CANCER AND VITAMIN C

A DISCUSSION OF THE NATURE, CAUSES, PREVENTION, AND TREATMENT OF CANCER WITH SPECIAL REFERENCE TO THE VALUE OF VITAMIN C

Ewan Cameron, M.B., Ch.B., F. R. C. S. (Glasgow), F. R. C. S. (Edinburgh)

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Preface

Some years ago we developed the idea that regular high intakes of vitamin C (ascorbic acid, or its several biologically active salts known as ascorbates) play some part both in the prevention of cancer and in the treatment of established cancer.

Evidence steadily accumulates to support this view.

Cancer, of course, is the major unsolved health problem with strong emotional overtones. Although not the major killer, it has become the most feared of all diseases and a major focus of biological research throughout the world. The repeated statement of our views and clinical results in the scientific literature has given rise to much fruitful discussion with colleagues in the scientific and medical fields, and it has also involved us in a massive correspondence with desperate cancer patients seeking advice and help, as well as with their families, friends, and physicians.

For some years we have tried to write personal letters to these patients, family members, friends, and physicians, but meeting this obligation is now beyond our resources. It seems increasingly clear to us that many of these despairing patients lack understanding of (a) the very nature of cancer, (b) the value and the limitations of all conventional (and some unconventional) forms of treatment of cancer, and (c) our own views as to how vitamin C might help them. This book is an attempt to answer these questions.

Cancer is an unpleasant disease. Death by cancer usually involves much more suffering than other ways of death, such as by a heart attack. The cancer patient may lead a life of misery for months or years before his suffering is brought to an end by death. Much of his misery may be caused by the treatment that is given him in the effort to control the disease.

In the United States about 1.9 million people will die this year. About 20 percent of the deaths, 395,000, will be from cancer. Every day about 2,100 people in this country develop cancer and about 1,080 die of cancer. If the incidence and mortality continue at their present rates, one adult in the United States in every three will develop cancer at some time in his life, and one in five will die of the disease.

During the last twenty years about ten billion dollars has been spent on cancer research, in the effort to get some control of the disease. The budget of the National Cancer Institute for the year 1979 is $900 million and that of the American Cancer Society is $140 million. Despite this great expenditure and the corresponding great effort, not much has been achieved. Some progress has been made in the treatment of some kinds of cancer, especially leukemia and Hodgkin's disease, by new regimes of treatment with high-energy radiation and anticancer drugs. For most kinds of cancer, those involving solid tumors in adults, which lead to 95 percent of the cancer deaths, there has been essentially no change in overall incidence and mortality during recent years.

One of us (Ewan Cameron) is a surgeon who for over thirty years has been involved in the treatment of cancer patients. During the early part of this period he developed the idea that the most important factor determining the progress and outcome of any cancer illness is the natural resistance of the patient to his disease. In his 1966 book *Hyaluronidase and Cancer* he pointed out that the resistance of the normal tissues surrounding a malignant tumor to infiltration by that tumor would be increased if the strength of the intercellular cement (also called ground substance) that binds the cells of the normal tissues together could be increased. This intercellular cement contains very long molecular chains, called glycosaminoglycans, that give it strength, and it also contains fibrils of the protein collagen, which further strengthen the cement in the same way as the steel reinforcing rods strengthen reinforced concrete. It is in fact known that some, and probably all, malignant tumors liberate an enzyme, hyaluronidase, that causes the glycosaminoglycans to be cut into smaller molecules, thus weakening the intercellular cement. Moreover, some, and perhaps all, malignant tumors also liberate another enzyme, collagenase, that causes the collagen fibrils to be split into small molecules, further weakening the normal tissues and making it easier for the malignant tumor to grow into them in the way characteristic of malignancies.

These facts indicate clearly that the effort should be made to strengthen the intercellular cement in the normal tissues of cancer patients and to inhibit the tumor enzymes that cause its breakdown. Until 1971, however, no one had found a way of doing this. Then in that year two new ideas, both involving vitamin C, were advanced. Cameron and Douglas Rotman, on the basis of some chemical arguments, suggested that an increased concentration of vita-

min C in the body would stimulate the normal cells to produce increased amounts of the substance hyaluronidase inhibitor, which would combine with the enzyme hyaluronidase liberated by the malignant tumor and prevent it from attacking the intercellular cement. At the same time the other author of this book (Linus Pauling) pointed out that it is known that vitamin C is required for the synthesis of collagen; accordingly increasing the intake of this vitamin would cause more collagen fibrils to be made, further strengthening the intercellular cement.

He suggested to Cameron, for reasons discussed in Chapter 14, that an intake of 10 grams of vitamin C per day be given to the patients with advanced cancer. Clinical trials were cautiously begun by Cameron in Vale of Leven Hospital, Loch Lomondside, Scotland, in November 1971. The patients who were treated with vitamin C during the first year were those with advanced cancer for whom the conventional treatments had ceased to be of benefit —patients considered in Scottish medical practice to be "untreatable."

Cameron soon was convinced that most of the patients who received vitamin C benefited from it, and with each succeeding year a larger fraction of the cancer patients in this hospital were given the vitamin. Over 500 patients in this hospital with advanced cancer and many with cancer in earlier stages have received vitamin C, in conjunction with other therapy, during the eight years since this treatment was instituted. The use of vitamin C has also spread to other hospitals in this region of Scotland, and to a smaller extent to other parts of the world.

The first observation that was made is that for many cancer patients the administration of vitamin C seems to improve the state of well-being, as measured by improved appetite, increased mental alertness, decreased requirement for pain-killing drugs, and other clinical criteria. This effect was described by Cameron and Campbell (1974) in their report on the first 50 ascorbate-treated patients in the following words:

> We should now like to describe what we have come to recognize as the standard response to large-dose ascorbic acid supplements in patients with advanced cancer. Subjective evidence of benefit is usually apparent by about the 5th to 10th day of treatment, and in many patients this response can be very striking indeed. The patient then enters a stage of increased well-being and general clinical improvement, and during this phase objective evidence accumulates to confirm that some retardation of tumor growth has been achieved. The objective evidence of benefit varies with the individual clinical presentation, but may take the form of relief of particularly distressing pressure symptoms such as pain from skeletal metastases, a slowing down of the rate of accumulation of malignant effusions, a trend toward improvement in malignant jaundice, or relief from respiratory distress, and is accompanied by a slow fall in the erythrocyte sedimentation rate and the serum seromucoid concentration. This phase of clinical improvement may be

> very transient, or it may last for weeks or months, and in a few patients may be so prolonged and accompanied by such convincing evidence of objective benefit as to indicate that permanent regression has been induced.

An unexpected and potentially valuable relation of vitamin C to addictive narcotic drugs was also noted. Many patients with advanced cancer, especially those with skeletal metastases, suffer severe pain because of the pressure developed by the growth of the tumor in a restricted space. This pain frequently requires the use of narcotic drugs. Cameron and Baird (1973) reported that the first five ascorbate-treated patients who had been receiving large doses of morphine or heroin to control pain were taken off these drugs a few days after the treatment with vitamin C was begun, because the vitamin C seemed to diminish the pain to such an extent that the drug was not needed. Moreover, none of these patients asked that the morphine or heroin be given to them —they seemed not to experience any serious withdrawal signs or symptoms. This observation was the basis of the recently reported successful use of massive doses of vitamin C in the treatment of narcotic addiction (Libby and Stone, 1976).

A careful study has been made of 100 of the first ascorbate-treated cancer patients in Vale of Leven Hospital, in comparison with 1000 cancer patients who were matched (10 to 1) with the ascorbate-treated patients with respect to age, sex, type of cancer, and clinical state and who were treated by the same physicians, in the same hospital, and in the same way except that they did not receive the doses of vitamin C. The results of this study were reported in two papers (Cameron and Pauling, 1976, 1978) and are discussed in detail in later chapters of this book, beginning with Chapter 18. Here we may mention that on the average the ascorbate-treated patients survived ten months longer than their matched controls. Twenty-two of the 100 ascorbate-treated patients (22 percent) lived longer than a year after being deemed to have reached the terminal stage, whereas only four of the 1000 controls (0.4 percent) lived this long. The average survival time of these 22 ascorbate-treated patients after being deemed terminal has now (15 September 1979) reached 2.8 years, and continues to increase with the passing of time because five of these patients are still alive; all of the controls have died.

In this study, in which the treatment with vitamin C was introduced only in the terminal phase of the illness, most of the patients were not so fortunate. After a period of sustained clinical improvement the malignant activity reasserted itself, and the patient died from his original disease. In many of these patients the mode of death was in itself unusual. After a period of comparative well-being and apparent tumor quiescence the patient very suddenly entered a rapid terminal phase with a precipitous downhill course and death within a few days from fulminating cancer. In some patients these events followed immedi-

ately the cessation, for one reason or another, of the intake of the large doses of vitamin C, and for these patients the rapid decline may well be attributed to this action. For other patients, however, who continued to receive the vitamin some other explanation of the sudden transition from apparent restraint to uncontrolled dissemination of the malignancy is needed. There is still uncertainty about the most effective dosage of vitamin C for cancer patients, and it is possible that permanent regression could have been achieved for some of these patients by giving them larger doses of the vitamin. In fact, amounts larger than 10 grams per day—as much as 100 grams per day—have been used in some cancer patients, both by intravenous infusion and orally, with apparent benefit. In one patient recurrence of the cancer that had been controlled for six months by intake of 10 grams per day was observed to follow the cessation of intake of the vitamin. The recurrent cancer did not respond to oral doses of 10 grams per day for 10 days but did respond by a second regression to 20 grams by intravenous infusion for 10 days, followed by a maintenance oral dosage of 12½ grams per day (Cameron, Campbell, and Jack, 1975; see also Chapter 20).

Many patients with cancer in earlier stages in Vale of Leven Hospital and elsewhere have been treated with a large intake of vitamin C, in conjunction with other therapeutic measures, often with great apparent benefit. No carefully controlled long-term trial to determine the amount of this benefit has been carried out. We believe, however, on the basis of our own observations (some of which are discussed in later chapters of this book) that vitamin C therapy against cancer is much more effective when it is begun early in the development of the disease than when it is postponed until the patient has reached the apparently hopeless stage.

There is also much evidence that an increased intake of vitamin C by healthy people significantly decreases the chance of developing cancer. This evidence is discussed in Chapter 22.

We have some information about how vitamin C works in the prevention and treatment of cancer, but much remains to be discovered. Vitamin C can inactivate viruses by a molecular mechanism that is understood, and it may function in this way to help control those human cancers that are thought to involve viruses. It also has rather general detoxifying powers for toxic substances that enter the human body, including carcinogenic chemicals (substances that cause cancer). Probably its most important modes of action are those in which it increases the effectiveness of the body's natural protective mechanisms, especially the various immune mechanisms. A detailed discussion of the mechanisms of action of vitamin C is given in Chapters 15 and 16.

It is our opinion that supplemental vitamin C has value for the prevention of all forms of cancer in healthy human beings and also is of some benefit in the

treatment of patients with cancer in every stage of the disease, and can be of great value to some patients. We believe that before long the use of this simple, safe, natural, and inexpensive substance will become an accepted part of all regimes for the prevention and treatment of cancer.

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Contents

PART I

THE NATURE AND CAUSES OF CANCER

1

The Nature of Cancer

The human body may be compared with a clay sculpture. Corresponding to the internal wire frame of the sculpture, we have a bony skeleton, which is hinged here and there to permit motion. In order to give this structure life and being there are some 10 trillion (10,000,000,000,000) cells scattered throughout, occupying, together with the body fluids, every available interstice. Each cell carries out some specialized functions. They range from those of the simple fibroblast, which is busily at work keeping the reinforcing material in good shape, and the lymphocytes and other white cells, which destroy invading bacteria and cancer cells, to the highly complex cells of the brain, which formulate and transmit the orders for all this corporate activity and which interact with one another in such a way as to fashion our consciousness, provide our memory bank, and permit us to think and reason. To hold the cells together and to fill us out to shapely proportions we have a ubiquitous material called the *ground substance* or intercellular cement, mentioned in the preface. Thoroughly mixed into this ground substance is a dense network of collagen and other fibers to give it extra strength and resilience.

These 10 trillion cells all function as subservient members of one highly integrated unit, the human body, obedient to the motto "Each for all, and all for one." They can be likened to the members of a highly organized national state with an extremely strict code of law and order, with each individual performing his allotted task for the good of the whole and with any disobedience or failure to serve the collective organization punished by immediate expulsion and death.

Most of these cells have the capacity for infinite multiplication and also for reversion to a more primitive and less specialized form. This capacity is demonstrated in the technique of tissue culture: a normal cell is taken from a human being or other organism and put in a glass flask where it is provided with the right nutrients and kept at the right temperature; it then divides into two cells, and the process of cell division continues without end, producing a vast succession of generations of progeny, so long as we provide the requisite artificial environment.

This capacity for repeated multiplication is continually operating in the perfectly healthy body, but always in a very carefully controlled manner. Cells of some kinds in the human body age and die and are constantly being replaced by fresh offspring, but always within the total ceiling of 10 trillion. Skin is a good example. Our complexion consists of a smooth patina of dead cells that are constantly being discarded and just as constantly being replaced by generations of new cells rising up from the deeper living layer, and yet the whole process is so nicely regulated and controlled throughout our whole lifespan that only a very few unfortunate persons, with rare genetic diseases, ever develop rhinoceros hides or pathologically thin skins because of a fault in this regulatory mechanism. The specialized cells of the gastrointestinal tract, millions and millions of them arranged in fronds and villi to increase their functional area and busily secreting digestive enzymes and absorbing the processed nutrients for distribution to their compatriots, also wear out and die and are then discarded, broken down into small molecules for recycling or elimination, to be automatically replaced by fresh vigorous young descendants ready to carry on the same function—and yet for most human beings we do not see an intestine choked and blocked by solid masses of such cells or a useless intestine completely devoid of them.

The proliferative capacity of cells is best seen in the process of repair after injury. In any healthy tissue of an adult at any time we have a stable number of cells that divide only now and then to replace their defunct brethren. But when a wound is inflicted on that tissue everything is galvanized into frenzied activity. All cells in the immediate vicinity leap into action, dividing rapidly to repair the defect. It is interesting to note that if one takes a small sample of such healing tissue and submits it to an experienced histopathologist without telling him that it has come from a recent wound his opinion after microscopic examination of the tissue may be that it is from a malignant tumor. But of course it is not malignant, because as soon as the healing process is complete the cells revert to their usual well-controlled existence and their life continues as before the injury.

This almost unbelievably precise and quite magnificent control mechanism enables the human being to survive as a completely integrated functioning

organism, instead of turning into a heterogeneous mass of warring cellular factions.

Cancer occurs when a cell and its descendants (or sometimes two or more cells of different kinds and their descendants) escape from this control mechanism and begin to behave in a renegade fashion. When we consider the total number of cells at risk and their continuing activity throughout life, we must conclude that the remarkable fact is not that people develop cancer, but rather that many people escape this fate throughout their lives.

Thus cancer occurs when a single cell (or a group of a few cells) escapes from regulatory control and is able to bequeath its independence to its descendants through every succeeding generation. The cancer cell exploits his newfound freedom to the utmost. No longer need he stay in place, wait in line for food, nor perform any function for the benefit of the whole organism. He can reproduce at will, building up an immense clone of equally ruthless offspring. Suddenly he and his offspring can travel throughout the body, taking over new areas of territory and, by leaping in and out of the circulatory systems, establish new colonies of equally ruthless aggressors in distant lands. He has acquired the trick of securing the lion's share of the available nutrients. He may cease to perform the functions that he formerly carried out for the benefit of the whole community of cells. He is the true wayward renegade rebel, creating his own largely independent colony within the corporate state of the human body.

For a time he may enjoy great success. He is efficient and aggressive. He and his progeny have the potential to be truly immortal, except for one thing: they are parasites who need the food, water, and oxygen and all sorts of metabolic services provided by the rest of the organism. The cancer cell attacks, has his initial success, enjoys a brief moment of supremacy, and then, as the source of the essential supporting services is destroyed, he also dies.

In the following paragraphs we outline the progressive stages of development, establishment, and dissemination of human cancer.

Although undoubtedly many changes go before, the first clearly detectable stage is that of *precancer*. Evidence of this stage may be seen by use of the optical microscope, which reveals changes in the appearance and configuration of cells that predict frank malignant change. In healthy epithelium (outer layer) of the skin, for example, the microscopist has before him an orderly array of identically shaped cells, each with its own sharply defined nucleus and each neatly mortised into its neighbors in a nearly perfect pattern of uniform thickness. But in precancerous change there is an obvious irregularity of the epithelial thickness, with peaks and troughs related to the profusion or scarcity of the component cells. Furthermore, the cells have lost their uniformity; there are dwarf cells and giant cells interspersed with cells of normal

size, and many cells show gross irregularity of the nuclei. This development of structural irregularity and confusion often precedes clinical cancer, but not always, as will be discussed in later chapters.

We may assume that such precancerous changes occur in every tissue, although their identification is possible only in situations accessible for surveillance. These are in the epithelium of the cervix of the uterus (by the Pap-smear technique), in the breast (by biopsy for intra-duct carcinoma), and in the urinary bladder (search for the so-called unstable transitional uroepithelium). What are observed are visibly abnormal cells, proliferating in an irregular fashion and clearly associated with malignant change, but as yet showing no migration and no evidence of malignant invasiveness.

The next stage is frank local cancer. Here the distortion of individual cell structure is more pronounced, with a tendency to reversion to a more primitive "undifferentiated" type of cells, and, more important, with infiltration of the abnormal cells from their normal locations into the surrounding tissues.

There are several grades at this stage, building up to the sizeable local "lump" or tumor that needs no microscope for its recognition. The tumor (which is called the *primary tumor*) consists of a steadily expanding mass of subdividing cells. It can grow rapidly: in only 25 cell divisions (25 generations) a single cancerous cell can have over 30 million progeny, forming a tumor the size of a baseball, if no loss of tumor cells takes place.

At this time signs and symptoms usually become evident. The mass, lump, tumor, or cancer (meaning the same, if it is a malignant growth) may have reached such size as to be recognized. If it is of the skin, we may see it as an indolent (painless) ulcer that will not heal; if it is in a prominent structure, such as the breast, we can begin to feel it as a suspiciously hard nodule different in consistency from the normal tissues. Elsewhere it might make its intrinsically painless progress known indirectly by the slow compression of involved or adjacent structures, producing such effects as increasing difficulty in swallowing in cancer of the esophagus, obstruction of the large bowel and consequent problems of elimination in cancer of the colon, difficulty in urination in cancer of the prostate, painless jaundice because of compression of the bile duct by cancer of the pancreas, and hoarseness caused by compression of the nerve to the larynx by hilar cancer of the bronchus (lung cancer). Or it might declare its presence by suddenly ulcerating through some vital membrane, producing anything from barely noticeable to massive bleeding, such as hemoptysis (coughing up blood), hematemesis (vomiting blood), melena (passing blood in the stools), vaginal bleeding (from some ulcerative lesion in the female generative tract), or hematuria (passing blood in the urine). Every one of these signs and symptoms can be caused by disorders other than cancer