is well understood by quantum physicists, acupuncturists and homeopaths.

Such energetic therapeutics have proven effective in restoring sight to sufferers from Macular Degeneration. This is a disorder for which "medical science" has no effective treatment, but which responds quite readily to energy treatments. Several other diseases which have no effective pharmacological treatment have been shown to respond well to the application of small electromagnetic vibrations applied to the body. The use of energy medicine shows great promise for the treatment of those chronic degenerative diseases which respond so poorly to pharmacological treatments.

### **Infectious Disease Resurgence**

In America we once naively believed that "medical science" would wipe out all of the infectious diseases which had plagued the human race through the use of antibiotics. The antibiotics failed and antibiotic resistance has caused the re-emergence of new and more virulent infections which are difficult to treat in today's world. Several bacterial and viral infections are

prevalent in the American population today.

### **Hepatitis C Infection**

It has been estimated that one in six Americans has an active viremia which will ultimately become manifested as Viral Hepatitis A, B, C, D, or G. The most pernicious is Hepatitis C, which has a relatively long period of asymptomatic development.

Patients with Hepatitis C are frequently found to have circulating autoantibodies and several immune mediated extra-hepatic manifestations of the virus have been reported including polyarteritis nodosa, thyroiditis, anemia, dermatitis, sicca syndrome, and non-Hodgkin's lymphoma. The extrahepatic manifestations that are most clearly associated with Hepatitis C infection are glomerulonephritis and mixed essential cryoglobulinemia.

Since there are now some newly developed effective treatments for viral hepatitis which may be able to eradicate the disease during the three decades long period between its contraction and the appearance of incurable damage, it would be advisable for testing for this disorder to become a routine part of comprehensive health assessment.

### **OVERVIEW OF CLINICAL MITOCHONDRIA DETOX, REOX AND EMT IN THE DIAGNOSIS AND TREATMENT OF CHRONIC DEGENERATIVE DISEASE**

Most of the chronic degenerative diseases which are classified by the signs and symptoms they produce may become manifest at various times in the sufferer's life. These manifestations of a common disorder are created by impaired mitochondrial function and a progressive failure in the production of ATP. Because of the failure in the production of ATP in diverse tissues and organs, these tissues and organs began to regress back towards a primordial anaerobic metabolism in which

lactic acid builds up and the mitochondria become either dormant or the cell reverts to a malignant cell.

Some of these cells begin with genetically impaired function due to maternally inherited mtDNA; others acquire dysfunctions from new mutations in mtDNA as well as toxic interference with their function.

With the knowledge that a decrease in mitochondrial function leads to chronic diseases, then the therapeutic approaches should be aimed at restoring mitochondrial function, detoxification and regeneration of the tissues and organs.

Successful treatment of degenerative diseases consists of reversing the core process at the root of these disorders rather than attempting to suppress these diverse symptoms produced by the pathological process one by one as they appear.

It is estimated by the Mitochondrial Disease Foundation that one in every four thousand Americans born each year suffers from an identifiable mitochondrial DNA defect which is manifest at birth or in early childhood.

Well over 60% of Americans will, as they mature and age, acquire one or more mitochondrial dysfunctions through the impact of environmental factors. These accumulate and are eventually manifest by the diseases which are collectively called chronic degenerative diseases, ranging from arthritis, diabetes, cardiovascular disease, loss of vision and hearing, muscular diseases and cancer. These disorders are preventable and are reversible.

The only treatments which offer hope of return to normal function are those which remove the causes of the regression and restore the capacity to return to normal function. These appear to be:

- (1) Detoxification
- (2) Orthomolecular nutrition
- (3) Oxidation
- (4) Pulsed electromagnetic stimulation at an appropriate frequency

These measures have been highly successful in restoring healthy function by restoring the function of the mitochondria.

Detoxification is a multiphase process which involves nutrition. These have recently been described and in detail by Josephine Krohn, M.D. and her co-authors in their book "Natural Detoxification," Point Roberts, Washington, Hartley & Marks Publishers (1996) which constitutes a definitive manual of detoxification procedures.

This manual includes measures for the restoration of normal bowel ecology which is important since the bowel is the route for virtually all the toxins capable of interfering with mitochondrial function. Much nutritional therapy is involved in detoxing processes. Orthomolecular nutrition means a basic diet which is appropriate for the individual's metabolic type. The cancer therapy of William Donald Kelly, one of the most consistently successful alternative cancer therapies developed to date is based largely on this concept. There are certain nutrients which support oxidative phosphorylation and the known antioxidants should be supplied along with the basic diet appropriate to the individual's metabolic type. Appropriate nutrition means not only the intake of nutrients which are correct but also the avoidance of the substances which can and do adversely affect mitochondrial function. The diet, both food and drink, must not contain any of the mitochondrial toxins. The water must be free of any traces of fluoride as well as the hundreds of chemicals which are routinely found in certain water supplies, such as chlorine and

its derivatives. The foods must be free of herbicides, pesticides, inorganic fertilizers, food colors or additives, including those approved by the Department of Agriculture and the FDA for use as food additives. The tolerance for such substances in the treatment of mitochondrial dysfunction is zero. The foods and beverages must not contain aspartame or Nutrasweet - a product which is currently found in over 5,000 commercial foods and beverages. It is reported to cause Multiple Sclerosis and Systemic Lupus, both of which are mitochondrial disorders. When this product reaches a temperature exceeding 86 degrees F. it converts to Formaldehyde and Formic Acid and below that temperature, it metabolizes to methylalcohol. Some of the metabolic type diets include meats - these meats must be free of antibiotic residues; seafoods should be confined to those originating and living well away from coastal waters, particularly waters near the mouths of rivers and inland streams. Seafood consisting of Northern fish should be caught at least 50 miles off shore. Poultry should be of the free-range variety and not that raised in crowded cages and fed antibiotics and other chemicals. Fruits and vegetables should be thoroughly ozonated before consumption to eliminate all herbicide and pesticide residues, as well as to destroy pathogenic bacteria such as E Coli 0157-H7, Salmonella and similar organisms involved in Food-borne Diseases<sup>8</sup>. The toxins produced by such microorganisms can destroy mitochondrial function. All bathing water should be purified by ozonation and not chlorination.

Another highly successful alternative cancer treatment, Essiac Tea, is an herbal detoxification formula. The tea must be brewed from absolutely pure water. Green tea is also reported to be an extremely efficient preventive of cancer - it too must be brewed from absolutely

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<sup>8</sup>See Fox, Nichols, SPOILED: The Dangerous Truth About Food Gone Haywire, New York, Basic Books (1997)

pure water.

Oxygenation: To the methods of oxygenation discussed in Krohn's et al's Natural Detoxification, the safest method of oxygen enhancement is by transdermal diffusion. The individual is immersed up to the neck in a tub of water through which Ozone is being bubbled. This leads to a rapid rise in tissue oxygenation which, reportedly, lasts longer than the increased tissue oxygenation achieved with hyperbaric oxygen and eliminates the drawbacks inherent in HBO. It can be used as often as necessary to maintain high levels of oxygen in the extracellular fluid where it is readily available to the cells, and it avoids problems such as oxy-hemoglobin disassociation shifts.

One pharmaceutical, Dichloroacetate, has been reported to be of any benefit in the treatment of mitochondrial diseases; all other pharmaceuticals should be suspected of being mitochondrial toxins. Some may not be, but until that is reliably established, they should empirically be handled as if they are. All synthetic compounds, those not occurring in nature, and synthesized from petroleum are capable of interfering with mitochondrial function.

Dental amalgam restorations are certainly capable of producing a mitochondrial toxin in the form of methylated mercury. Most other heavy metals should be avoided and where present in fat stores, should be removed by detoxification.

In the regenerative treatment of mitochondrial dysfunctions, if at all possible, pharmaceutical treatments should be replaced by herbal, nutritional, homeopathic or other natural therapies. During and after treatment, the principles of Natural Hygiene should be followed.

There is quite a lot that can be accomplished in this regard. Air and water can be filtered, oxygenated and sometimes electrostatically treated to remove pollutants.

Geopathic stress can be avoided. Bedding can be replaced by air mattresses, which should be placed on wooden platforms to avoid all coil springs and other metallic support which can generate or accumulate electromagnetic frequencies. Some household appliances which generated high gauss magnetic fields can be eliminated. Quartz watches should not be worn on the body. Areas of Geopathic stress should be avoided, particularly for work and sleeping areas.

Acupuncture by a skilled practitioner can support many systems and organs energetically and can be a valuable aid for maintaining good bowel function.

Spinal manipulation by a skilled Chiropractor or Osteopath can be crucial where the nerve supply to organs arises from the spinal nerve as well as the autonomic nervous system, the ganglia of which originate from the spinal nerves. Body work, Rolfing and massage therapies are also valuable.

Psychological and spiritual counselling are of inestimable importance in all treatment programs.

All psychopharmaceutical drugs should be completely avoided in persons being treated for mitochondrial dysfunction, particularly the Selective Serotonin Re-uptake Inhibitors and diazepam derivatives. These can be replaced by herbal remedies such as St. John's Wort. Drugs which alter brain chemistry almost certainly are mitochondrial toxins.

Blood pressure medications can and should be replaced by herbal and nutritional programs when possible.

Non-steroidal anti-inflammatory drugs are absolutely contraindicated in people suffering from mitochondrial dysfunctions.

Carbonated beverages should be avoided, especially those which are sweetened artificially

with Aspartame.

Alcohol should be avoided. If this is not done, the intake should be strictly limited to one ounce of alcohol daily, preferably red wine.

Electromagnetic Treatment: While there are a number of electromagnetic treatments and devices available, the one which appears to be most efficacious for the treatment of mitochondrial dysfunction is the treatment devised and successfully used by Dimetro Sodi Pallares, M.D. of Mexico City.

This treatment utilizes a pulsed electromagnetic pad which operates at 1 to 600 Gauss at 60 cycles. It is used in conjunction with a polarizing solution first developed several years ago by Dr. Sodi Pallares consisting of a high potassium, low sodium glucose solution with insulin.

Using the combination of the solution, pulsed electromagnetic therapy and a high potassium, low sodium diet, Dr. Sodi Pallares has successfully reversed cardiomyopathy, as well as reversed extensive metastatic cancer. Two fairly brief reports from the 4th International Symposium on Biologically Closed Electric Circuits serve to illustrate this:

"This 32 year old female had a history of breast cancer treated by mastectomy. She subsequently developed metastasis to the right hip which failed to respond to radiation and chemotherapy. When first seen in February 1996, she complained of severe pain in several parts of her body, and X-rays confirmed spread of the cancer to the right femur, skull, and both hands and wrists.

She was given polarizing solution twice weekly, pulsed magnetic field therapy for 4-5 hours daily, and started on a low sodium-high potassium diet. After ten days, her pain had significantly lessened, and her strength and energy were considerably improved. Four months later, she was completely free of all complaints, and, as noted below, her X-rays had essentially returned to normal. Unfortunately, this cannot be fully appreciated, since the size of these, as well as the other X-rays in this Newsletter are drastically reduced. This patient now leads a completely normal life, has no pain or any other symptoms and continues her daily

full time working activities as a biochemist.

A 42-year old man had severe heart failure due to cardiomyopathy that was resistant to treatment. A heart muscle biopsy at a leading cardiovascular center confirmed myocardial necrosis, and he was told that unless he had a heart transplant, he would be dead in a few months. While waiting for a donor, he developed increasing shortness of breath, chest pain, and abdominal distention. When first seen, he was in severe heart failure, his heart was tremendously enlarged, and there were numerous abnormalities in his electrocardiogram. After only two weeks of treatment with polarizing solution, magnetotherapy, and diet, all of his symptoms had disappeared, and there was a remarkable reduction in heart size, as can be seen in the following X-rays. Almost four years later, this patient is in excellent health and lives a completely normal life. He continues to follow the diet, but requires no medication."

An additional example of the effects of electromagnetic treatment of degenerative diseases involving mitochondria is the reversal of Macular Degeneration by the use of Electromagnetic treatments using the Transcutaneous Electrical Nerve Stimulation (TENS) device.

Macular degeneration is a disorder of the Rods, Cones and Pigmented Epithelium of the retina in which these cells become dormant, leading to a loss of visual acuity and the accumulation of drusen over the macular area.

Electrical Nerve Stimulation of the macula as a treatment for macular degeneration thusly:

"To create a closed circuit when stimulating the eyelids, a brass cylinder or rod is held in one hand of the patient, and a brass eyelid probe with a shielded handle is held in the other hand. The eye is treated by providing a micro-current to four points on each upper and lower eyelid. When stimulating the upper eyelid, the patient is asked to look downward with eyes closed. Four points are stimulated on the upper lid and lower lid using microamperage between 200 and 250 micro amps. The amperage is brought up until the patient sees light flashes and/or feels the tinge of electricity. It is then dropped until no detectable light or feeling is noted. This is the amperage then used. Each of the eight eyelid points are stimulated for 12 seconds using one of the three frequencies. Each of the eight eyelid points are stimulated for 12 seconds with frequency of 0.3 cycles/second, 9.1 cycles/second, and 30 cycles/second by a .5Hz biphasic pulse.

A square waveform is used on the eye because square waveforms cause

better responses on neural tissue than sloped waveforms.

New patients are treated once a week for eight weeks and once a month thereafter. I feel more frequent long-term treatment would give us even better results.

The Michael-Allen study showed significant stability in the rate of visual acuity loss with the above regimen.

In my case studies, I have found significant visual acuity increases - sometimes 2-3 lines on the Snellen Chart - with patients who just begin to show a rapid drop in vision over 3 to 6 months. Every one of these patients showed an increase in visual acuity after one to two treatments. I will cover case studies later.

I feel that retinal function is lost for a time period before the macula cells are destroyed. *If we can intervene at the time of rapid acuity loss, we can recover significant retinal function.* If we wait too long before treatment, the macula cells are lost and cell function recovery will be minimal.

Normal retinal cell function is a photochemical reaction converting light energy to an electrical impulse which travels to the brain and vision occurs. Diseased, inflamed retinal cells eventually lose cell function, ATP levels drop, protein synthesis drops, the electric resistance goes up and cell electricity potential goes down. The cells seem to go dormant for a time before they die. *If we begin electric stimulation before the cells are lost, we re-establish a more normal cellular electrical potential, ATP levels increase, protein synthesis occurs and normal cell metabolism is restored.* With this, normal photochemical reactions again occur and visual acuity returns.

In 1982, Dr. Ngok Cheng studied the effect of microcurrent on Adenosine TriPhosphate (ATP) concentrations and protein synthesis in mammalian skin. ATP is the source of energy for normal cell activity. It is the carrier molecule for free energy derived from foodstuffs and sunlight. It is necessary for protein synthesis in a cell. ATP supplies the energy for the cellular sodium pump, which removes metabolic waste from a cell and transports metabolic substrates from the blood to the cell.

Dr. Cheng demonstrated the ATP concentration increased by as much as 300% to 400% in cells stimulated with microcurrents between 25 micro amps and 1,000 micro amps.

The electrical resistance of tissue with chronic pathology is higher than that of surrounding normal tissue. Regeneration is a series of endothermic,

electrochemical reactions. Electricity used in minuscule quantities is used by cells to regenerate.

I have found that to restore significant visual acuity, we have only a small window of time to begin treatment before the cells are permanently lost and good recovery of acuity is achievable. We must find and treat these patients at the proper time."

When the oxidative and energy producing functions of mitochondria suffer a loss of the effective function, they have a tendency to regress back toward the primordial state. This regression has been termed Oxidative Regression to Primordial Encoding - ORPEC.<sup>9</sup> The result of such regression is that the cells become dormant, decreasing energy production, becoming unable to function, until eventually, they either die or reach the ultimate primordial state, malignancy. Some cells can remain dormant for long periods of time - for years.

The regression to the primordial state can be reversed and normal function restored. The treatment is generally prolonged and return to normal or  $\beta$  state function can take quite a while to occur, and is being accomplished in progressive centers where Eclectic treatments are employed.

Since each sufferer is individual and possesses his or her own biochemical and electromagnetic individuality and the causes of the degeneration are highly individual, arising from personal lifestyles, experiences and living habits, the treatments must be individualized and treatment must be by a team or staff approach. Few practitioners of any discipline, medicine, chiropractic, Oriental medicine, Osteopathy possess all the skills needed to reverse the degeneration. The patient must be carefully examined, and an exhaustive toxic substance intake history must be taken. Laboratory analysis of blood, hair, urine, stool and other specimens must be

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<sup>9</sup>Ali, Majid Op Cit Fn 4

obtained. The patient's treatment plan must be coordinated by the staff of therapists who will participate, and monitoring of the patients response evaluated periodically.

The treatment's four general phases, must go on simultaneously. Dietary and life style must be changed and a new healthier lifestyle be adopted. If the stage of malignancy is in the later stages, the treatment must be intensive. If the malignancy is at the beginning stages, a less intensive program may be indicated.

The treatments outlined are generic, and the total extent the program is followed is a decision which must be made on a case-by-case basis. The ultimate decision in the end after advice and guidance will be made by the patient or patient's family.

The treatments outlined here are outpatient treatments for chronic degenerative diseases which are not immediately life threatening. The treatment of cancer, in advanced stages, should probably be undertaken at a residential facility.

Over the past seventy-five years, a large number of what are known as Alternative Cancer Therapies have been developed. Many of these have demonstrated to be very effective.

Since the Allopathically-oriented "War on Cancer" began in the 1970s has now been conceded to have been less than successful, a significant percentage of patients have sought and received such alternative therapies with a success rate not completely known, but generally conceded to be significantly higher than has been realized by the allopathic approach.

There are a number of books about alternative cancer therapies currently in press, for the purpose of this discussion, three of these which seem to use an even-handed and analytical approach have been reviewed; these are:

1. Falcone, Ron, THE COMPLETE GUIDE TO ALTERNATIVE CANCER THERAPIES, New York, Citadel Press (1994)
2. Moss, Ralph, CANCER THERAPY, New York, Equinox Press, (1992)
3. Walters, Richard, OPTIONS, THE ALTERNATIVE CANCER THERAPY BOOK, New York, Avery Publishing Group (1993)

These three books cover the following therapies:

Burzynski's Anti-Neoplastin Therapy  
Gaston Naessens 714X  
Revicci Therapy  
Burton's Immune Augmentative Therapy  
Livingston Therapy  
Issels Whole Body Therapy  
Hoxsey Therapy  
Essiac Tea  
Wheatgrass Therapy  
Macrobiotic Therapy  
Moermann's Anti-Cancer Diet  
Gerson Therapy  
Kelley Nutritional-Metabolic Therapy  
Hans Nieper's Therapy  
Oxygen Therapy  
Hyperthermia  
DMSO Therapy  
Live Cell Therapy  
Bioelectric Therapies  
Ayurvedia  
Chinese Medicine  
Amygdalin  
Arginine  
BGC and Coley's Toxin  
Gonzales Therapy

When analyzed, all of these therapies can be classified as falling into one or more of the four approaches to chronic disease treatment.

The recent emergence of Cell Specific Cancer Therapy on electromagnetic treatment and the electromagnetic therapies which are reported at the Fourth International Symposium on

Biologically Closed Electric Circuits, October 26-29, 1977, amplify the information on the electromagnetic approaches.

However, there remains a very important aspect of cancer therapy which is exhaustively analyzed in the PhD Dissertation of Alice Rose at Georgia State University in 1979. This is the psychological and spiritual aspects of cancer treatment. The main thrust is that in many cases, cancer is associated with an attitude of psychological or spiritual despair, which must be alleviated if any therapy is to be successful.

Experience in a large number of alternative cancer clinics both in the United States and offshore has demonstrated the crucial importance of residential cancer patients living in and around the facility forming friendships and bonding during the treatment experience to provide a form of psychological and spiritual support not possible to obtain in other circumstances.

Its impact on the success or failure of the treatment programs cannot be overestimated in overcoming the psychological and spiritual despair which characterizes the disease.

With their interactions each with the other, these patients facing an identical problem literally seem to heal each other.

Therefore, a residential facility where such interaction can occur during a cancer treatment program may be essential to its success.

In the studies of David Spiegel, a psychiatrist at Stanford University,<sup>10</sup> Dr. Spiegel's treatment of terminally ill breast cancer patients included mutual support and discussion groups among such patients. Those who served as untreated controls received no such treatment. The

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<sup>10</sup>Spiegel, D.A., A psychosocial Intervention and Survival Time of Patients with Metastatic Breast Cancer advances: The Journal of Mind-Body-Health, volume 7, pp. 10-19, 1991.

results showed that the treatment group lived twice as long after the time they entered the study as the control group. Survival on average was 18.9 months for the controls and 36.6 months for those in the program. The time between the recurrence of illness and death was significantly prolonged in the treatment group and the more patients who participated in the group, the greater the effect.

### **An Example of the Analysis of One Treatment**

Perhaps the most hotly debated and contested alternative cancer therapy to have emerged in the past half-Century is the use of Amygdalin or Laetrile, which continues to be a mainstay of therapy at most offshore cancer therapies.

The use of Laetrile was the subject of one of the most prolonged lawsuits in America, during which the FDA was enjoined by the Court from interfering with its use by cancer patients for over a decade. Some 26 states passed legislation legalizing the use of Laetrile within those states.

One dispassionate and thoughtfully analytical appraisal of the possible role of Laetrile in the treatment of cancer, contained in an Expert's Affidavit used in that case, which in applicable part reads:

"Perhaps the clearest evidence accumulated since 1977 of the effectiveness of Laetrile in the treatment of cancer is the report of the National Research Council, Committee on Diet, Nutrition and Cancer, "Diet, Nutrition and Cancer", Executive Summary, page 11 states:

Foods and numerous ...nonnutritive components of the diet have been examined for their potential to protect against carcinogenesis ...In laboratory experiments, vitamins, trace elements, nonnutritive food additives, and other organic constituents of food, ...indoles, phenols, flavones, and isothiocyanates have been tested for their ability to inhibit neoplasia.

...A number of nonnutritive...compounds that are present in these vegetables also inhibit carcinogenesis in laboratory animals.

Section A The Relationship Between Nutrients and Cancer, page 51 states:

Yet, as the data reviewed in Chapters 13 and 14 indicate, at least some of the compounds in food (e.g., flavones, isothiocyanates) that have been implicated in the causation or prevention of cancer are food constituents other than nutrients ...

On page 52, it is stated:

...For example, the constituents of cruciferae responsible for their apparent effect on the occurrence of cancer may be, as Chapter 15 suggests, indoles, isothiocyanates, or other nonnutritive substances demonstrated to affect carcinogenesis in the laboratory.

Page 358 states:

In recent years, a number of ...constituents of foods have been studied for their inhibitory effects on carcinogenesis.

Chapter 15, "Inhibitors of Carcinogenesis, pp. 362:

Aromatic Isothiocyanates. Benzyl isothiocyanates and phenethyl isothiocyanate are also constituents of cruciferous plants. These aromatic isothiocyanates have been shown to inhibit neoplasia induced by polycyclic aromatic hydrocarbons (PAH's) when they were administered during the initiation phase under several different experimental conditions. These results were obtained when the aromatic isothiocyanate was fed both before and during administration of the PAH's (Wattenberg, 1977, 1979b).<sup>11</sup> Little is known about their mechanism of inhibition other than the fact that benzyl isothiocyanate is a potent inducer of glutathione X-transferase activity. In further studies, mammary tumor formation resulting from exposure to DMBA was inhibited by the administration of benzyl isothiocyanate subsequent to the carcinogen. It has also been demonstrated that this compound inhibited 1,2-dimethylhydrazine-induced neoplasia of the large intestine when the exposures were begun 1 week after administration of the carcinogen. (Wattenberg, 1981b)<sup>12</sup> The mechanism of these inhibitory effects is not known.

The report in Life Sciences Vol. 27, pp. 659 (1980) by Heikkila and Cabbatt, entitled: "The Prevention of Alloxan-induced Diabetes by Amygdalin" provides the clue to understanding the anticarcinogenic properties of Laetrile. That report states:

"Firstly, amygdalin most likely was a good hydroxyl radical scavenger since amygdalin contains both a benzene ring and a sugar moiety and compounds with these groups have very high rate constants for reactivity with the hydroxyl radical.<sup>13</sup>

Secondly, amygdalin like all of the other agents which we have found to be protective, can be tolerated by experimental animals at rather high doses - - -

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<sup>11</sup>Wattenberg, L.W. (1977) Inhibition of carcinogenic effects of polycyclic hydrocarbons by benzyl isothiocyanates and related compounds. J. Natl. Cancer Inst. 58:395

<sup>12</sup>Wattenberg, L.W. Inhibition of carcinogen-induced neoplasia by sodium cyanate, tert-butyl isocyanate and benzyl isothiocyanate administered subsequent to carcinogen exposure. Cancer Res. 41:2991-2994.

<sup>13</sup>Dorfman, L.M. and Adams, G.E., National Standard Reference Data System, NBS, 4 1-59 (1973)

It has previously shown that high doses of several good hydroxyl radical scavengers...dimethylsulfoxide ...given to mice at various times prior to alloxan, were able to protect against the diabetogenic action of alloxan ...in a recent report it was shown that catalase, superoxide dismutase, and several potent hydroxyl radical scavengers could prevent some of the toxic actions of alloxan on isolated islet cells. - - - In the present study we report that amygdalin can protect against alloxan. Although, as mentioned above direct rate constants for amygdalin's reactivity with the hydroxyl radical, to our knowledge have not been published, one would expect that the rate constant for reactivity of amygdalin with the hydroxyl radical is very high. - - - The rate constant for amygdalin has been recently directly determined with a pulse radiolysis technique and found to be  $4.1 \times 10^9 \text{M}^{-1}\text{S}^{-1}$ . Thus, one might reasonably add amygdalin to the list of hydroxyl radical scavengers able to protect against alloxan. It is interesting that the chemical structure of amygdalin is quite different from most of the other hydroxyl radical scavengers previously reported to protect against alloxan. - - -

It should be mentioned, however, that hydroxyl radical scavengers in general are known to be radioprotective due to their scavenging of the deleterious and reactive hydroxyl radical, which is thought to be the damaging species generated by ionizing radiation ..."

Levine and Kidd<sup>14</sup> report:

- - - There is a great deal of evidence that nutrient-derived and synthetic antioxidant factors can successfully intervene to halt the progression of chemical carcinogenesis at any point. Various antioxidants protect against the actions of initiator carcinogens in the "model" skin tumor system (Slaga, 1984). Antioxidant compounds also can block the promotion process (Demopoulos, et al., 1980, Slaga, 1984). Progression past promotion to neoplasia can also be protective against antioxidants. Vitamin A and its related retinoid derivatives are widely recognized as tissue growth regulators and have also been shown to protect by antioxidant mechanisms.

Dietary antioxidant factors can be potent inhibitors of malignant progression. Exposure of all-trans-retinoic acid (a synthetic vitamin A analog) can effectively block further progression of preneoplastic skin growths, skin (basal cell) carcinoma, and bladder papillomas. Other retinoids caused the regression of chemically induced pulmonary adenomas. Glutathione, the tripeptide nucleosorbophylic antioxidants, may cause the regression of established malignant tumors. Rovi reported in Science that dietary supplementation with reduced glutathione (GSH) caused the regression of hepatocellular carcinomas induced in rodents by the highly potent carcinogen aflatoxin. Two subsequent studies failed to

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<sup>14</sup>Levine, Stephen A., Ph.D. and Kidd, Parris M., Ph.D., Beyond Antioxidant Adaptation - A Free Radical-Hypoxia-Clonal Thesis of Cancer Causation, Journal of Orthomolecular Psychiatry, Vol. 14, No. 3 (1984)

confirm this finding, Novi, et al (1982) cautioned that the route by which glutathione is administered is important; a second group has reported that reduced glutathione causes hepatocellular carcinomas to regress. - - -

In the cancer cell the major mode of ATP generation appears to be non-mitochondrial, i.e., glycolytic. Cancer cells respiring glycolytically may encounter a major limiting factor in their capacity to generate ATP by this means: a relative glut in the reduced electron carriers NADH and NADPH, and a relative deficiency in their corresponding oxidized forms NADP<sup>+</sup> and NAD<sup>+</sup>. These occur as a result of the impaired cellular ability to utilize these electron carriers in electron transfer to the ultimate electron acceptor - oxygen. Hence an extra-reduced cellular state has developed, i.e., a state beyond antioxidant adaptation. The cell in this state has markedly lower reliance on oxygen for metabolism, and fewer oxygen radicals are available to present an oxidizing challenge to the cell. The drawback for the cancer cell is that it now lacks a full complement of antioxidant enzymes and the flexibility to mount an effective antioxidant response to oxidant attack.

While other hypotheses for the anticarcinogenic properties of Laetrile have been reported and there may, of course, be several modes of action, it can now be reasonably deduced from the available scientific literature that one of the chief effects of Laetrile and its metabolites responsible for its ability to shrink tumors is its effect as a free radical scavenger in cancer cells, which are known to be largely developed in anaerobic glycolysis and have severely restricted oxidative phosphorylation.

Frank after an elegant series of experiments demonstrated that the high rate of mitosis in cancer cells is due to the cytoplasmic accumulation of reduced pyridines, which become available for various synthetic processes of tumor growth and drive mitosis.<sup>15</sup>

Tumors having a relatively anaerobic metabolism, with a much higher rate of glycolysis than normal tissues, at least in part due to a relative inhibition of pyruvate dehydrogenase, pool Lactic acid which serves as a reservoir of hydrogen for cytoplasmic reduced pyridines, which do not efficiently cross the mitochondrial membrane by the glycerophosphate and malate-aspartate shuttles. These non-mitochondrial reduced pyridines are the critical stimulus for the abnormal growth (mitosis) of cancer cells, particularly NADH and NADPH<sub>2</sub>. Tumors in which this pool of extra mitochondrial pyridines is decreased shrink rapidly, probably by reduction of the pool of reduced pyridines as NADPH<sub>2</sub> and NADPH which then decrease mitosis in such cases.

It is likely that the interference with glycerophosphate and malate aspartate

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<sup>15</sup>Frank, Benjamin, Nucleic acid as antioxidant therapy of Aging and Degeneration. N4, Royal Health Books, Ltd., New York (1977)

shuttles necessary to transport the hydrogen ions across the mitochondrial membrane is due to free radicals in the cytoplasm and that Amygdalin which is a very potent free radical scavenger may assist in making pyruvate more accessible to the Krebs cycle by assisting in the oxidation of NADH to NAD and thus reduce the cytoplasmic pools of reduced pyridine.

If this is the case, then Laetrile can be considered a non-toxic antimetabolic therapeutic which achieves its results not by damaging the apparatus of mitosis but by diverting to oxidative phosphorylation the excess pool of reduced pyridines which fuel excessive mitosis, and that this is achieved with no deleterious and indeed, perhaps a salubrious effect on non-malignant cells so that the toxicity and interruption of mitosis in normal cells prevalent in the use of toxic antimetabolites does not require the interrupted administration necessary in toxic chemotherapeutic agents.

Therefore, Laetrile can exert its antimetabolic and anticarcinogenic effects in a prolonged and continuous fashion and thereby bring about rapid tumor regression without adversely impacting the immunological status of the patient, indeed, perhaps improving that status.

It may be significant in this regard to note that leukocytes contain significant amounts of NADH oxidase which may account for some of the ability of leukocytes to produce tumor shrinkage through a similar mechanism as NADH oxidase could likewise shrink the pool of reduced pyridine available to drive abnormal mitosis.

A great deal of research during the past decade has been focused on the probability that cancer cells can be converted back to normal or near normal cells by agents which influence intracellular biochemistry and restore the cells to aerobic metabolism.

Booyens, et al<sup>16</sup> have demonstrated that human melanoma cells can be reversed by addition of gamma linolenic acid and have successfully treated a number of cases of malignant melanoma by the administration of gamma linolenic acid.

Indeed, the FDA has granted Phase I approval to E. I. Dupont, Co. for testing of n-methylformamide, a solvent similar to Dimethylsulfoxide, both of which were discovered by David Dexter and his colleagues at Brown University to have the property of transforming malignant cells into near normal cells.

In this regard Heikkila and Cabbert note that dimethylsulfoxide is a good hydroxyl radical scavenger while, like amygdalin, protects against the effects of alloxan when administered prior to alloxan.

Thus it may be reasonable to investigate whether or not Amygdalin and DMSO, as well as dimethylformamide achieve their effects by restoring normal or near normal oxidative phosphorylation and decreasing the malignant cells

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<sup>16</sup>Booyens, et al, Second International Congress on Essential Fatty Acids, Prostaglandins and Leukotrienes (London) March 24-27, 1985 (Abst).

dependence on anaerobic glycolysis for energy production and thereby depleting the cytoplasmic pooling of reduced pyridines which appear to drive abnormal mitosis in malignant cells.

Certainly all of the hydroxyl-scavenging agents may also help normalize other enzyme systems, as does gammalinolenic acid and improve the metabolism of malignant cells in other fashions as well.

For instance, it is reasonable to assert that GLA achieves its effects by conversion to Prostaglandin E<sub>1</sub> which influences intracellular adenylyl cyclase and cyclic AMP.

For this reason it would be well to test Amygdalin together with other nutrients which have been found clinically to produce tumor shrinkage as their action may be synergistic.

This synergism could be expected since both GLA and Amygdalin occur in nature predominately as components of seeds.

In "Nutritional Factors with the Potential to Inhibit Critical Pathways of Tumor Promotion"<sup>17</sup> a Chapter in Modulation and Prevention of Cancer by Vitamins, Flavin and Kolbye of the Nutrition Education and Food and Drug Administration Bureau of Food, state:

"Nutritional factors potentially can inhibit critical phases of tumor promotion. The proper combination of these factors is more effective in this inhibition than isolated substances because of their ability to complement each other in their mechanisms of action".

The hypothesis advanced here also finds support in the report of Shearer in "Modulation and Mediation of Cancer by Vitamins"<sup>18</sup>

"Amygdalin use by humans with cancer indicates that the effect of the 'laetrile' regimen must be on controlling growth of the cancer cells rather than killing them.

Effect on Cancer Initiation. The ability of vitamin A or amygdalin to alter the rate of cancer initiation by 3'me DAB in rat liver was assayed by competitive hybridization of normal rat liver nuclear RNA to normal fetal rat DNA.

Effect on Cancer Growth. The ability of vitamin A or amygdalin to alter the rate of growth of hepatocellular carcinomas previously initiated and promoted by 3 months of feeding 0.06% 3'meDAB was assayed by lifetime feeding studies.

...Rats on the high vitamin A diet and amygdalin diet survived on the average somewhat longer than those on the control diet (93 days, 99 days, and 76

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<sup>17</sup>Meyskens, F.L. and Prasad, K.N. (Eds), Modulation and Mediation of Cancer by Vitamins, (Karger, Basel 1983) Flavin, D.F., Kolbye, A.C., Jr., Nutritional Factors with the Potential to Inhibit Critical Pathways of Tumor Promotion, pp. 24-38.

<sup>18</sup>Modulation and Mediation of Cancer by Vitamins, Editors: Meyskens, Prasad (1983) Karger, Basel, Chemoprevention of Azo-Dye-Induced Liver Carcinogenesis in the Rat by a Natural Carotenoid, R. W. Shearer, pp. 89-94.

days, respectively, after stopping the carcinogen) and rats fed both high vitamin A and amygdalin survived significantly longer (128 days). 4 rats in these groups which died early were cannibalized, but all of the rest were either dead or moribund with huge liver tumors when the experiment was terminated 7 months after stopping the carcinogen treatment, with the exception of 1 rat on the amygdalin diet which had only small cancers and would have lived probably another month.

The fetalism of malignant tumors must be explained by any potentially valid theory of the fundamental nature of the malignant process. The currently popular mutation theory is inadequate for this reason. These results suggest the usefulness of both vitamin A and amygdalin in modulating rat liver carcinogenesis in the study of tumor fetalism and other promotion-specific events". "

Since that time, Laetrile and other Betaisothiocyanates which are commonly found in cruciferous vegetables have been acknowledged to be of great value in the prevention of cancer by the National Research Council as well as the American Cancer Society.

As early as 40-50 years ago, scientists felt that measures which supported mitochondrial function, the production of ATP were crucial in the treatment of cancer. It appears that laetrile may do this by acting as a highly efficient antioxidant.

The cancer therapies listed in these three books must of course, undergo similar penetrating analysis before being incorporated into an integrated cancer treatment program designed to cure cancer.

The metabolic typing and dietary adjustments based on such typing are discussed in Moss's book in conjunction with Nicholas Gonzales' approach. This originated as an integral part of the highly successful cancer therapies of William Donald Kelley.

Nicholas J. Gonzales, M.D., became interested in Kelley's method while a student at Cornell University Medical College in the late 1970's. After graduating, Dr. Gonzales did post-graduate work with Robert A. Good, M.D., Ph.D., then president of Sloan-Kettering Institute, and thoroughly investigated Kelley's treatments. In a lengthy unpublished monograph, One Man Alone,

Dr. Gonzales reports that the Kelley method, when used properly, achieved a remarkably high success rate, even in such seemingly incurable forms of cancer as carcinoma of the pancreas and liver. Robert G. Houston, author of *Repression and Reform, an Evaluation of Alternative Cancer Therapies*, argues that this report constitutes proof of the effectiveness of Kelley's method.

"The Gonzales Monograph documents results dramatic enough to constitute formal proof even with a single arm study. The survival of 5 or more years for all 5 pancreatic cancer patients on the full program was significant statistically compared to the standard 5-year survival of 3%.

These results mandate that Kelly's method of metabolic typing and prescription of an appropriate diet for each metabolic type should be an integral part of any alternative cancer program which relies to any measure on nutritional therapies.

Such metabolic typing into the two main classifications and the four subclassifications of each can be determined by analysis of mineral patterns during mineral hair analysis. This type of metabolic analysis is performed at Trace Elements, Inc., 4501 Sunbelt Drive, Addison, Texas, 75001, Telephone: 1-800-824-2314.

Diet therapy for people with cancer is variable; diet should be determined by the individual's metabolic type. Research has developed the ability to recognize metabolic types through tissue mineral patterns of the hair. Dr. David L. Watts has found that certain mineral patterns reveal metabolic characteristics that correlate well with the descriptions of earlier investigators.

*Metabolism is a term used to describe nutrient utilization or efficiency on a cellular level resulting in energy production and maintenance. Cellular metabolism is controlled by neurological and endocrine function, which will affect nutrient absorption, retention, and excretion.*

Clinical research, conducted by Dr. Watts correlated over 100,000 tissue mineral analyses

with specific physical and biochemical characteristics. Through a properly obtained and assayed sample, eight distinct metabolic categories were identified. These include, the fast and slow metabolic types, each with their four sub-types.

The metabolic types with their sub-categories can generally be associated with the various stage of stress, whether acute or chronic in nature. Developed by Hans Selye, these stages are the alarm, resistance, recovery and/or exhaustion stage. Metabolic typing through TMA allows these stages of stress to be more easily determined, and therapy can then be made more specific by working with rather than against the body's normal responses to stress.

The following descriptions briefly define the characteristics of Fast and Slow Metabolism and the neuroendocrine combinations of the sub-categories.

#### **FAST METABOLISM:**

Fast Metabolism is synonymous with Sympathetic Dominance, Fast Oxidation, and Type A Personality. Excessive sympathetic nervous system activity increases the availability of glucose for rapid metabolism via epinephrine release from the adrenal medulla. The adrenal medulla stimulates other areas of the body that are not directly innervated by sympathetic nerve fibers and can increase the metabolic rate by as much as 100 percent.

The fast metabolizer's cellular oxidation is more than adequate in pyruvate and oxaloacetic acid production, but inadequate in the production of acetates. This results in incomplete energy production in the Krebs cycle. The fast metabolizer is in a state of rapid glycolysis, which accounts for the high metabolic rate. High HCL with tissue acidity and low pancreatic enzyme production are usually present also.

The fast metabolizer is usually experiencing a considerable amount of stress (physical,

emotional, or a combination of both). He or she often enjoys stressful situations and may even seek them. This type of person is usually late for appointments, somewhat agitated or hyperexcitable, and is often considered a workaholic. If the metabolism becomes too fast, he begins to experience more emotional stress, especially anxiety about the future. The blood pressure may become elevated, with accompanying dental problems and excessive perspiration. Frequently, an increased need to eat develops in order to maintain high energy levels. Weight gain will usually occur in the abdominal region.

**FAST METABOLISM TYPE # 1:** Classified as sympathetic dominant with increased adrenal activity and increased thyroid function. This synchronous neuro-endocrine combination will frequently result in increased energy levels. However, if an imbalance develops between the adrenal and thyroid glands, the ability to sustain energy levels may become diminished. The Fast Metabolizer Type # 1 can develop TMA patterns associated with alarm, resistance, or recovery stage of stress.

**FAST METABOLISM TYPE # 2:** Classified as sympathetic dominant with increased adrenal cortical activity and lowered thyroid function. This imbalanced neuro-endocrine combination reflects the alarm stage of stress. When the adrenal cortex becomes dominant over thyroid activity, energy fluctuation may become dramatic. Often the Type #2 individual will experience an increase then a decrease in energy levels, which can contribute to significant mood swings.

**FAST METABOLISM TYPE # 3:** Classified as sympathetic dominant with decreased adrenal cortical activity in conjunction with increased thyroid function. This imbalanced neuro-endocrine combination is indicative of the resistance or exhaustion stage of stress and is often

associated with depression and irritability if chronic.

**FAST METABOLISM TYPE # 4:** Classified as sympathetic neurological dominance with decreased activity and decreased thyroid glandular function. This neuro-endocrine combination is associated with the exhaustion stage of stress, often reflected in extreme fatigue, depression, and anxiety.

### **SLOW METABOLISM**

Slow metabolism is synonymous with Para-sympathetic Dominance, Slow Oxidation, and Type B personality. Generally speaking, the slow metabolic types metabolize glucose at a reduced rate. If slow metabolism is severe, energy production and maintenance of normal energy levels will become inadequate. This is a result of the inability to split glucose molecules to form adequate amounts of pyruvates and oxaloacetic acid in the glycolysis cycle. This leads then to the inability to produce citric acid in the Krebs cycle. Low HCL and tissue alkalinity are also usually present.

Slow metabolizers are most often well organized and methodical. They tend to start projects and see them through to completion. Somewhat regarded as perfectionists, they perform best when not under stress. If the metabolic rate becomes excessively reduced, they become subject to fatigue, requiring extra amounts of rest. They eventually experience depression, often dwelling upon the past. Blood pressure may decrease below normal, along with the development of cold hands and feet. Weight gain will usually be noticed on the thighs and hips. If the metabolism continues to decrease, protein foods, especially meats will become poorly tolerated which may then increase their tendency toward vegetarianism.

**SLOW METABOLISM TYPE # 1:** Classified as para-sympathetic dominant with decreased adrenal medullary activity and decreased thyroid function. This synchronous neuro-

endocrine combination will result in sustained energy levels (endurance); however, the production of energy will be below optimum. The Slow Metabolizer Type # 1 can experience any one of the four stages of stress.

**SLOW METABOLISM TYPE # 2:** Classified as para-sympathetic dominant with increased adrenal cortical activity and decreased thyroid function. This imbalanced neuro-endocrine combination is indicative of the alarm stage of stress. When the adrenal cortex is dominant relative to the thyroid, energy fluctuations may become pronounced. The slow metabolizer Type # 2 will normally experience both elevated and depressed energy levels, which can contribute to significant mood swings.

**SLOW METABOLISM TYPE # 3:** Classified as parasympathetic dominant with decreased adrenal cortical activity and increased thyroid function. This imbalanced neuro-endocrine combination is indicative of the resistance or exhaustion stages of stress. When chronic, slow metabolism Type # 3 is often associated with depression and irritability.

**SLOW METABOLISM TYPE # 4:** Classified as para-sympathetic dominant with high adrenal activity in conjunction with elevated thyroid function. This imbalanced neuro-endocrine combination is usually a result of an acute alarm stage of stress that has progressed into the stage of resistance.

The alternative cancer therapies do not lend themselves well to double blind studies, since they are integrated therapies, not dependent on one substance or approach which can be isolated for such tests.

Many of the alternative modalities discussed in these three books as well as the electromagnetic therapies discussed above should be integrated into the program.

The results will be appraised by outcome rather than by process analysis and the only control will be the patient's progress as contrasted to outcomes from conventional treatments which are well documented and well known.

Since the aim of these therapies is the conversion of malignant cells back to normal function, outcome analysis is the only method of comparing the relative efficacy of such therapies.

Cancer has been cured in hundreds of thousands of patients, both in the United States and in offshore clinics, for the past 30 years. While formal statistics are not available, the reports of many patient-oriented support groups such as the Cancer Control Society, People Against Cancer, and Cancer Victors and Friends constitute an impressive selection of experience and data concerning such therapies which are significant statistically when compared with the known survival rates of conventional therapies. These therapies integrated into the newly emerging knowledge about electromagnetic treatments and the possibility of reversing degeneration due to mitochondrial dysfunction are sufficient to mandate widespread adoption of alternative therapies by anyone who prefers such treatments over the surgery, radiation and toxic chemotherapy which has consistently failed to produce significant cure rates.

### **Symptoms of Metabolic Disease**

Seizures

Pre-existing developmental delay

Hypotonia or weakness, particularly if there is no evident cause

Combined central and peripheral cause for hypotonia or weakness

Increased anion gap and/or acidosis

Unexplained myopathy or cardiomyopathy

Retinopathy

Unusual MRI findings, particularly basal ganglia or unusual white matter abnormalities

Recurrent or cyclic episodes of vomiting and dehydration

Feeding difficulties, vomiting or reflux

Fasting intolerance

Failure to thrive despite adequate caloric intake  
Unexplained hearing loss  
Recurrent episodes with changes in mental status, particularly if associated with vomiting or ataxia  
Liver or kidney disease  
Peculiar body odor  
Short stature when combined with any of the above signs and symptoms

**Family history of:**

Known mitochondrial or metabolic problems  
Muscle or brain diseases  
Unexplained hearing loss  
Unusual heart diseases  
Developmental delay or regression  
Epilepsy  
SIDS  
Diabetes  
Blindness or retinopathy  
Parkinson disease  
Alzheimer disease  
Unexplained illness or death

**THE ANTIOXIDANT SYMPHONY**

There is an array of substances which have a biologically antioxidant and free radical scavenging property in the body and there is an array of free radicals produced during the process of electron transport and oxidative phosphorylation with the conversion of ADP to ATP in the mitochondria, in normal and under abnormal conditions.

There are several metabolic types and several haplotypes of mitochondrial DNA, as well as several point deletions and mutations in mitochondrial DNA which are passed along with mitochondria from mother to offspring. The interplay of these as well as some nuclear DNA mutations all have an influence on who and under what circumstances will develop arteriosclerosis and subsequent coronary heart disease or stroke.

Heart function is determined mitochondrially, and the health and function of the

myocardium is dependant on the state of function of its mitochondria.

The cardiovascular system does not exist in splendid isolation from the body; it is a vital and essential part of it and is subject to the same nutritional and bioenergetic influences which affect all the organs.

Nutrients are far from standardized in the American diet in raw fruits and vegetables grown in American soil. The only way of ensuring a constant and dependable level of nutrient intake is through supplementation.

Antioxidant and mitochondrial medicine will dominate the early years of the 21st century. Nutritional supplementation, herbs, energy medicine and detoxification will replace pharmacology in the prevention and treatment of the major killer diseases.

The medicine of the 21st century will be eclectic in its philosophy; health oriented, not disease oriented, and far more effective than anything developed and used in the 20th Century.

Clinical trials and meta-analysis of clinical trials, conducted according to standards set by regulatory agency requirements, are used extensively in allopathic medicine. They have little to do with the treatment or prevention of chronic degenerative diseases.

Such trials are sponsored and paid for by manufacturers of pharmaceuticals. Clinical trials are uniquely designed to determine whether or not a particular pharmaceutical is or is not effective in the treatment of a particular disease in relatively large population of people who have been diagnosed as suffering from a particular disorder. They are useful to determine which of two drugs may be the most efficacious for the pharmaceutical treatment of a particular disease.

For testing hypotheses about the long-term use of multiple nutrients on multifactorial diseases, such trials are inappropriate.

In treatment programs which do not include the use of pharmaceuticals, other approaches to approve the efficacy must be derived. Laboratory research together with epidemiological evidence and careful appraisal of treatment results, will be the most effective to determine outcome.

Chinese medicine represents the accumulation of thousands of years of experience in the treatment of human diseases. Because its methodologies are largely non-pharmaceutical and deal with modalities which are never considered in allopathic medicine, there has been a tendency to ignore its impressive results.

A Western tradition and accumulation of hundreds of years of empirical experience in the treatment of diseases, has likewise been ignored in the enthusiasm of 20th Century Allopathic teachers who felt that all the answers were to be found in synthetic chemical compounds which block one or more life processes in the body.

The accumulated results of 20th Century Allopathic medicine in the treatment and prevention of chronic degenerative diseases is far from impressive.

Chinese medicine on the other hand, has been working well for thousands of years and the same may be said of the Western empirical approaches.

The shift away from Allopathic towards more experienced based medical practice is underway throughout American medicine. This internal movement within the medical profession is characterized by the laying aside of Allopathic gold standards which simply do not work and an open willingness to learn about older methods which were cast aside in the mid-20th Century.

Traditional Chinese medicine is based upon herbology and energy, two subjects which were excluded from 20th Century Allopathic medicine in the United States. The rich traditions of Chinese Medicine continue to be practiced there, as it has for thousands of years. It has much to

offer in the management of chronic degenerative disease.

While Chinese Medicine has been practiced predominantly within Chinese populations for well over a Century and a half, it was little known or appreciated in this country until the late 1970's when an influential American journalist, James Reston, accompanying President Nixon on a State visit to the Chinese mainland. He developed appendicitis and was treated in a Chinese hospital where he underwent acupuncture treatment for post-operative pain. Mr. Reston was impressed and wrote glowing reports about acupuncture and Chinese medicine. This focused national attention on Chinese medicine and led in a few years to the licensing of Oriental medical practitioners or Acupuncturists in several states such as California, New York, Nevada and Arizona. Now acupuncture and Oriental medicine is a licensed profession in most states, and there are several colleges of Oriental Medicine in the United States.

#### CONCLUSION

Presently, there are a number of excellent books in print which describe the use of antioxidant and herbal remedies in the treatment of cancer by nationally known experts. These are listed below at the beginning of the bibliography and should be of great benefit in designing specific antioxidant and herbal treatments for individuals being treated for cancer.

What Drs. Warburg and Szent-Gyorgi told us around a half-century ago is that when the respiratory apparatus of the cell is compromised sufficiently, that cell will either die or become malignant. That if it does become malignant, it may eventually find its way back to normal function but it may not. If it becomes malignant it usually spreads until it kills the organism. They offered us clues to how to help these cells find their way back to normal function. If their ideas had been accepted, rather than rejected, by the cancer research establishment a half-century ago, the

cancer problem would probably have been solved by now. Since it was not accepted at that time, it will be necessary to go back to that turning point and armed with a half-century of research on mitochondria which has taken place since that time, carry their ideas out to fruition, if the problem is going to be solved.