

Vitamin C

“If an elderly but distinguished scientist says that something is possible he is almost certainly right, but if he says that it is impossible he is very probably wrong.”

Arthur C. Clark

The aim of cancer research is to find a safe agent that can destroy a wide range of cancers. Recently, we described the action of vitamin C (ascorbate) in such terms.¹⁵ In this chapter, we revise and update our earlier description.

An effective treatment must either prevent cancer cell proliferation or increase cancer cell death.¹ Vitamin C can do both. Evidence suggests that high dose Vitamin C eradicates cancer cells selectively, while leaving healthy cells unharmed.^{216,217} In fact, rather than damaging normal cells, the vitamin’s antioxidant properties may improve the patient’s health.

Vitamin C belongs to a class of chemicals whose importance is only just being realised: effective cancer treatments that have few side effects. The idea that vitamin C could provide a useful treatment for cancer originated over half a century ago.⁶⁴⁷ Since then, hundreds of research papers, including laboratory, animal and human studies, have been published on the effects of ascorbate on cancer. The evidence continues to accumulate; for example, Mark Levine’s group at the US National Institutes of Health (NIH) recently confirmed reports of the selective cytotoxic action of vitamin C on cancer cells.⁶⁴⁸ Levine’s report indicates that the cytotoxic actions of vitamin C are no longer considered controversial.

Vitamin C is a widely used nutritional supplement. It has been the subject of large claims, from Linus Pauling and others, as well as numerous attacks by government authorities. The medical establishment’s attitude towards vitamin C is, at best, ambivalent. For example, a book on medical blunders includes the establishment’s response to Linus Pauling’s proposals on vitamin C.⁶⁴⁹

The story of vitamin C is one of the most fascinating in modern medical science.¹⁵ Humans, unlike most other animals, do not synthesise vitamin C in their bodies. As a result, people need to obtain vitamin C from their food to avoid the disease scurvy. For decades, there has been a controversy about the appropriate levels of intake for optimal health.

Our current model, which supports high dose intakes, is called dynamic flow.^{15,470} According to this, frequent doses of vitamin C are required to maintain high blood levels, leading to excretion in the urine. Dynamic flow ensures the body is constantly in a reducing state. Repeated high doses provide a mechanism for humans to restore their physiology to a state close to that of most other animals, which synthesise the vitamin.

Low blood levels of vitamin C lead to sickness and ill health,⁶⁵⁰ while higher levels are associated with prevention of cancer and general good health.⁶⁵¹ Dynamic flow level oral intakes or intravenous doses of sodium ascorbate may be beneficial in treating cancer.^{652,675,676,693,694,695,697,698,701,703,704,710,711,712,713,721} Intravenous administration is generally more effective as a treatment for disease,⁶⁵³ although it is possible that oral doses, sufficient to maintain dynamic flow, could be an effective treatment. Frequent, gram level oral doses can lead to sustained plasma concentrations, at up to 250 $\mu\text{M/L}$. Intravenous doses can produce higher, but transient, plasma levels in the millimolar range (i.e. above 1000 $\mu\text{M/L}$).⁶⁵² However, as we shall see, certain synergistic supplements increase the potency of vitamin C against cancer cells. These supplements may allow an effective oral therapy for many forms of this disease.

Further indications that vitamin C could be an effective treatment arise from the finding that ascorbate prevents cancer cells from growing. Ki Won Lee and colleagues, from the University of Seoul, have described a mechanism by which vitamin C stops cancer cells proliferating.^{654,655} Normal cells stop growing when they receive signals from neighbouring cells; these signals are induced by hydrogen peroxide and other oxidants. Cancers can continue spreading, because they do not respond to the signals that inhibit growth in normal cells. Ki Won Lee showed that vitamin C enabled cancer cells to receive and act on such messages to stop growth.

Reduction and oxidation

Vitamin C normally acts as a reducing agent in the body. It is the main water-soluble antioxidant in the diet and the most important in the extracellular fluid. Despite these properties, under certain circumstances, it can also act as an oxidant. It shares this ability to act as either an oxidising or a reducing agent with many other dietary antioxidants, including vitamin E.

People critical of high doses have used the possibility that vitamin C acts as a pro-oxidant as a justification for not taking supplements.

However, both antioxidant and oxidant properties of vitamin C offer health benefits. In particular, the oxidant properties of vitamin C are believed to be a central feature of its anticancer action.^{217,656} Ironically, the property that detractors use as a key point against the use of high doses of vitamin C could form the basis of one of its clinical benefits.

Ascorbate kills cancer cells

Ascorbate has powerful effects on the metabolism of cancer cells.^{217,657} It has been shown to inhibit the growth of several cancer cell lines,^{217,658} and is effective in inhibiting tumour growth in animal experiments.⁶⁵⁹ Vitamin C kills cancer cells by oxidation and, more specifically, by generating hydrogen peroxide inside the cell body.^{660,661,662,663,664,665,666} Furthermore, the hydrogen peroxide produced in this way breaks down to give additional oxidants, such as the hydroxyl radical, which can severely compromise cancer cells.⁷¹⁸

In cancer, when vitamin C cycles between ascorbate and dehydroascorbate, hydrogen peroxide is produced.^{667,853,668,669,670} These effects are increased by the presence of free iron and copper,⁶⁷¹ and a combination of vitamin C and copper has been suggested as a possible cancer treatment.²¹⁷ Cancer cells contain high levels of iron and some other metals.^{672,673} As we have explained, the cells are short of antioxidant enzymes, including catalase, which converts hydrogen peroxide to oxygen and water.^{674,675} Consequently, they are unable to detoxify the large quantities of hydrogen peroxide produced by high levels of vitamin C. This hydrogen peroxide damages and kills the cancer cells.

Intravenous administration

Intravenous ascorbate can kill cancer cells,^{711,676,1028} but the blood levels obtainable with oral doses have generally been shown to be less effective. When vitamin C is given intravenously, high levels (up to about 15 mM/L) can be achieved. This is far greater than the concentration required to kill cancer cells. A thin layer of cancer cells may succumb to even a short exposure at levels of 1 mM/L.

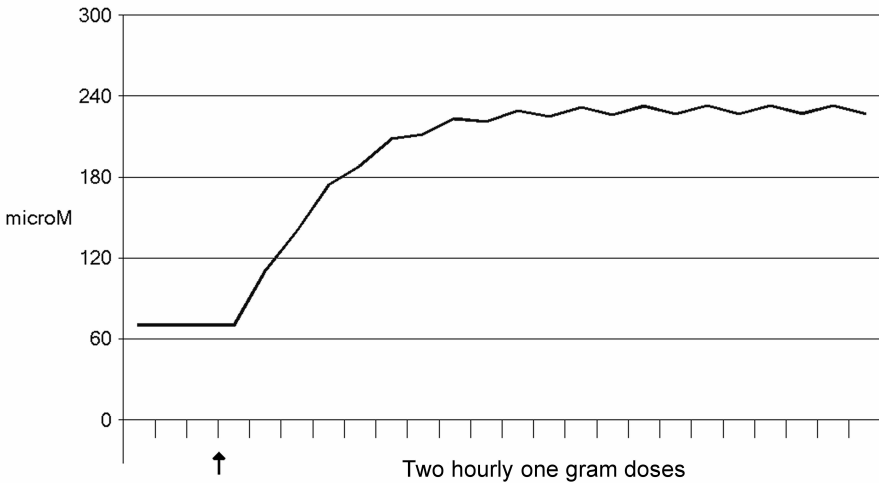
For many years, there has been confusion about the difference between intravenous and oral doses of ascorbate. Intravenous doses of sodium ascorbate are reported to be more effective, consistent with the increased blood levels obtained. Following an intravenous injection, the high blood levels of ascorbate fall rapidly. Typically, therefore, the dose is infused over a period of several hours, to maintain blood levels.

The intravenous doses of sodium ascorbate required to be cytotoxic to cancer cells can exceed 100 grams. This is a massive dose, even when compared with the “megadose” or gram level intakes suggested by Linus Pauling and others. Typically, these massive infusions will be accompanied by an oral intake of more than 10 grams per day.

Oral doses

It is sometimes claimed that it is not possible to reach cytotoxic levels of vitamin C with oral intakes. However, this assertion is based on incomplete and inappropriate data. In a well-nourished individual, the background blood plasma level is about 70 $\mu\text{M/L}$. Above this concentration, ascorbate is rapidly excreted from the blood, with a half life of about 30 minutes. Large oral doses raise blood levels to a peak in about 2-3 hours, after which the level decays back to the baseline. Frequent oral doses can sustain blood plasma levels of, perhaps, 250 $\mu\text{M/L}$, in a dynamic flow. Such levels are toxic to some cancer cell lines.

Blood plasma levels of ascorbate



This graph shows computed plasma levels for gram level doses of ascorbate, taken orally, at two-hour intervals. The first dose is given in the third hour.

Repeated large oral doses can establish plasma vitamin C levels equivalent to those that, in test tube studies, kill some types of cancer when administered for even a short period. It is not yet known what the result of sustained high oral doses would be on cancer in humans. Oral doses have been reported to be effective in clinical cases of cancer.^{15,581,677} However, Robert Cathcart, a physician highly experienced in the use of vitamin C, reports that he has never succeeded in curing cancer with oral doses and warns against hubris in this area.⁶⁷⁸ It is possible that dynamic flow intakes could be effective in destroying cancer, but this hypothesis has yet to be subjected to clinical trials.

Bowel tolerance levels, as described by Cathcart,⁶⁷⁹ produce blood levels in the region of 250 $\mu\text{M/L}$; these can be sustained by repeated dosing at short intervals. In a healthy adult, bowel tolerance is typically reached by a single oral dose above about five grams. Intakes of approximately 20 grams per day, in frequent divided doses, can sustain these high plasma levels. In sick people, the bowel tolerance increases greatly. A mild cold can increase the tolerance level to above 50 grams per day, while influenza and other severe viral infections can raise the level to approaching 200 grams.

Uptake by cancer cells

Like people with infections, cancer sufferers have an increased bowel tolerance to vitamin C. This probably reflects higher requirements for ascorbate. Cancer patients' tissue vitamin C levels are lower than are those of healthy people. Patients undergoing conventional treatments have even lower values: the body's ascorbate reserves appear to be inversely related to the intensity of conventional treatment.⁵⁸¹

Hugh Riordan's research group have described an interesting example, which relates to this finding.⁶⁸⁰ A 70 year-old man from Kansas, with cancer of the pancreas, was given a 15-gram infusion of sodium ascorbate, over a period of one hour. Immediately following the treatment, his blood vitamin C levels were far lower than expected.^a Our explanation for this finding is that cancer cells absorb and metabolise high levels of ascorbate.⁶⁵⁹

Cancer cells can absorb ascorbate by a different mechanism than is used by most healthy cells. Healthy cells take up vitamin C from the surrounding plasma, using biochemical pumps. Some cells contain

^a The quoted value was 34 mg/dl compared with 120-200 mg/dl for a healthy subject. These figures seem to relate to measurements following intravenous infusion.

specific ascorbate pumps, while others absorb oxidised vitamin C, or dehydroascorbate, using glucose pumps.^{681,682,683} Oxidised vitamin C is structurally similar to glucose, so can be transported by glucose pumps. Some specialised white blood cells take in vitamin C by oxidising their local surroundings, absorbing the resulting dehydroascorbate and then reducing it back to ascorbate.²

Tumours have a similar mechanism, which can accumulate high levels of ascorbate within cancer cells.⁶⁸⁴ When glucose levels are low, tumours absorb more vitamin C. However, high levels of glucose inhibit uptake of both dehydroascorbate and ascorbate.⁶⁸⁵ Cancer can inhibit active transport of the vitamin,⁶⁸⁶ hence reducing its antioxidant effects. Despite this, cancer cells absorb higher levels of vitamin C than might be expected. The importance of the relationship between glucose and vitamin C, in cancer and its treatment, has been stressed by John Ely.⁸³¹

A general feature of malignant tumours is that they are in an oxidising state. Cancer cells use the oxidising conditions to assist their growth and cell division. Consequently, when ascorbate molecules enter the tumour's environment, they become oxidised to dehydroascorbate and may produce hydrogen peroxide.⁶⁸⁷ Glucose transporters in the cancer cells' outer membranes are then able to transport the dehydroascorbate into the cell bodies.⁶⁸⁸ Moreover, cancer cells have a higher than normal dehydroascorbate transport rate.⁶⁸⁹ In animal models, tumour cells that accumulate only oxidised ascorbate have been shown to take in the vitamin, rapidly.⁶⁹⁰

Malignant melanoma is one of the most aggressive of human cancers; it is derived from melanocyte cells in the skin. It requires large amounts of glucose to power its growth and activities. Like other cancers, melanoma cells have large numbers of glucose transporters. Some melanoma cells actively facilitate the uptake of the dehydroascorbate form of vitamin C.⁶⁹¹ Melanoma cells transport ascorbate with similar levels of efficiency to those of healthy melanocytes. By contrast, melanoma cells transport the oxidised form, dehydroascorbate, 10 times faster than melanocyte cells.⁶⁹² This increased rate of dehydroascorbate transport is achieved using glucose transporters. Melanoma cells can concentrate dehydroascorbate to levels 100 times greater than those in the surrounding medium.

Cancer cells absorb oxidised ascorbate

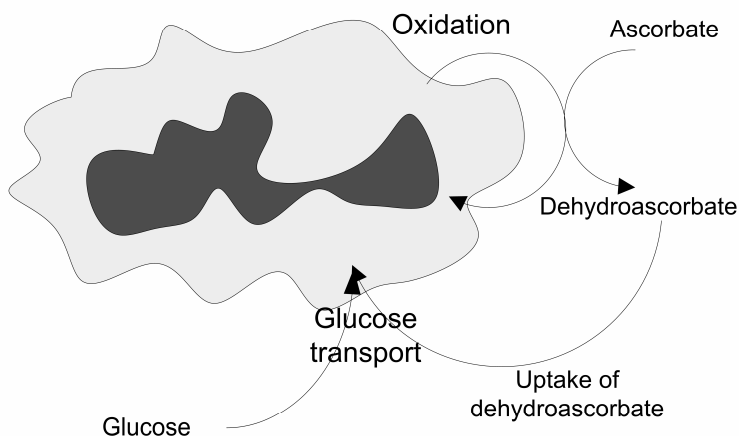


Diagram showing the uptake of dehydroascorbate by glucose pumps in cancer cells.

Clinical studies of cancer

The history of vitamin C as a cancer treatment is a catalogue of errors. Many experiments were poorly performed and lacked controls. Other researchers failed to give the vitamin C by injection, thinking an oral dose would be as effective. Where trials did use oral intakes, the doses were given infrequently and were not adequate to sustain the patients' blood levels.¹⁵ Scientists on both sides of the debate have been subjected to personal abuse and had their motives challenged.^b However, we are not interested in debate or argument, only in the facts.

The idea that vitamin C could be used to treat cancer was popularised in 1976, by Linus Pauling and Ewan Cameron, a Scottish surgeon. Cameron was a respected and established cancer specialist, who believed that the critical factor in recovery from cancer was the person's biological response. At first, he was sceptical that vitamin C could work against cancer. However, he realised that his patients had little to lose. Some were in the terminal stages and, even if vitamin C were ineffective, it would not do harm. He started giving 10 grams per day of vitamin C to patients with terminal disease, and convinced himself of the benefits.

^b We considered whether to describe these allegations, but decided they were not pertinent to the discussion.

Initially, Cameron and Pauling published case reports of 50 patients, who were given sodium ascorbate injections, together with oral supplements. They increased the number of patients to 100, and found that cancer patients treated with vitamin C survived three to four times longer than untreated controls. The control group consisted of 1,000 patients, who received no vitamin C. They were matched (10 to 1) with the experimental patients, with respect to age, sex, type of cancer and clinical status of “untreatability”. They were treated in the same hospital, by the same staff and were managed identically, except for the vitamin C.

Traditionalists argued that the selection of patients in Cameron’s studies could have been biased. They also suggested that the vitamin C and control groups were not properly matched and might have had a different severity of disease. They further claimed that taking control patient details from medical records might introduce additional bias. Such a selection bias, as suggested by the detractors, might explain the positive results, but would need to be extreme.

Cathcart has raised another objection to the Vale of Leven studies, namely, that the dose of vitamin C was too small. Ten grams is at the low end of clinical doses and would not provide relief from a common cold. Animals that manufacture their own vitamin C get cancer. Since these animals often have high tissue levels of ascorbate, this sets a lower limit on the effective dose. Pauling and Cameron’s positive findings for such low doses are therefore unexpected, but can be attributed to their choice of the intravenous route, which leads to higher tissue levels.

Pauling and Cameron provided an estimate of the benefits of vitamin C, at these relatively low doses.⁵⁸¹ These figures appear to derive from their experience of clinical case studies and apply to patients with terminal disease considered untreatable by conventional means. As we shall show, higher doses might be expected to give a greater response. The doses used by Pauling and Cameron were only a fraction of the doses normally found to be cytotoxic to tumours. However, we now know that tumours preferentially accumulate ascorbate.^c

The response of Pauling and Cameron’s patients to vitamin C therapy is indicated in the following table:

^c Tumours preferentially take up L-ascorbate by active transport. This form of the vitamin, which is now becoming more available in supplement form, may therefore be a more effective cytotoxic agent.

Response	Percentage of patients
None	20
Minimal	25
Tumour retardation	25
Tumour unchanged	20
Tumour regression	9
Tumour death	1

The patients used to derive these figures would not have reached and sustained plasma levels of vitamin C likely to kill the cancers. Pauling and Cameron could have been conservative in their estimates of the number of patients who might benefit from vitamin C therapies.¹⁵

A later study was conducted from 1978 to 1982, in the same region of Scotland. This included 294 patients, treated with ascorbate, and 1532 controls. Patients received either vitamin C or palliative care, according to which doctor admitted them. Patients receiving vitamin C had an average survival period of 343 days, almost twice as long as the controls (180 days). Moreover, the supplemented patients appeared to have an improved quality of life. However, the controls were not subject to exactly the same conditions as treated patients. Cameron, being convinced of the efficacy of the treatment, was ethically unable to deny vitamin C treatment to dying patients. Differences in survival figures could reflect unconscious bias by physicians, or errors in diagnosis.

In 1979, Morishige and Murata published a report confirming the results obtained by Cameron.⁶⁹³ In this Japanese study, the death rate for higher dose ascorbate patients was only one third that of patients receiving lower doses. They studied 99 patients, of whom 44 subjects received four grams of vitamin C or less per day and 55 received five grams or more. Patients receiving the low dose of vitamin C lived an average of 43 days. Those receiving five to nine grams lived 275 days and subjects receiving 10 to 15 grams lived an average of 278 days. Surprisingly, patients receiving the highest doses, 30 to 60 grams, lived an average of only 129 days. This period is three times longer than the

lowest dose patients, but only half as long as the 5-15 gram groups. However, the highest doses were given to the patients with the most advanced disease, which could explain these findings.

The Japanese experiment appears to confirm Cameron's study, as the ascorbate treated patients lived far longer. Regrettably, like Cameron's, this study was not a double-blind trial. Detractors used this fact to suggest the study was invalid. Despite this objection, the groups with different dose levels acted as internal controls. Unless there was a large selection bias, this experiment confirmed that vitamin C prolongs life in patients with cancer. Nonetheless, the medical community found the results of the Japanese study questionable and did not accept its validity.⁶⁹⁴ It appears that it is necessary for someone suggesting a new approach to cancer to provide comprehensive evidence before the treatment will even be tested.

Pauling's reputation as a world-leading scientist gave Cameron's results publicity and the medical establishment was forced to reply to his findings. The prestigious Mayo Clinic decided to conduct its own controlled trial.⁶⁹⁵ However, some writers have suggested that their real aim was to quash the claims for vitamin C as a cancer treatment.⁶⁹⁶ Linus Pauling himself thought the Mayo Clinic studies were an example of scientific fraud.⁸²⁷ The Mayo Clinic study did not answer the problems raised, but fuelled further controversy.^{697,698}

In a later study, concerning the anticancer effects of laetrile, Moertel would write,

"it would be unconscionable to randomise people between a drug and a standard therapy that would hold a known potential for cure or [life] extension."^{699,700}

This is the same argument used by Ewan Cameron to defend his uncontrolled clinical trials of vitamin C.^d Such inconsistency supports Pauling's questioning of the motives behind Moertel's investigation.

The Mayo Clinic study was prospective and double-blind, with randomised controls. Ten grams of vitamin C were given *orally* to the subjects, and a placebo to the controls. A single dose of this size would raise blood levels only transiently. The 63 controls matched the 60 supplemented subjects. Both groups survived for about the same length of time, seven weeks. The study concluded that there was no benefit

^d We ignore the fact that there is poor evidence for Moertel's assertion of chemotherapy being curative or extending life expectancy, at least for the majority of solid tumours in adults.

from vitamin C. Following numerous complaints about the adequacy of the initial clinical trial, the Mayo Clinic conducted another study, to confirm the negative result.⁷⁰¹ This study also used oral supplementation and an inappropriately low and infrequent dose. Despite repeated requests, the Mayo Clinic refused to release their raw data for analysis by other scientists. This refusal to release the data suggests the researchers lacked confidence in their published analysis. The limited data available indicate that patients who survived had their treatment changed in such a way as to increase the death rate. A plausible explanation might be that chemotherapy reduced the life expectancy of the surviving patients.

It is unfortunate that Linus Pauling did not explain the crucial difference between intravenous and oral vitamin C. The Mayo Clinic's use of oral doses would clearly have biased the results. In 2002, Gonzalez and colleagues reported that intravenous sodium ascorbate gives results that are more consistent in cancer patients, as higher blood levels are attained.⁷¹³ Sebastian Padayatty and Mark Levine, of the US National Institutes of Health, have also reported that intravenous sodium ascorbate is more effective in cancer treatment, since it enables higher blood levels to be reached.⁷⁰² They suggest that the change in method of administration could explain the differences between the Pauling and Mayo Clinic studies.

Back in 1969, a study by Dean Burk showed direct killing of cancer cells by ascorbate.⁷¹⁸ Burk suggested that,

“The future of effective cancer chemotherapy will not rest on the use of host-toxic compounds now so widely employed, but upon virtually host-non-toxic compounds, that are lethal to cancer cells, of which ascorbate represents an excellent prototype.”

Dean Burk was correct. In the intervening three decades, enough data has accumulated to indicate that both oral and intravenous non-toxic anticancer therapies are a practical possibility.

Further positive reports

Reports on the efficacy of vitamin C as a treatment for cancer have continued. Perhaps most notable are those from Abram Hoffer, the first physician to use a double-blind clinical trial in psychiatry. His results confirm those of Cameron, Morishige and Murata, in showing greatly increased survival times.^{703,704} Hoffer's book provides a wealth of information on his studies, including analysis of results and case study presentations. Other physicians who have used vitamin C to treat cancer over recent decades include Robert Cathcart⁷⁰⁵ and Selva Kumar. Kumar

reports positive results with intravenous sodium ascorbate in renal cell carcinoma and lymphoma.⁷⁰⁶

In an important step, laboratory studies by Riordan and others confirmed that vitamin C is toxic to cancer cells.⁷⁰⁷ This finding has been replicated in animal studies,⁷⁰⁸ and in humans.⁷⁰⁹ Riordan published case studies demonstrating that vitamin C is an effective cancer treatment,^{709,710} and has published a detailed mechanism of action.^{711,712,713} Derivatives of vitamin C have been shown to have anti-tumour effects,^{714,715} and a recent paper proposes encapsulation of vitamin C in micro-particles, for use as an anticancer treatment.⁷¹⁶

With the accumulation of scientific evidence, the establishment view is changing. Recent papers on vitamin C and cancer from Mark Levine's group at the National Institutes of Health support the anticancer actions of vitamin C.^{648,652}

Vitamin C kills cancer

The idea that vitamin C might be effective against cancer originated in the 1940s. By 1969, it was known that vitamin C could kill cancer cells directly.⁷¹⁸ Fred Klenner suggested the use of massive-dose intravenous ascorbate as a treatment for cancer, back in 1971.

It is difficult to extrapolate from laboratory studies to an anti-cancer effect in the body. First, the effect must be demonstrated in test tube studies. Next, researchers must show that the effect can also occur in the body. Finally, they must obtain clinical results to indicate an increased life expectancy. In the case of vitamin C, this has all been done. The only thing that remains is for the experiments to be replicated and suitable double-blind clinical trials to be performed. However, the bulk of clinical trials are by drug companies and, unfortunately for patients, vitamin C offers no profit incentive.^{9,11}

Recently, Mark Levine's group has confirmed that vitamin C is toxic to tumour cells in both tissue studies and animal models.^{648,652} These experiments involved applying vitamin C to several types of cancer and normal cell lines, for a period of only one hour. As we might expect from the preceding three decades of results, vitamin C killed the cancer cells but did not harm normal cells. Based on these findings, Levine concluded that vitamin C is only effective when used intravenously.⁶⁴⁸ This conclusion does not take account of longer periods of exposure, which might allow oral dynamic flow level doses to be effective against cancer.

Levine examined the dose response in human lymphoma cells, which were highly susceptible to the action of vitamin C in a one-hour exposure. Over the following day (18-22 hours later), the number of cells dying was recorded. At high intravenous dose levels (1-5 mM/L) more than 80% of the cancer cells died, mainly by necrosis and apoptosis. This implies a massive poisoning of the cells and the potential for rapid destruction of tumours. However, doses consistent with blood plasma levels in the dynamic flow range of oral doses (200-300 $\mu\text{mol/L}$) also produced cell death. In this case, exposure for one hour produced death in 10-30% of the cancer cells. Importantly, dynamic flow levels from oral doses can be maintained indefinitely. Levine's results suggest that oral doses of vitamin C, at sustained dynamic flow levels, are likely to be a safe and effective way of treating cancer.

Levine claims that vitamin C acts by generating hydrogen peroxide in the plasma surrounding the cancer cells, rather than inside the cells. The evidence presented for this suggestion is flawed. The cancer cells were apparently preloaded with a low dose of vitamin C. Levine assumes that a low dose of vitamin C in the extracellular fluid saturates cancer cells to a maximum internal concentration, so they cannot absorb more.^{e,2} No data is provided to support this idea, which is probably incorrect. Since the initial low dose does not kill the cells, but a subsequent higher dose (2 mM/L) does, Levine assumes the action must be extracellular. Levine's results are generally consistent with earlier descriptions by Holman, Riordan and others, in which healthy cells have a full complement of antioxidant enzymes to prevent the build up of hydrogen peroxide. For example, red cells in blood prevent the formation of hydrogen peroxide. In tumours, where the catalase and other antioxidant systems are deficient, hydrogen peroxide can accumulate and destroy sensitive cells.

A new treatment?

The first step in developing a new treatment is to show that a chemical kills tumour cells at lower concentrations than it harms human cells. In most cases, a new therapy has to go through detailed toxicity testing and must be capable of delivery to the target tumours. With vitamin C, many of these issues simply do not apply, as ascorbate is a normal and essential part of the body's biochemistry. It is important,

^e Levine believes that normal body cells contain millimolar amounts of vitamin C, which overestimates the true value by about an order of magnitude.

however, to show that a suitably high concentration of vitamin C can reach the cancer.

Riordan tested samples of human serum from patients receiving intravenous ascorbate. His measurements confirm that the levels obtained are equivalent to those that are cytotoxic to tumour cells in experimental studies. Riordan also showed that samples of blood plasma, taken following ascorbate injections, killed cancer cells in tissue culture.

Riordan and others have proposed that ascorbate does not kill cells directly, but acts by producing hydrogen peroxide.⁷¹⁷ Riordan confirmed that the concentration of the enzyme catalase, which breaks down hydrogen peroxide, is up to one hundred times greater in normal cells than in tumour cells. This suggestion agrees with the findings of Holman, who discovered the acute sensitivity of cancer to hydrogen peroxide, back in the 1950s.

As we have explained previously, Holman and others reported that preparations of hydrogen peroxide selectively kill cancer cells in test tube and animal experiments. Such preparations also slow growth and destroy tumours in humans. The results with vitamin C are in harmony with this earlier research. Both lines of evidence are consistent with the mechanisms of action of current radiation and chemotherapy treatments. They also agree with the known biochemistry of cell signalling and cell division.

Agents that cause hydrogen peroxide to be generated in cancer should be toxic to cancer cells, while being safe for normal tissues. Both ascorbate and metabolites of ascorbate have anti-tumour activity in isolated tissues. Thus, sufficient doses of vitamin C should kill tumour cells, without toxic effects to healthy cells. The evidence suggests that vitamin C could be the elusive magic bullet.

Dean Burk's research at the US National Cancer Institute indicates that ascorbate is highly toxic to carcinoma cells.⁷¹⁸ Notably, the toxicity increases if a catalase inhibitor is present. Bram reported that vitamin C is preferentially toxic to experimental cell lines of malignant melanoma (skin cancer).⁷¹⁹ He also found that copper increases this toxicity. The presence of copper and some other metals can cause ascorbate to act as a pro-oxidant, rather than an antioxidant, leading to greater production of hydrogen peroxide in cancer.

In 1990, Helgestad reported that a new malignant lymphoma T-cell line was sensitive to ascorbate in culture, at concentrations attainable in human blood.⁷²⁰ Additional research confirms that several leukaemia cell

cultures are sensitive to vitamin C concentrations achievable in the human body, while normal blood-forming cells are not suppressed.^{853,721,722,723} Research into the joint actions of vitamin C and selenium on gastric cancer has suggested that that the combination may be a useful treatment.⁷²⁴

Occasionally, it has been reported that high dose intravenous ascorbate can destroy a tumour too quickly for the patient to be able to cope with the resulting mass of dead tissue. These clinical observations reinforce the obvious need for medical supervision. However, on the plus side, these effects show that vitamin C certainly can destroy tumours within the human body.

Case study

Hugh Riordan has described a number of case studies on the use of vitamin C in cancer. In 1995, he saw a female patient with metastatic end-stage breast cancer.⁶⁸⁰ She presented with cancer in “nearly every bone in her skeleton” and blood clots in both of the large veins that run behind the collarbones, draining the arms and head. One of the bed-ridden woman’s arms was badly inflamed, because of the lack of blood flow. The blood clots were treated with an anticlotting drug,^f and she was given an initial daily infusion of 30 grams of sodium ascorbate. This was increased to a five-hour infusion of 100 grams per day. Within a week, she was reportedly able to walk about the hospital and looked like a new person. She was discharged from the hospital and her treatment continued, with 100-gram infusions of sodium ascorbate, three times a week. Three months after starting the therapy, several tumours in her skull were no longer visible on x-ray. Sadly, six months later, she fell while walking in a shopping mall and died from complications of the resulting fractures.

^f Activase was used to dissolve the clots.

Conclusions

We have described evidence that vitamin C can kill cancer. Indeed, the properties of ascorbate reflect, perfectly, the requirements for a chemotherapeutic agent.

- The effects of vitamin C on cancer can be explained theoretically.
- The results can be predicted from earlier research on hydrogen peroxide.
- Cell culture studies demonstrate the killing of cancer cells.
- Animal studies show anticancer activity.
- In humans, measurements show that blood levels that would be expected to kill cancer cells can be reached, with intravenous injection or oral dynamic flow intakes.
- The blood plasma of people injected with vitamin C can kill cancer cells.
- A large and increasing number of clinical reports find that ascorbate is an effective treatment.
- Case studies report that people with metastatic cancer have been cured.

The only item missing from this list is a randomised, double-blind, clinical trial, showing that vitamin C is an effective treatment or cure. Such trials can be prohibitively expensive to perform and most are conducted by pharmaceutical companies. The absence of such trials with vitamin C and associated redox agents may simply reflect the lack of potential financial reward.

With powerful evidence of efficacy and a large degree of safety, lives may be saved with little financial or health risk to the patient. In the following chapters, we provide evidence that the beneficial effects of vitamin C in cancer have been underestimated. This suggests that large and frequent oral doses vitamin C could form the basis of a powerful new approach to cancer therapy.