

Ascorbate Persistence, and the Rationale for Treating Cancer with Continuous IVC Plus Integrations

Abstract

The mystery of Pauling, Cameron, and Hoffer's low-dose Intravenous Vitamin C efficacy (wherein they only used 10g/day) may finally be settled. New research shows a newly discovered cytotoxic mechanism for IVC (intravenous vitamin c) is ATP depletion, such that very low dose IVC can be very cytotoxic if ascorbate-persistence is continuous and long-lasting. Continuous IVC can be even much more tolerable than conventional IVC, possible more effective, and even safe even for G6PD-deficient patients. Continuous IVC was tried in a 1998 pilot study, but was limited, and without integrations or conventional intermittent bolus injections. Ascorbate-Persistence, as a concept, is gaining popularity as an integrative cancer-treatment strategy. There are substantial additional advantages of using an Ascorbate-Persistence maximized protocol.

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History

Linus Pauling and Ewan Cameron's landmark 1972 study on treating Cancer with IVC (Intravenous Vitamin C) resulted in a reported 4X increase in lifespan that shook the world. The results were shortly then confirmed at Japan's Saga University by Dr. Murata with a 5.7 increase in lifespan. It now appears we've learned of one more thing they did right the first time, which we may have been doing wrong ever since, and it may be the most important thing that we should have learned from the start.

Recent studies shed light on what was most likely Pauling and Cameron's main cytotoxic mechanism, resolving a number of seemingly anomalous data points within the preponderance of IVC research data. This cytotoxic mechanism for H₂O₂, when expressed by IVC, kills cancer by diminishing cancer's energy supply.¹ The implications of this mechanism are very *substantial*, and 3 implications are particularly poignant:

1. The mystery of Pauling, Cameron, and Hoffer's low-dose efficacy may finally be settled

Pauling and Cameron, and then reproduced by Dr. Murata, experienced unparalleled success at 10 gram IVC doses (now considered to be a considerably low IVC dose level) and thereby increased life extension by an average of 4.2X among 100 cancer patients¹⁰ ... a feat which has baffled many an IVC researcher since then. What has made it especially bewildering is that the protocol contradicts the popular conventional strategy about IVC dose that "more is better". Today, often the target for blood-ascorbate-concentration is 30 times higher or more than what Pauling used in that first study (presuming Pauling administered at only 1g/hour, see "Evidences" below).

Finally, we can show what made those 10 gram doses so surprisingly effective: it was the *method* whereby those 10 grams were administered. In short, they induced a millimolar concentration of ascorbate in the bloodstream that was persistent for likely 12 to 16 hours, 5 days per week. This leverages the diminishing cancer cell energy caused by H₂O₂-expressed IVC, or in other words the 12- 16 hour unabated millimolar blood ascorbate persistence starved cancer of energy, to death.

Unabated millimolar blood ascorbate persistence, or *ascorbate-persistence* as we'll call it herein for convenience sake, should therefore be a key parameter that should perhaps even rival dose potency when treating cancer with vitamin C. This is the amount of time that blood-level ascorbates are perpetually (continuously) at or above the millimolar range necessary to kill most cancers, and according to the 2015 study results *ascorbate-persistence (given in terms of minutes, or hours)* should be maximized to effect maximum cancer cell death.

Similarly it should now no longer be a mystery how Abram Hoffer was also able to successfully treat cancer with only oral doses and a biweekly IV of only 2.5 grams of sodium ascorbate ², who also stretched out *ascorbate-persistence* as long as possible with his similarly low-dose methods. His results, like Pauling's, otherwise seemed impossible according to contemporary IVC pharmacokinetic theory and use that has mostly ignored *ascorbate-persistence* as a key IVC parameter for the last 45 years since Pauling's landmark study.

2. Very low dose IVC can be very cytotoxic if *ascorbate-persistence* is continuous and long-lasting

Consider a battleground analogy wherein an enemy is 90% to the point of death by starvation. If he eats a biscuit, though nearly dead, what then happens? In a very short time all the previous starvation is thereby *entirely* lost as a tactical advantage. In short, it does little good to starve the enemy of their energy unless the starvation is unabated until the enemy dies. Being *almost dead*, like in a Monty Python movie, is futile and even poses a risk when those nearly dead cancer cells suddenly get a boost of energy and feel like getting up and taking a walk. Similarly, with respect to cancer, a persistence strategy *should not let up one iota until the cancer is entirely destroyed*. This is a "slow and steady wins the race" protocol, not the "fast-and-furious" protocol normally employed by very high-dose IVC.

Even a very brief daily cessation of the low-dose treatment, however brief, may be ill advised, as a cessation may allow cancer to feast on the metaphorical "biscuit" of energy otherwise available. Besides, the low-dose IVC used in *ascorbate-persistence* methodology can be so remarkably tolerable in the range of 1g - 10g per hour, there is really little need for for the patient to 'take a break', as no break is needed at such low doses.

By extending that battle analogy we may consider the conventional shock-and-awe approach of IVC, as it is generally deployed today. The shock-and-awe strategy is a fast and furious to hit cancer as hard as possible (ie. with as much ascorbate as possible) all at once. Sadly, after just a few hours after the conventional shock-and-awe protocol of 50+ grams (administered itself within 3 hours during which time it is well protected within its own cancerous infrastructure) the enemy, cancer, is typically back restoring its energy to full capacity. This represents, again, a tremendous loss of tactical advantage since IVC kills cancer by starving cancer of its energy.

Additionally, shock-and-awe protocols are justified based on the presumed correlation between dose and patient recovery which correlation may even be a misinterpretation of the results. See Evidences #4, and 5, below for more explanation.

3. IVC can be even much more tolerable, effective, and safe even for G6PD-deficient patients.

Compared to current IVC protocols *ascorbate-persistence* can be facilitated with easily administered and very tolerable administrations as low as 1g per hour, similar to what was used

in Pauling's 10g/day protocol (supplemented with oral C throughout the day) as a continuous drip *until all cancer is gone*. Continuing a single treatment *until all cancer is gone* represents a substantial paradigm shift, but for energy starvation to be fatal the administration must be continuous until all cancer is destroyed, which can take days or weeks. As a result the perceived challenge is no longer patient tolerance for the treatment, but rather the immediate inconvenience for the patient and the practitioner who are accustomed to IVC being comprised of many short outpatient visits.

The practitioner ready to leverage *ascorbate-persistence* may be tempted to mimic exactly what Pauling and Cameron did, or even Hoffer, but their protocols both suffer from potentially inadequate persistence. Success should not depend on spurious unknowns such as patient compliance with scheduled doses, or a "dynamic flow" (a process proposed by Hickey & Roberts whereby the human body stores and uses ascorbates ⁵) that might periodically put the body in a low-ascorbate state, even if for only 5 minutes. Cameron noted occasional "explosive" tumor growth during low-dose IVC where only oral doses were used¹⁰, depending on dynamic flow, and which were possibly caused by short rebound scurvy incidences that wouldn't happen with continuous IVC. The risk to repeat those responses simply is not worth it.

It thereby seems sensible to hedge the practitioner's bet, perhaps by utilizing an ambulatory pump administering a 24/7 low-dose ascorbate-persistence maximized IVC protocol unabated for a full week or maybe even longer. Many weeks if possible. Again, this may initially seem extreme to practitioners who are accustomed to outpatient IVC, especially when high doses seem only tolerated for just a few hours, but these administration rates are at least 10X times lower than convention. Very few of the challenges with high-dose IVC are even an issue anymore with an *ascorbate-persistence* maximized protocol.

See "Advantages" and "Disadvantages" for more considerations.

Continuous IVC was Tried in a Pilot Study, but not with Integrations and Intermittent Bolus Injections

In 1998 a study through the University of Nebraska the Riordan Clinic, which has done more research on IVC than any other organization, investigated continuous IVC on 24 refractory patients.¹³ Doses ranged for the average weight patient from roughly 10g per day to 50g per day (adjusted for patient mass), and the mean treatment schedule lasted for 8 weeks, though one patient did it for 4 years with stable disease, who was on the medium level dose (430mg/kg/day). Unlike the results from Pauling and then validated by Dr. Murata, survival statistics were not collected, mostly because at 8 weeks most patients stopped the protocol at the scheduled end of the trial. There was one patient who opted to stay on the protocol for 4 years who experienced stable disease progression despite having refractory cancer. Additionally, most measured bio-markers were either stable (within expected statistical variation) or did improve for most of the 24 patients, regardless of dose, during the study.

Additionally a lot was learned from this study, paving the way for doing the study with some new integrations that should significantly potentiate the results. For example, now that we know the IVC has a glucose starving effect on cancer (ATP reduction), it can be paired with a ketogenic type diet. Additionally potentiating factors have been identified since the original study such as hypoxia which is known to deplete the H₂O₂ at the tumor (H₂O₂ is responsible for most of the anti-cancer effects of vitamin C), and that can be mitigated with O₂ potentiating mechanisms. Other IVC potentiating supplements which have since been discovered, such as alpha-lipoic acid that can triple IVC cytotoxicity, can be added to protocol.¹⁴ Lastly, combining the low-dose continuous IVC (and it appears only 10g/day is needed) with periodic bolus IVC dosing (targeting 20mmol/L) should make the combined strategy very cytotoxic to most any cancer that is responsive to conventional chemo.

Lastly, ambulatory continuous pump technology has come a long way since the University of Nebraska study and now this protocol can be done quite easily with a battery-free pump that is hidden, easily refilled/replaced, and which allows for a very active lifestyle.

Ascorbate-Persistence Is Gaining Momentum

Although envisioned differently, a strategy of lower-dose with longer-duration administrations has been formally considered in the past by some of the most respected researchers in the IVC community^{6,7}. In these papers the Riordan Clinic developed a hypothesis of "Systemic Saturation" based on clinical patient and pharmacokinetic observations. They hypothesized that over-saturation of ascorbic acid could possibly prevent the expression of H₂O₂, and thereby recommended a lower dose with extended treatment times. This was also an effort that included the contributions of Hickey regarding the "Dynamic Flow" Hickey had described elsewhere⁵.

Dr. Thomas Levy MD, JD - similarly another bedrock in the IVC research community, has advocated an *ascorbate-persistence* maximized protocol with respect to liposomal C, yielding higher blood ascorbates than is otherwise orally possible extended over an extended continuous term of treatment. The new research also supports the liposomal C approach which can similarly lead to a diminished ATP production in cancer cells.

Evidences for The Need for *Ascorbate-Persistence* Maximized Protocols

What we attempt to show here is that unabated millimolar persistence may be more important than the conventional dose-maximized IVC protocols, as evidenced by the following:

1. "vitamin C inhibited energy metabolism through NAD depletion, thereby inducing cancer cell death."¹ In this 2015 study it was shown that H₂O₂ (provided by the IVC) essentially starved cancer to death by inducing metabolic changes during glycolysis. This mechanism may be more effectively realized with an *ascorbate-persistence* maximized protocol than the conventional potency-maximized protocol.
2. Early 1970's IVC successes with only 5g and 10g IVC may be due to long durations, administered at a low-rate throughout each day. To date the unparalleled results have

only been attributed to imagined design-of-experiment problems, when in fact the all-day-long protocol combined with oral administrations throughout out the day now seem to solve this mystery. Although the administration rate was only disclosed as "per day" (which is not useful in this analysis), Cameron's comments support an all-day scenario with the two following comments that:

- a. they used 2 liters of ringers lactate solution per day¹ suggesting such a low dose was delivered very slowly by today's standards, for it is unlikely they used that much solution just to keep the port open,¹⁰
- b. The mention that that administrations were "very tentative" ¹, as should have been expected, considering that they were the first to try IVC for cancer in this manner.
- c. Similarly they administered oral vitamin C in 4 small doses throughout the day, so it appears on multiple fronts that they killed cancer by much longer *ascorbate-persistence* ranges than is currently done¹⁰. This would also take advantage of the "dynamic flow" model as proposed by Dr. Steve Hickey⁵ to hedge likelihood that the persistence of cytotoxic levels of ascorbate were as unabated as possible.

The documented successes seen during the earliest testing of IVC (4.2X increased life span for example) at these low of doses to date has seemed unrepeatable until now. Similar patient outcomes using today's relatively high-dose high-rate protocols have only been observed at doses approaching 10X higher than these pioneering efforts, enough that in general current recommendations are to focus mainly on higher doses.⁸

3. According the Cameron those receiving 45g throughout the day did not experience "any clear therapeutic advantage" compared to those receiving 10g.¹⁰ This contradicts findings today where an obvious advantage should be observed when increasing IVC dose by 450%, but it's likely that Cameron administered the 45g over the same duration as the 10g (by dissolving each into the 2 Liters solution specified and administering both at the same drop rate), so the *ascorbate-persistence* was the same for both doses (10g vs 45g). By spreading the administration over a longer period he never achieved to concentrations necessary to cause oxidative damage to cancer cells. This then (oxidative damage) is related more closely to rate than total dose. It appears now that up to 30g/hr is needed for sufficient oxidative damage, and 1-10 grams per hour are needed to deplete ATP in cancer. The ideal protocol will combine these, periodic 30g/hr dosing with a base of 1g/hr to 10g/hr done continuously.
4. The very real dose correlation between dose and patient recovery generally ignores the simple fact that high doses also put the patient in a higher persistence of blood levels of millimolar ascorbates. A patient receiving 50g of IVC will therefore maintain cytotoxic ascorbate levels for up to 5-6 hours, whereas a patient receiving 80 grams of IVC will maintain cytotoxic ascorbate levels for up to 7 hours. The correlation therefore may be as much an argument for causal relationship of duration as it is for dosage.
5. If IVC cytotoxicity is purely potency-modulated then it stands to reason that there is no point of diminishing returns for dosage. To the contrary there is generally a point of diminishing returns at roughly the 100g point of administration for most patients. Positive

patient outcomes should correlate more linearly with of *ascorbate-persistence* since it also diminishes relative to the dose at higher doses (eg. $f(50g)=5.5hr/50g=1.1hr/g$ which is greater than $f(80g)=7hr/80g=0.88hr/g$, ie. ascorbate-persistence diminishes along with dose). By removing dose, the nonlinearity is removed, identifying a potentially more direct causal relationship of cytotoxicity with ascorbate-persistence than with dosage.

Potential Advantages of the Ascorbate-Persistence IVC Protocol

The following assumes that the patient only receives 1g-10g per hour over a 24/7 time frame.

1. Designed to wipe-out cancer in one step of very well tolerated (low dose) IV administration (however long that duration may be, 24/7 proposed as a potential starting point).
2. Most G6PD patients (of African ancestry) are not reactive to the protocols where only few grams are intravenously administered given over a period of a couple hours. Such G6PD patients could therefore feasibly be administered 1g/hr and up to 3g/hr continuously, 24/7, with little to no complications.¹²
3. Lower rate, smaller needle, less IV irritation, easier on veins.
4. No tremors / shakiness caused by blood sugar fluctuations.
5. At 10x lower doses, bladder function should be relatively unchanged, allowing patients with renal challenges (kidney problems, dialysis) to be candidates.
6. At 10x lower doses, Herxheimers reaction is easier to mitigate and troubleshoot
7. The impact of potentiating substances such as vitamin K or artemisinin can be more easily controlled, and monitored considering that the 10x lower-dose vitamin C provides a relatively quiet and more constant baseline.
8. Patient always feels well enough to engage in other simultaneous synergistic potentiating therapies, and since the therapy is constant they are also easier to schedule to work simultaneously. This is often generally the case with IVC, but should always be expected with low-dose *ascorbate-persistence*. These may include oxygen therapies, simultaneous chemotherapy, and aerobic exercise (stationary bike).
9. No diminishing-ascorbate headaches (often occurs after a massive IVC dose).
10. Lower IVC fluid costs. This may not necessarily be true though, since it may be advisable to change the IVC fluid every 2-3 hours to maintain as reduced of a solution as possible. Reduced IVC contributes twice as many bioavailable electrons at the cellular level compared to oxidized IVC, which situation may or may not affect efficacy.
11. Decreased hospital costs: (a) The patient will not need to come in 2-3 times per week for many weeks on end, (b) The low rates likely significantly reduce IVC complications (see 'advantages' above) the overall drain on nursing staff may be negligible, if not reduced, (c) If done during chemo treatment the patient will be there anyway. (d) These costs of course could also be defrayed by setting up administration at home, started by a nurse in the morning at low dose (1g/hr to 10g/hr) who may return in the evening to end the dosage. Again, in most cases with low kvo rates there should be negligible

complications that might require onsite assistance throughout the day so 2 short visits should be adequate.

12. Significant travel savings (time, money, parking, logistics) for the patient compared to scheduling many dozens of outpatient visits.
13. Patients don't require any recovery (which is common for many IVC patients after each high-dose IVC, with hypoglycemic symptoms or other symptoms often extending into the following day).
14. Since over time all the tissues in the human body will eventually absorb millimolar ascorbate from a 24/7 low-dose protocol, theoretically it seems it would be the best adjuvant cancer protocol any patient could hope for because it will kill all cancer, no matter how infinitesimal within the body, in a way no conventional chemo agent can do, and in a way that can't be done with conventional shock-and-awe IVC protocols (which don't penetrate as well as *ascorbate-persistence* protocols).
15. The University of Nebraska pilot study from 1998 demonstrated that this protocol is extremely safe, especially at the low doses which provided mostly the same level of blood ascorbates as the higher doses.

Potential Disadvantages of an Ascorbate-Persistence IVC Protocol

1. Some patients may find it inconvenient. Some IVC patients may rather get a very high dose (50+ grams) and easily get on with their day. For them an ascorbate-persistence maximized protocol can be a challenge with patients who wish to ignore that cancer is a serious disease that may require significant inconvenience on their part.
2. May require a diet and supplement adjustment (example antioxidant supplements should be entirely suspended during the treatment). IV glutathione, and other antioxidant IV fluids must also be abandoned during treatment. Patients should be encouraged to continue to get all their antioxidants only from oral consumption found in a standard healthy diet, preferably of whole foods, which some patients might resist. Since the main cytotoxic mechanism leveraged here is via cancer-specific energy-starvation, all foods with high glycemic index must be avoided since they can often cause a short spike in blood glucose, whereby one slip-up can give cancer a gasping chance at survival. A quick web-search for "low-gi diet" should provide good guidance.
3. Diabetics, who need to regularly monitor their blood glucose will not be able to use simple finger-stick blood-glucose measurements, as they are falsely high readings during IVC treatment. If the patient needs their blood glucose tested it should be laboratory tested using the hexokinase glucose reference method. ⁹

Conclusion

At a minimum there exists a large population of G6PD deficient patients who until now have been deprived of IVC, who can benefit from a low dose 24/7 *ascorbate-persistence* maximized protocol.

Although not expected to be an immediate replacement for conventional IVC protocols, a 24/7 (or similar) *ascorbate-persistence* maximized protocol should pose no danger for prime candidates of conventional IVC, and as a preliminary treatment to conventional IVC (which is even far easier to tolerate than conventional IVC). It can only improve the patient's chances against cancer. If perchance the protocol leaves them cancer-free prior to conventional IVC then the original ascorbate-persistence practices by Pauling et al., then it will finally find its rightful place within the IVC community.

IVC has been much maligned over the simple fact that it challenges conventional oncological thought. The proposal that *ascorbate-persistence* as a key parameter for improved IVC efficacy against cancer may similarly face doubt as it challenges the status quo within the IVC community, and the protocols used today have reached convention status. It is therefore with hope that key leaders in IVC community can be an example of the kind of open mindedness that is sought from the rest of the oncological world when presented with data that challenges the status quo.

Doubtlessly, the 24/7 *ascorbate-persistence* protocol is the best adjuvant therapy for all presumably cured cancer patients.

Footnotes and Citations

- (1) Uetaki M, Tabata S, Nakasuka F, Soga T, Tomita M. Metabolomic alterations in human cancer cells by vitamin C-induced oxidative stress. *Scientific Reports*. 2015;5:13896. doi:10.1038/srep13896.
- (2) Abram Hoffer, M.D., Ph.D - *Clinical Procedures in Treating Terminally Ill Cancer Patients with Vitamin C*
- (3) Monti DA, Mitchell E, Bazzan AJ, et al. Phase I Evaluation of Intravenous Ascorbic Acid in Combination with Gemcitabine and Erlotinib in Patients with Metastatic Pancreatic Cancer. Perez-Gracia JL, ed. *PLoS ONE*. 2012;7(1):e29794. doi:10.1371/journal.pone.0029794.
- (4) Moertel, Charles G.; Fleming, Thomas R.; Creagan, Edward T.; Rubin, Joseph; O'Connell, Michael J.; Ames, Matthew M. "High-Dose Vitamin C versus Placebo in the Treatment of Patients with Advanced Cancer Who Have Had No Prior Chemotherapy"; 1985/01/17 doi: 10.1056/NEJM198501173120301, *New England Journal of Medicine*
- (5) "The Real Story Behind Vitamin C" Steve Hickey, PhD; Hilary Roberts, PhD; https://www.peakenergy.com/news/VitaminC_Cancer_w_Comments.pdf
- (6) Gonzalez MJ, Miranda Massari JR, Duconge J, Riordan NH, Ichim T. Schedule Dependence in Cancer Therapy: Intravenous Vitamin C and the Systemic Saturation Hypothesis. *Journal of orthomolecular medicine : official journal of the Academy of Orthomolecular Medicine*. 2012;27(1):9-12.
- (7) Jorge Duconge, Ph.D.1 ; Jorge R. Miranda-Massari, Pharm.D.2 ; Michael J. Gonzalez, Ph.D.3 ; Neil H. Riordan, Ph.D.4; "Schedule-Dependence in Cancer Therapy: What is the True Scenario for Vitamin C?" *Journal of orthomolecular medicine : official journal of the Academy of Orthomolecular Medicine*. Vol. 22, No. 1, 2007 pg21-26

- (8) Monti DA, Mitchell E, Bazzan AJ, et al. Phase I Evaluation of Intravenous Ascorbic Acid in Combination with Gemcitabine and Erlotinib in Patients with Metastatic Pancreatic Cancer. Perez-Gracia JL, ed. PLoS ONE. 2012;7(1):e29794.
doi:10.1371/journal.pone.0029794.
- (9) James Jackson, PhD; Ronald Hunninghake, PhD; Chad Krier, ND, DC; Rebecca Kirby, MD; Glen Hyland, MD; Special Report "False Positive Finger Stick Blood Glucose Readings After High Dose Intravenous Vitamin C", The Center for the Improvement of Human Functioning International, Inc. Wichita, KS; brightspot.org
- (10) Ewan Cameron; Allan Campbell; The Orthomolecular Treatment of Cancer II. Clinical Trial of High-Dose Ascorbic Acid Supplements In Advanced Human Cancer; Chem.-Biol. Interactions 9, 1974, 285-315
http://www4.dr-rath-foundation.org/NHC/studien_pdf/old/the_orthomolecular_treatment_of_cancer.pdf
- (11) Ewan Cameron; "Vitamin C and Cancer: A Personal Perspective";
<http://scarc.library.oregonstate.edu/coll/cameron/cameron-personal/page1.html>)
- (12) Rees DC, Kelsey H, Richards JD. Acute haemolysis induced by high dose ascorbic acid in glucose-6-phosphate dehydrogenase deficiency. Bmj. 1993;306(6881):841-2.
Epub 1993/03/27.
- (13) Riordan HD, Casciari JJ, Gonzalez MJ, Riordan NH, Miranda-Massari JR, Taylor P, Jackson JA. A pilot clinical study of continuous intravenous ascorbate in terminal cancer patients. P R Health Sci J 2005, 24, 269-276.
- (14) Casciari JJ, Riordan NH, Schmidt TL, Meng XL, Jackson JA, Riordan HD. Cytotoxicity of ascorbate, lipoic acid, and other antioxidants in hollow fibre in vitro tumours. Br J Cancer 2001, 84,1544–1550.