

CANCER RESEARCH and the DI-CARBONYLS

A Century of Progress

By Paul M. Koch

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Cancer Research and the Di-Carbon A Century In Review

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INTRODUCTION

The cause and treatment of cancer is of vital importance to all of us. In the search for the answers to the cancer problem, a researcher should consider the research of such scientists as Otto Warburg, Ph.D., M.D., N.L., Albert Szent-Gyorgyi, Ph.D., M.D., N.L. and Professor Joseph Henri Maisin, M.D., Director, Institut du Cancer, Louvain University, Belgium. Drs Warburg and Szent-Gyorgyi conducted extensive research on the cellular chemistry of cancer and Dr. Maisin conducted research with the peroxide of diformaldehyde and organic unsaturated compounds just prior to World War II. The independent cancer research of yesterday, that has been put on the back shelf by so many researchers of today, should once again be given a second look. If we want to resolve the mystery of the basic cause of cancer and its allied disease¹, and at the same time come up with an effective method of treatment for these serious disease conditions it will be necessary for each researcher to open his mind to all possible theories on the causes and treatment of these diseases. To have an ostrich like mentality will never solve these medical problems.

“WHAT IS CANCER?”

In 1995, the American Cancer Society defines cancer as:

“Cancer is a word for a large group of diseases characterized by an abnormal seemingly unrestricted growth of body cells. Normal cells divide and grow in an orderly fashion, and during the early years of an individual’s life, cell division is rapid. Once full growth is attained, normal cells of most tissues divide only to replace worn-out tissue and repair injuries. Cancer cells divide and grow out of control. When a mass of cancer cells build up, a tumor is formed that spreads and destroys surrounding normal tissue. Cells that break away from the original tumor may be carried by the lymph system or the bloodstream to other areas of the body where they may settle and form ‘colony’ tumors. When this occurs, the tumor is said to have METASTASIZED and the new growths are called METASTASES. Not all tumors are cancerous. Benign tumors, which are contained and limited in their growth, are usually not life threatening.” (Document 001881, printed 08/04/95)

This Document (001881) goes on to say:

“Approximately 3 out of 10 Americans will develop cancer. Of that number, 40% will be considered ‘cured,’ that is, they will be living 5 years after diagnosis and be free from any signs of cancer. The survival rate increases with the early detection and treatment of the cancer.

(Words in bold print are the emphasis of Paul M. Koch, Esq.).

Additionally, positive changes in a person’s lifestyle can help prevent many forms of cancer. There are more than 100 different types of cancer, classified by the part of the body in which they arise and of their microscopic appearance. Because the behavior of each type of cancer and its response to different treatment varies, it is necessary to treat each cancer and each cancer patient individually.”

Dorland’s Illustrated Medical Dictionary (23 Ed., 1961) defines cancer as:

“A cellular tumor the natural course of which is fatal and usually associated with formation of secondary tumors.” (p. 223)

BASIC MEDICAL RESEARCH

In September 1950, Dr. Albert Szent-Gyorgyi was a guest lecturer who spoke on the subject: The Next Half Century in Biochemistry at the dedication exercises for the new research laboratories for the Sterling Winthrop Research Institute, Rensselaer, New York. In his talk he made the following specific reference to “basic research” and “applied research” (62, O):

I often hear distinction drawn between ‘basic’ and ‘applied’ research with the unspoken implication that ‘basic research’ is that which cannot be applied and thus is useless. There is no such difference for all knowledge is useful, all research is but applied research. The difference is merely in timing and dimension. ‘Applied research’ is the application of knowledge already acquired, paying cash return. Basic research, which seeks new knowledge for knowledge’s sake, new truth for truth’s sake, is the foundation of the applied research of tomorrow. All really important progress of today was abstruse, apparently useless research yesterday, and if we neglect basic research today we have

cut out the roots of progress tomorrow. Antibiotics were a few years ago merely the subject of the curiosity of two people who were interested in the theoretical problem of natural defense regulations. A big scale reduction in human suffering can come only by such extension of basic knowledge.” (p. 46)

Dr. Szent-Gyorgyi was a strong believer in the importance of “basic medical research.” This is the foundation for all scientific medical knowledge. Without basic research, there can be no foundation for applied research. Applied research is but a mere extension of basic research of yesterday. He spent his whole life conducting basic medical research for the benefit of mankind. It was this research that made it possible for him to isolate ascorbic acid from the adrenal glands and from various plant juices and then prove that this ascorbic acid (hexuronic acid) was identical to Vitamin C. Subsequently he isolated flavones from paprika and gave them the name of Vitamin P. This biological research opened the door for him to conduct “basic research” in the field of cancer, which is the utmost importance to everyone.

In his 1963 paper *Cancer Therapy: A Possible New Approach* (62, C), Dr. Szent-Gyorgyi identified a substance he called “Retine” which inhibited cancer growth and “Promine” which makes cancer cells grow faster. In this paper he suggested that both Retine and Promine were of small molecular weight and of high potency and that they control normal cell division. He also wrote in 1963 that in animal experiments with retine, that daily injections of retine produced no observable toxic effect (62, d). In 1967, Dr. Szent-Gyorgyi also made reference to glyoxal derivatives as having antiviral properties (62, f).

In 1968 Dr. Szent-Gyorgyi wrote about the cancerostatic action of methylglyoxal (62, d). In his paper Bioelectronics — Intermolecular electron transfer may play a major role in biological regulation, defense, and cancer (62, h) he wrote:

“The simplest alpha-keto-aldehyde is methylglyoxal (pyruvic aldehyde); this fact seemed most exciting because, as far as we know, all cells contain a very powerful enzymic system for the conversion of alpha-ketoaldehydes into the corresponding unreactive oxyacids — for converting, for instance, methylglyoxal into lactic acid. This enzymic system, called the ‘glyoxalase,’ occupied the attention of several of the most outstanding biochemists in the first half of this century, but the interest later faded out, for no glyoxal derivative could be found on the main

metabolic pathways, nor could such a substance be isolated from tissues under normal conditions. And what is the use of an enzyme without a substrate?

“Should the inhibitor of growth prove to be a dicarbonyl, like methylglyoxal or a compound thereof, then I had an excuse for not having been able to isolate it, for the isolation of the expected trace amounts of such a very **reactive substance** would be very difficult indeed.”

Dr. Szent-Gyorgyi concludes his paper with this paragraph:

“A Tentative New Theory of Cancer, one could ask what would happen if a cell lost its ability to bind its own glyoxalase? Then it would have to go on multiplying senselessly and endlessly, behaving like a cancer cell. As far as we know, the only difference between a normal cell and a cancer cell is the fact that the latter divides when no proliferation is needed. All this leads, tentatively, to a new theory of cancer: a cancer cell is a cell, which has lost its ability to bind its own glyoxalase. Whether this theory is right or wrong remains to be demonstrated. It recommends itself by its clarity, its simplicity, and its ability to explain why such a great variety of noxious influences can lead to the same end, cancer. The theory also has the earmark of a good theory: it can be proved or disproved. What may lend it additional value is the fact that it suggests various ways of seeking a therapy for cancer. It is regrettable that, owing to cuts in the budget, this research will have to be discontinued...”

In 1972, Dr. Szent-Gyorgyi was interviewed by Jane Kinderlehrer for *Prevention Magazine*. She titled her article: Liver May Hold The Secret of Cancer Prevention (62, 1). In this article Dr. Szent-Gyorgyi tells of finding an unidentified substance which he called **Retine, a substance that had the ability to retard neoplastic cell division and growth**. I quote excerpts from the article:

“A world-famous Nobel Laureate believes he is on the track of the body substance that prevents cancer in healthy people — and might cure those stricken.

“THE KEY TO A CURE for cancer may be just around the Corner.’ This is a direct quote — not from the Cancer Society on the eve of a fundraising drive, nor from some mysterious witch doctor in Upper Slobotnik.

“The man who believes the cancer problem is nearly licked is a Nobel prize winner, one of the world’s leading scientists, a biochemist and an M.D., Dr. Albert Szent-Gyorgyi. Dr. Szent-Gyorgyi is one of the most productive researchers the world has ever known...

“The famous Nobel Laureate believes that his laboratory is on the verge of isolating a substance for which the world has long yearned — **a nontoxic, cell specific substance with anti-cancer activity.**

“The source of this anti-cancer agent is liver, although the compound appears to be present in all normal (non cancerous) tissues.”

Ms Kinderlehrer, in her article, goes on to describe Dr. Szent-Gyorgyi’s basic research with “Retine”; how he found it and how it functions to prevent cancer cells from dividing. To continue this important research, Dr. Szent-Gyorgyi had applied to the National Institute of Health for a research grant. Unfortunately, his application was rejected.

“Our grant application has a poor prospect,’ Dr. Szent-Gyorgyi explained because, ‘a discovery is, by definition, at variance with existing knowledge.’

“‘Retine’ is indeed at variance with the current search for chemotherapeutic answers to the growing problem of cancer. It does not destroy tissue but plays a key role in growth regulation. Dr. Szent-Gyorgyi said that he and Dr. Egyud have found that ‘retine stops the growth of cancer cells without poisoning other cells.’

“When ‘retine’ is present in sufficient concentration, no cell division can occur while vital cellular processes go on unhindered, research done at the laboratory has revealed.

“And what is a good bit of luck, and not my cleverness,’ the white-haired scientist pointed out, ‘is that if a cancer **cell cannot grow, it dies by itself.**’

“According to the researchers, **‘retine’ is normally produced by the body and, when it is, it prevents the growth of existing cancer cells. But the body can lose its ability to produce this**

substance... Putting the ‘retine’ back in the body, just as we put insulin back into a diabetic’s body, can stop the growth of cancer, he believes... The scientists at Woods Hole found that **cancer cells are much more sensitive to retine than normal ones, and so cancer cells may be inhibited** specifically... ‘Retine’ can easily be measured even in small quantities of serum because it has a strong and specific florescent emission.”

In this article, references were made to Dr. Frank Rauscher, Jr., the new director of the National Cancer Institute, appointed in May of 1972, and to the discovery of a virus called, the Rauscher virus, that produces a form of leukemia in mice. Also, it was pointed out, that a lion’s share of the billion dollar research budget was earmarked for virus research. This article also made reference to the following research of Otto Warburg, Ph.D., M.D., N.L.

“As another Nobel prize winner, Dr. Otto Warburg, pointed out in his address to the Nobel-Laureates at Lindau in 1966, ‘It is true that some virus caused cancers occur in animals, but no one is sure human virus-cancer has been observed so far, whereas innumerable substances cause cancer without viruses in animals and man. Thus, viruses do not meet the demands of Pasteur, that it **must be possible to trace the prime cause in every case of the disease.** Therefore, **science classifies viruses as remote causes of cancer, leading to anaerobiosis (ability to live without oxygen) which is the prime cause, that meets the demands of Pasteur.**”

“Dr. Szent-Gyorgyi estimated that \$200,000, which is merely a crumb of the big cancer fund pie, would allow him in two years time to come ‘very close to an actual cure for cancer.’

“Some day, there is no doubt, that this cancer retarding substance must be isolated, identified, synthesized, and made available for testing on human beings. How long must we wait?”

In his 1973 paper, Bioelectronics and Cancer (62, i), **Dr. Szent-Gyorgyi made a complete review of his biological and cancer research over the years.** He pointed out the importance of the biological function of the two enzyme systems which involved glyoxalase I and II and of the coenzyme, SH-glutathione and the transformation of glyoxal derivatives into the corresponding hydroxyacids and methylglyoxal into lactic acid. He explains the importance of C = O, the “carbonyl group”, and O = C — C = O, the “di-carbonyl group”, the simplest being glyoxal. He identifies “retine” as the substance that keeps cells at rest, the “off” switch to

cell division, and “glyoxalase” as the “on switch” which bring about uncontrolled cell division. It is glyoxalase that changed the reactive, dicarbonyl, glyoxal derivatives into the corresponding inactive hydroxyacids. He wrote:

“If ‘retine’ is glyoxal or a glyoxal derivative; then the enzyme which starts proliferation could be the glyoxalase which transforms the carbonyls into inactive hydroxyacids. As shown by L. Egyud, animal cells do contain glyoxal and methylglyoxal. They contain also glyoxalase so when no proliferation is needed, these two, glyoxalase and the glyoxal derivatives must be kept separated, and damage could induce proliferation by creating disorder and letting them meet. This could explain the biological role of glyoxalase which has been a mystery.” (p 554-5)

On page 560 (making a reference to Dr. Koch’s book *The Survival Factor in Neoplastic and Viral Disease, An Introduction to Carbonyl and Free Radical Therapy*, 1961) (33), Dr. Szent-Gyorgyi wrote:

“The possible importance of carbonyls in regulation and carcinostatis was emphasized by W. F. Koch.”

And in his conclusion to this paper, Dr. Szent-Gyorgyi said in part:

“The cancer problem is finite and solvable. What is needed for its solution is imagination, the high spirit of inquiry, and the wonderful new tools of research. It is not solvable by the combined arrogance and ignorance of politicians now trying to command science, nor is it solvable by bureaucratic dullness.

“In the present paper a wide alley is opened for an attack on cancer. It is made possible to pinpoint and correct disturbance. The road is marked out: it leads over extensive basic studies, a thorough study of all the components of the regulatory system. There are shortcuts only to failure.

“The progress of science is marked by the penetration into increasingly small dimensions. From macroscopic anatomy biology moved to microscopy, from light microscopy to electron microscopy. At present it is dominated by the molecular concept. The next natural step will be a penetration into the electronic dimension. Cancer, partly, is a disturbance in the electronic dimension.

“Progress in the art of healing has always been induced by progress in basic knowledge. The present regrettable emphasis on **applied research at the expense of basic research, and the search for a cure before an understanding, can only delay the final solution.** Our inability to cope with diseases like cancer indicates major gaps in our basic knowledge, which have to be filled before progress can be made.

“The carbonyls with extended **(pi) systems may be the key not only to cancer but also to other ‘degenerative diseases’**, like schizophrenia, muscular dystrophy and various pathological conditions of the heart muscle. These substances represent a specific field of research, which demands for its exploration, specific experience. The substances in question cannot be isolated and identified without use of the most modern analytical methods, and the idea must be accepted that the days ‘string and sealing wax’ are past also in biochemistry. It is for society, or rather its government, to decide whether it wants to meet the expense of having these diseases eliminated. The writer is paralyzed by the lack of means, his last three applications having been rejected by the main granting agency in biomedical research, the National Health Institutions...

It was through this extensive research that Dr. Szent-Gyorgyi was able to reach the scientific conclusion that the **identity of Retine** was in reality the dicarbonyl, methylglyoxal; **the nontoxic chemical substance that he had isolated years earlier which was able to inhibit cancer cell division.** Subsequently, he wrote: “The Search For A Natural Cure For Cancer”, (62, I). In this paper, he summarized his theories on cancer research with a constructive approach to finding an effective treatment for cancer.

“There is a great need for a drug which cures or prevents cancer without harming the patient. Such an action can be expected only from a natural substance. I have to explain what I mean by ‘natural’.

“The cell is an exceedingly complicated and subtle machinery in which all functions are carefully regulated. A normal cell divides only when division is needed. A cancer cell divides also when no division is needed. The regulators are out of order. All efforts to show the difference between the chemical makeup of a normal and a cancer cell have hitherto failed. The cellular structures are

identical, only the regulators are disturbed. Something has gone wrong that has to be repaired.

“In order to be able to repair any mechanism, we must know how it is built and how it works... We can control only what we understand. To be able to repair, we must find out what has gone wrong, which screw is missing or which bolt has loosened. To replace the new part which takes over the function of the old one, is what I call a ‘natural cure.’ Only by replacing the failing part, can we expect a real cure which does not damage the host. Putting in all sorts of substances which we take from the shelf, or synthesize are not ‘natural,’ even if taken from some plants. The same holds for high energy radiation. All these artificial therapeutics agents interfere with some basic function on which both the cancer and the normal host cell depend. They have thus to damage both.

“For years my laboratory has worked in silence to find out how the living cell regulates its proliferation. We have arrived at a fairly clear concept and hope to be able to identify soon the part which is not working properly. In my opinion, this is the only hopeful approach. It is not an easy one because the living machinery is very complex and subtle. This is not a new approach either. It is the oldest approach but it is not a sensational one and so it is very difficult to find support for it. The National Institutes for Health, the main granting agency for biomedical research, rejected my application thrice. I had no luck with the cancer society either. Everybody wants a quick cure, but there are no shortcuts to basic research. There are shortcuts only to failure.

“...Oxygen makes oxidation, burning possible, and oxidation produces energy. Warburg, the great German biochemist, made energy responsible for the development. But energy cannot transform, build machines, it can only drive them. But if it was not energy which provoked the development, then it had to be oxygen itself which made the difference. ‘Oxidation’ in scientific language means taking ‘electrons,’ electric particles from oxidized material. All matter is built of an atomic nuclei and electrons. Taking electrons from a substance means oxidizing it. The oxygen of the air does not take electrons from the living protein, but there are atomic groups, called carbonyls, which contain oxygen which can take single electrons from protein, bringing the proteins hereby into a most reactive form, called ‘free radical.’ The transformed proteins have very special properties, like electric conductivity, **It is here in the electronic dimension that something is out of order in cancer.**

Carbonyls arrest cell division and my laboratory was led to the conclusion that it is still the carbonyls which arrest cell proliferation and it is the carbonyl which make the cell return to the resting state, after it completed division, If the carbonyls are missing, proliferation has to go on, and cancer results. We were not the first to be led to such a conclusion. A decade ago a very intuitive researcher, W. F. Koch, came to the same conclusion. Unfortunately, he did not leave us enough information to enable us to follow his trail.

“By having carbonyls as regulating agents, the problem is by no means solved. We have to find out how the carbonyl fits into the regulation, how it is produced, destroyed and how it acts. There is still a long way to go, but I am very confident that this is the right way and the end is not too far.”

Dr. Szent-Gyorgyi, in his book *Electronic Biology and Cancer, A New Theory of Cancer*, Chapter 5, Oxygen and Dicarbonyls (1976) (62, m) describes the importance of molecular oxygen and its central role in biology and its ability to oxidize by taking electrons from other molecules. He explains the relationship between the oxygen atom and the carbon atom, the carbonyl ($C = O$) and the dicarbonyl ($O = C - C = O$) and he points out that the simplest dicarbonyl is glyoxal and that the methyl derivative is methylglyoxal. Also, he points out that the simplest di-aldehyde is also glyoxal and the simplest ketone aldehyde is also methylglyoxal. He further points out that since the dicarbonyls are highly unsaturated compounds, they cannot exist in a strongly reducing anaerobic atmosphere, the alpha state (the simplest or unstructured state) of cellular life. Thus, the dicarbonyls become a specific features of his beta state (aerobic or structured state) of cell life. To obtain the full benefit of Dr. Szent-Gyorgyi's research, one has to fully study this booklet and his subsequent booklet “Living State and Cancer” (1978) (62, n)

In Chapter 20, “Notes On History”, of this booklet, Dr. Szent-Gyorgyi made a brief reference to the research of Dr. William F. Koch with the dicarbonyls in the sixties, and Dr. Koch's claim of therapeutic action for quinones. (*The Survival Factor In Neoplastic And Viral Diseases, A Study of the Phenomena of the Free Radical, the Double Bond, and Its Alpha placed Hydrogen Atom in the Pathogenesis and Correction of Neoplastic, Viral and Bacterial Diseases*, 1961)(33). Dr. Szent-Gyorgyi felt that the data given by Dr. Koch was not detailed enough to allow

repetition. Dr. Szent-Gyorgyi further pointed out that quinones did inhibit cell division but that they were very toxic and that the quinones, that he tested, he found to be devoid of therapeutic activity.

Dr. Szent-Gyorgyi was right when he said that quinones inhibit cell division but are very toxic. However, he did not indicate which quinones he worked with in his research and the type of experiments that he conducted. Because of the toxicity of quinones, they have to be used in high (homeopathic) dilutions of (6x) 1×10^{-6} . When Professor Maisin was doing his research in Belgium with some of Dr. Koch's products, Dr. Maisin found that he received his best results using these products at dilutions from 1×10^{-9} to 1×10^{-18} . Though these are very high dilutions (1×10^{-18}), he said that these products still contain several thousand molecules per cubic centimeter. (52) I only wish that Dr. Szent-Gyorgyi had learned more about Dr. Koch's research before working with quinones.

In 1979, Dr. Philip Garber contacted Dr. Szent-Gyorgyi in regards to my father's research and he had suggested that Dr. Szent-Gyorgyi meet with me in order that he (Dr. Szent-Gyorgyi) might learn more about Dr. Koch's theories, etc. Dr. Szent-Gyorgyi's wrote the following in his letter of November 1, 1979 to Dr. Garber.

"I can tell you, I have a great admiration for Koch. He must have been a very outstanding man. My feeling is that he **had a strong intuitive feeling about the role of C=O group and especially its conjugated form as C=OC=O as one of the great regulating forces in nature.** It is very unfortunate that he never expressed this clearly and definitely in any (of) his writings known to me. I have been working myself on these lines now for years and the subject has made very great progress and it is doubtful whether the notes of Dr. Koch could help any further.

"I would not like to become involved in the controversy around his name and, maybe, reproached later that I am led in my studies in by the posthumous notes which Paul could put at my disposal. I also doubt whether I could find the time for their study they undoubtedly deserve. I would not like either to revive the controversy around his work. That he has met by hostility is not doubtful for me. I know it from my own experience that people with intuition are regarded as an enemy by those who have none."