BOAI-Film zu Vitamin C:

https://www.youtube.com/watch?v=Mq30FyW1x84&t=362s&index=3&list=PLgtKw1QgfYrmAOjhZ 1vitjpzc9J5Y3iRA

http://pyrmont.vonabisw.de/niacin

Orthomolecular Therapy

Medical Mavericks Vol. 3 - by Hugh Desaix Riordan, M.D. | Published: January 2005 | Length: 259 pages

https://riordanclinic.org/wp-content/uploads/2014/12/Medical Mavericks Vol3-riordan-clinic-web.pdf

https://riordanclinic.org/books/

Das Arbeitsbuch zum Isernhagener Workshop "Wege zur Gesundheit" – 700 Seiten – Ebook € 0,99 – ISBN-13: 9783744872713 – € 16,90 – BOAI

https://www.amazon.de/lsernhagener-Workshop-Wege-Gesundheit-B%C3%BCrgervereinigung-ebook/dp/B0753L1JT9/ref=sr 1 1?ie=UTF8&qid=1522822451&sr=8-1&keywords=wege+zur+gesundheit++isernhagener

Vitamin C als hochdosiertes Therapeutikum bei chronischen Krankheiten – Der Korruptionsskandal in deutschen Arztpraxen

https://www.youtube.com/playlist?list=PLgtKw1QgfYrkCJTJPUuXemFQS-iZw0GTW

80 Years of High-Dose-Vitamin C Research

https://www.bod.de/buchshop/80-years-of-high-dose-vitamin-c-research-f-klenner-9783752812756

Als freies PdF

http://d.mp3vhs.de/RobertCathcart/1.pdf

http://astrologischefachliteratur.vonabisw.de/dr-med-robert-cathcart-on-vitamin-c

Compendium Vitamin C – täglich ab 18.000 mg – bei Grippe, Fieber, Bakterien, Viren, Entzündungen und als Antihistamin bei Heuschnupfen

Das diesbzgl. Buch gibt es hier bei BoD:

 $\frac{https://www.bod.de/buchshop/compendium-vitamin-c-taeglich-ab-18-000-mg-bei-grippe-fieber-bakterien-viren-entzuendungen-und-als-antihistamin-bei-heuschnupfen-f-r-kl-9783752812251$

als freies PdF:

http://d.mp3vhs.de/BoD2019ff/1.pdf

Logbuch zu Vitamin C in Hochdosis

Vitamin C Saves Man Dying of Viral Pneumonia by Jeffrey Dach MD

The Allan Smith Story

http://jeffreydachmd.com/vitamin-c-saves-dying-man/

http://jeffreydachmd.com/2017/06/intravenous-vitamin-c-cancer-chemotherapy/

http://astrologischefachliteratur.vonabisw.de/dr-med-robert-cathcart-on-vitamin-c

Bücher / ebooks:

80 Years of High-Dose-Vitamin C Research – als freies PdF

http://d.mp3vhs.de/RobertCathcart/1.pdf

Das diesbzgl. Buch gibt es hier bei BoD:

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http://d.mp3vhs.de/BoD2019ff/1.pdf

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Vitamin C bis zu 180.000 mg täglich bei Grippe, Fieber, Bakterien, Viren, Entzündungen und als Antihistamin bei Heuschnupfen

https://www.bod.de/buchshop/vitamin-c-bis-zu-180-000-mg-taeglich-bei-grippe-fieber-bakterien-viren-entzuendungen-und-als-antihistamin-bei-heuschnupfen-volker-h-sch-9783744886222

in der Tradition der Dres. Pauling, Stone, Klenner, Cathcart, Riordan, Hoffer, Rath, Saul, Levy, Hunninghake

Vitamin C: The Real Story: The Remarkable and Controversial Healing Factor: The Remarkable and Controversial Story of Vitamin C

https://www.amazon.de/Vitamin-Remarkable-Controversial-Healing-Factor/dp/159120223X/ref=sr_1_1?ie=UTF8&qid=1521990352&sr=8-1&keywords=vitamin+c+the+real

Prof. Dr. mult. Linus Paulin – How to Live Longer and Feel Better

https://www.amazon.de/How-Live-Longer-Feel-Better/dp/0870710966/ref=sr_1_sc_1?s=books-intl-de&ie=UTF8&qid=1521990438&sr=1-1-spell&keywords=pauling+feel+livving

Prof. Dr. med. Abram Hoffer – Putting It All Together: The New Orthomolecular Nutrition

https://www.amazon.de/Putting-All-Together-Orthomolecular-Nutrition/dp/0879836334/ref=sr_1_1?s=books-intl-de&ie=UTF8&qid=1521990516&sr=1-1&keywords=hoffer+putting

(2006-09) Robert Cathcart – Mega C for Viral & Other Diseases

https://www.youtube.com/watch?v=PKD3BXL8ESA&t=1s

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Dr. Robert Cathcart – Vitamin C Pioneer

https://www.youtube.com/watch?v=VkkWDDSti_s

http://d.mp3vhs.de/RobertCathcart/2.mp4

Cathcart Part 3: The Rationale for High Doses of Ascorbate

https://www.youtube.com/watch?v=qbdVs6cx6oY

http://d.mp3vhs.de/RobertCathcart/3.mp4

Cathcart Lecture on Titrating Vitamin C to Bowel Tolerance

https://www.youtube.com/watch?v=KOmAxiR0SHE

http://d.mp3vhs.de/RobertCathcart/4.mp4

bert Cathcart on Vitamin C

Bücher / ebooks:

80 Years of High-Dose-Vitamin C Research – als freies PdF

http://d.mp3vhs.de/RobertCathcart/1.pdf

Das diesbzgl. Buch gibt es hier bei BoD:

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Compendium Vitamin C – täglich ab 18.000 mg – bei Grippe, Fieber, Bakterien, Viren, Entzündungen und als Antihistamin bei Heuschnupfen

als freies PdF:

http://d.mp3vhs.de/BoD2019ff/1.pdf

Das diesbzgl. Buch gibt es hier bei BoD:

https://www.bod.de/buchshop/compendium-vitamin-c-taeglich-ab-18-000-mg-bei-grippe-fieber-bakterien-viren-entzuendungen-und-als-antihistamin-bei-heuschnupfen-f-r-kl-9783752812251

Logbuch zu Vitamin C in Hochdosis

http://d.mp3vhs.de/RobertCathcart/Logbuch.pdf

Vitamin C bis zu 180.000 mg täglich bei Grippe, Fieber, Bakterien, Viren, Entzündungen und als Antihistamin bei Heuschnupfen

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2018 – Dr. med. Robert Cathcart, MD on Vitamin C – 30.000 Patients – Herausgegeben von der Bürgervereinigung Orthomolekulare Aufklärung Isernhagen

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Curing with High Doses of Ascorbic Acid (Vitamin C)

https://www.bod.de/buchshop/curing-with-high-doses-of-ascorbic-acid-vitamin-robert-f-cathcart-iii-m-d-9783743116726

Vitamin C: The Real Story: The Remarkable and Controversial Healing Factor: The Remarkable and Controversial Story of Vitamin C

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Prof. Dr. mult. Linus Paulin – How to Live Longer and Feel Better

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(2006-09) Robert Cathcart – Mega C for Viral & Other Diseases

https://www.youtube.com/watch?v=PKD3BXL8ESA&t=1s

http://d.mp3vhs.de/RobertCathcart/1.mp4

Dr. Robert Cathcart - Vitamin C Pioneer

https://www.youtube.com/watch?v=VkkWDDSti_s

http://d.mp3vhs.de/RobertCathcart/2.mp4

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https://www.youtube.com/watch?v=KQmAxiR0SHE

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Robert Cathcart: Preparation of Vitamin C (Sodium Ascorbate) for IV Use

https://www.youtube.com/watch?v=iuRTLoQlSks

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https://www.youtube.com/playlist?list=PLgtKw1QgfYrlyhDayTRpVa2ig0-w7Ohuv

VITAMIN C, TITRATING TO BOWEL TOLERANCE, ANASCORBEMIA, AND ACUTE INDUCED SCURVY

http://www.doctoryourself.com/titration.html

Die Mega-Vitamin-C Methode von ROBERT F. CATHCART III, M.D.

http://www.vitamine-und-mehr.com/therapeuten/mega-vitamin-c-methode-robert-f-cathcart

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How Doctors Use (Or Should Use) Vitamin Therapy

http://orthomolecular.org/resources/omns/v06n25.shtml

The Method of Determining Proper Doses of Vitamin C for the Treatment of Disease by Titrating to Bowel Tolerance

http://orthomolecular.org/library/jom/1981/pdf/1981-v10n02-p125.pdf

Vitamin C Material: Where to Start, What to Watch

http://orthomolecular.org/resources/omns/v13n20.shtml

OMArchives.org – Dr. Robert Cathcart MD – Publications Index

OMArchives.org – Dr. Robert Cathcart MD – Preparing Vitamin C for IV Use

http://omarchives.org/dr-robert-cathcart-md-preparing-vitamin-c-for-iv-use/

Papers by Klenner, Cathcart and Stone

http://www.mv.helsinki.fi/home/hemila/klenner.htm

W. J. McCORMICK, M.D.

VITAMIN C IN THE PROPHYLAXIS AND THERAPY OF INFECTIOUS DISEASES

 $\underline{\text{http://www.seanet.com/\%7Ealexs/ascorbate/195x/mccormick-wj-arch_pediatrics-1951-v68-n1-p1.htm}$

In Memoriam

http://www.orthomolecular.org/library/jom/1984/pdf/1984-v13n04-p285.pdf

Dr. Irwin Stone: A Tribute

http://www.orthomolecular.org/library/jom/1985/pdf/1985-v14n02-p150.pdf

Eight Decades of Scurvy. - The Case History of a Misleading Dietary Hypothesis

http://www.orthomolecular.org/library/jom/1979/pdf/1979-v08n02-p058.pdf

Fifty Years of Research on Ascorbate and the Genetics of Scurvy:

From a Better Flavored Beer To Homo Sapiens Ascorbicus

Irwin Stone, D.Sc.

http://www.orthomolecular.org/library/jom/1984/pdf/1984-v13n04-p280.pdf

Vitamin C-THE HEALING FACTOR

Vitamin C, TITRATING TO BOWEL TOLERANCE, ANASCORBEMIA, and ACUTE INDUCED SCURVY

http://www.medical-hypotheses.com/article/0306-9877(81)90126-2/references

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http://d.mp3vhs.de/Cathcart/1mp4/2.mp4

http://d.mp3vhs.de/Cathcart/1mp4/3.mp4

http://d.mp3vhs.de/Cathcart/1mp4/4.mp4

http://d.mp3vhs.de/Cathcart/1mp4/5.mp4

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Papers by Klenner, Cathcart and Stone

Pdfs Dr. med. Cathcart

http://d.mp3vhs.de/RobertCathcart/Pdf/Cathcart/1.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Cathcart/2.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Cathcart/3.pdf

Pdfs Dr. med. Klenner

http://d.mp3vhs.de/RobertCathcart/Pdf/Klenner/1.pdf

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http://d.mp3vhs.de/RobertCathcart/Pdf/Klenner/8.pdf

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Pdfs Dr. rer. nat. Stone

http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/1.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/2.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/3.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/4.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/5.pdf

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http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/7.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/8.pdf

http://d.mp3vhs.de/RobertCathcart/Pdf/Stone/9.pdf

https://www.vitamincfoundation.org/squares/

BOAI-Film "Wege zur Gesundheit" (3:41:33)

BOAI – Bürgervereinigung Orthomolekulare Aufklärung Isernhagen

 $\frac{https://www.youtube.com/watch?v=Mq30FyW1x84\&t=362s\&index=3\&list=PLgtKw1QgfYrmAOjhZ1vitjpzc9J5Y3iRA}{}$

Vitamin C Saves Dying Man



Vitamin C Saves Man Dying of Viral Pneumonia by Jeffrey Dach MD

The Allan Smith Story – TV Documentary

Allan Smith, a New Zealand Dairy farmer, contracted Swine Flu while away on vacation in Fiji. When he returned home, the flu quickly evolved into severe pneumonia which left him in a coma on Life Support in the Intensive Care Unit. Chest Xrays showed the lungs were completely filled with fluid with an "opaque" appearance called "white out". After three weeks of this, Allan's doctors asked the family permission to turn off the machines and let him die. Allan's wife Sonia had a brother with some medical knowledge, so he stepped in and said, "you haven't tried everything, You have got to try high dose IV vitamin C on Allan". At first, the doctors resisted, saying it was useless. Next, the three sons weighed in with a persuasive argument to try the IV vitamin C, saying there was nothing to lose.

This article is part one. For part two <u>click here:</u> http://jeffreydachmd.com/2017/06/intravenous-vitamin-c-cancer-chemotherapy/.

Above Left image: IV Bag with Vitamin C, Courtesy of wikimedia Commons.

Doctors Agree to Try IV Vitamin C

The Doctors were in unanimous agreement that IV Vitamin C would be useless and a waste of time, and that the patient will certainly die. However, one doctor "felt slightly uneasy" with the decision to turn off life support, without first acceding to the family's wishes, and so they reluctantly agreed to give the IV Vitamin C. Their plan was to give the IV Vitamin C, show it was useless, and then turn off life support.

Dramatic Recovery

That day, Allan Smith was given 25 grams of IV Vitamin C in the evening and another 25 grams in the morning. The next day, a CAT scan of the lungs showed improving air flow and a few days later the Chest Xrays showed the lungs were no longer white, indicating air movement. The improvement was dramatic, clear and plain for all to see. However, the doctors denied it was the Vitamin C, and instead, attributed the improvement to "turning patient into a prone position".

Soon after starting the IV vitamin C, Alan could be taken off ECMO life support, and started breathing on his own. However, unexpectedly, a different physician consultant came in, took over the case and stopped the IV vitamin C. Alan Smith's condition promptly deteriorated. Allan's wife, Sonia, called a meeting with this new doctor to no avail. The new doctor rolled his eyes, looked up at the ceiling and uttered, "No More Vitamin C ". Not giving up so easily, the three brothers again weighed in, and demanding the IV vitamin C for dad. The three brothers again used their powers of "persuasion", and the new doctors reluctantly gave in, restarting the life saving IV vitamin C, but only at low doses of one gram a day. The brothers said, "Mucking about with the Vitamin C showed in his fathers health". "You had to be thick not to see it."

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Left upper image: Vitamin C molecule chemical structure, Courtesy of wikimedia Commons.

Oral Lyposperic Vitamin C

Allan's condition continued to improve and was eventually transferred to a hospital closer to home, still breathing with ventilator assistance. Here, the family had yet another battle with a new doctor who again stopped the IV Vitamin C. This time. the family brought in a lawyer who sent a warning letter to the hospital threatening legal action. The hospital was forced to restart the vitamin C, however, allowing only low dosage. Finally, Allan Smith was able to sit up in bed and take oral liquids. On their own, the family gave dad 6 grams a day of oral vitamin C. This was a highly absorbable form called Lypo-Spheric Vitamin C, from Livon Labs (Dr Thomas Levy).

Allan continued to improve and was discharged home from the hospital. At home, Allan's neighbor John joked with him, and said, "Allan, you owe me the 15 dollars I paid to have my suit dry cleaned for your funeral, and you bugger, you came back." They laughed together at the joke.

Video: 60 Minutes New Zealand TV – the Alan Smith Story, recovery from terminal viral pneumonia with high dose IV Vitamin C. Part One.

Part Two of Documentary- Denying the Obvious New Zealand 60 Minutes- Vitamin C Living Proof.

Interviewed in part two was the Principle Advisor to the Health Ministry and Senior Intensive Care Specialist, **David Galler**, who denied that the intravenous Vitamin C was a contributing factor in the Allan Smith's recovery. He proclaimed that the recovery could have been just as likely from a "bus driving by" as the high dose Vitamin C. When asked what he would need as proof to that Vitamin C is effective, he replied he would need a randomized controlled trial, such as those for new drug approval funded by a pharmaceutical company.

Three Randomized Placebo Controlled Studies

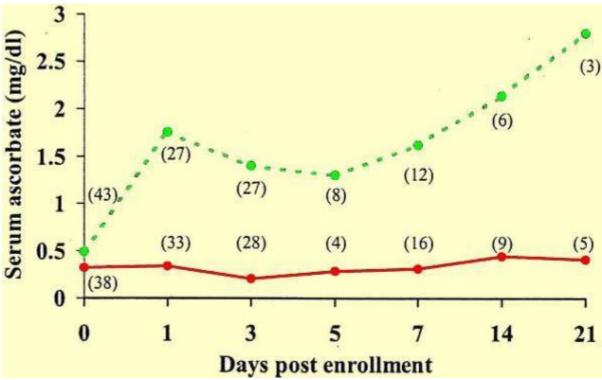
Apparently Dr Galler is unaware of three double blind placebo controlled studies of IV Vitamin C in critically ill patients in the ICU. These studies were published in Dr. Galler's own peer reviewed specialty medical literature. (1-5)

These three studies showed reduced mortality and reduced time on ventilators for septic and critically ill patients in the ICU setting. In addition, numerous other studies have measured blood vitamin C levels in critically ill patients in the hospital showing Vitamin C is typically depleted with levels below 25 % of healthy individuals.(6-11) As Dr Levy points out in Part Four of the Series (see below), there are thousands of studies over 70 years in the medical literature showing effectiveness, and safety of Vitamin C for viral illness.

Dr Levy's book, <u>Curing the Incurable: Vitamin C, Infectious Diseases, and Toxins, 3rd</u> Edition cites 1200 such articles supporting the use of Vitamin C.

Below Chart is from <u>Nathens et al</u>, showing serum vitamin C levels in Critically Ill Surgical patients. Red Line shows subnormal Blood Vitamin C values in untreated patients.

Green Line shows high normal Blood Vitamin C values in patients treated with IV Vitamin C. Normal range is 0.5 to 2.0 ng/dl. Vitamin C treated patients (green line) had less pulmonary morbidity, less multi-organ failure and less ventilator dependency when compared to untreated patients (red line).



Left chart shows low vitamin C (red line) in Critical care ICU patients, compared to treated patient (green line). Our routine test panel includes a serum vitamin C level for all patients.

Denying the Blatantly Obvious

Dr Galler appeared on New Zealand television claiming to be an authority and medical expert in the care of the ICU critically ill patient. To then make statements amounting to a public admission of ignorance of his own specialty literature is a profound embarrassment to him and to the Ministry of Health that appointed him Advisor. For Allan Smith's ICU doctors to witness a patient's dramatic recovery from sure death, and then deny the effectiveness of the treatment is astounding display of denying the obvious, and an embarrassment to the medical system in New Zealand. This is tantamount to holding up a hand in front of a person's face who then steadfastly denies a hand is in front of his face. It can also be compared to the ridiculous scenario of "denying" that parachutes are lifesaving, and insisting on "proof" by requiring a placebo controlled study. Two men jump out of a plane, one with a parachute and one without a parachute, to "prove" parachutes are effective.

Part Three of Documentary, - Dr Levy to the Rescue

This is a Video interview of Dr Thomas Levy on New Zealand TV – Campbell Live Show. Dr Levy says he was not surprised at the dramatic recovery of Allan Smith from terminal Swine Flu Pneumonia, and he says there is no doubt the Vitamin C was the treatment that saved Allan Smith's life. Dr Levy sees these types of results regularly from IV Vitamin C and he expects them, just like any well trained doctor would expect prompt recovery from bacterial pneumonia with IV antibiotics.

Transcript of Interview Part Three Dr Levy

TV Journalist to Dr Levy: Why do you believe in Vitamin C?

Dr Levy: This is not a belief like its a religion. Data has accumulated over the past 75 years. Studies are published at Harvard and New England Journal. Its amazing that a result is published in a journal and still doesn't make its way into practice

Experts say we don't see the proof this is efficacious.

Vitamin C by injection is a registered medicine for treatment of vitamin C deficiency in Zealand. Vitamin C is registered for IV injection.

Where is the evidence it is the kind of cure you say it is?

"I wrote a book, <u>Curing the Incurable: Vitamin C, Infectious Diseases, and Toxins</u>. This book contains 1200 references in the medical literature over the past 85 years, Vitamin C is enormously effective in eradicating infection and toxins."

Experts say we cannot recommend it. We can find no evidence? Why is this?

"I would have to know the motivation because this information is readily available. It's not information that is hidden, it's readily available. I would suggest they are closed minded....I know for a fact by personally using Vitamin C and giving it to my patients and discussions with hundreds of other doctors. What you saw that happened to Allan Smith happens on a regular basis."

How do you know it was vitamin C? Are you singing for your supper? You passionately believe this works.

"I passionately know it works. This is not something I have any uncertainly about. If someone treats a dozen patients with pneumococcal pneumonia and they recover, it is the same thing. I've seen and done the same thing with Vitamin C."

Buy Buffered Vitamin C from Pure Encapsulations.

Buy Lipospheric Vitamin C on Amazon.

This article is part one. For part two <u>click here.</u>

Update 2016 Vitamin C **in Sepsis:** Dr Paul Marek reports on IV vitamin C, corticosteroids and thiamine in Sepsis patients.(13) "<u>Hydrocortisone, Vitamin C and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study." *CHEST Journal* (2016).</u>

"Mortality was 8.5% (4 of 47) in the treatment group compared to 40.4% (19 of 47) in the control group. Vasopressors were weaned off all patients in the treatment group, a mean of 18.3 ± 9.8 hours after starting treatment with vitamin C protocol. The mean duration of vasopressor use was 54.9 ± 28.4 hours in the control group."

Update 12/16/14:

Fisher, Bernard J, and Ramesh Natarajan. "Phase I Safety Trial of Intravenous Ascorbic Acid in Patients with Severe Sepsis." Journal of Translational Medicine 12 (2014): 32. PMC. Web. 17 Dec. 2014.

Update Dec 2014

Review: Vitamin C revisited by Heleen M Oudemans-van Straaten*, Angelique ME Spoelstra-de Man and Monique C de Waard Critical Care 2014, 18:460 Published: 6 August 2014

Update 7/15: New York Times Scurvy in a Young Child

Dr. Suzanne Humphries on Vitamin C:

Links to articles with related content:

Doxycycline Vitamin C Anti Cancer Synergy

IV Vitamin C as Chemotherapy

MegaDose Vitamins in The ICU by Jeffrey Dach MD

My Vitamins Are Killing Me!!

Heart Disease Vitamin C and Linus Pauling by Jeffrey Dach

Dr Fred Klenner

Use of Vitamin C as Antibiotic Fred Klenner 1953

The Use of Vitamin C as an Antibiotic. Fred R. Klenner, M.D., Reidsville, N.C. Journal of Applied Nutrition, 1953, Vol. 6, pp. 274–278

Ascorbic Acid Fred klenner 1971

Journal of Applied Nutrition Vol. 23, No's 3 & 4, Winter 1971. Observations On the Dose and Administration of Ascorbic Acid When Employed Beyond the Range Of A Vitamin In Human Pathology Frederick R. Klenner, M.D., F.C.C.P. (1907-1984)

Clinical Guide Vitamin C Lendon Smith 2006

Clinical Guide to the Use of Vitamin C, The Clinical Experiences of Frederick R. Klenner, M.D., summarized by Lendon H. Smith, M.D. 2233 SW Market Street, Portland, Oregon 97201

Update 12/16/14: Dr Suzanne Humphries talks about Vitamin C in Stockholm at Orthomolecular Meeting

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http://www.naturalmedicine101.com/

http://www.truemedmd.com/ http://www.bioidenticalhormones101.com/

References:

Vitamin C Benefits Critically Ill, Septic Patients- Three randomized placebo controlled trials.

(1) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2767105/?tool=pubmed

Biofactors. 2009 Jan-Feb; 35(1): 5-13.

Mechanism of action of vitamin C in sepsis: Ascorbate modulates redox signaling in endothelium John X. Wilson

Subnormal ascorbate concentrations in plasma and leukocytes are common features of the critically ill in general and of patients with sepsis in particular [19–25]. Furthermore, plasma ascorbate correlates inversely with multiple organ failure [19] and directly with survival [21].

Parenteral administration of ascorbate may decrease morbidity and mortality in critically ill patients who are septic or at risk of becoming septic. In a randomized, double-blind, placebo-controlled trial with 216 critically ill patients, 28-day mortality was decreased in the patients who received combined ascorbate and vitamin E by intravenous infusion compared with those who did not [48]. A second randomized trial with 595 critically ill surgical patients found that a combination of ascorbate (1,000 mg q8h by intravenous injection) and vitamin E (1,000 IU q8h by naso- or orogastric tube), begun within 24 h of traumatic injury or major surgery, decreased relative risk of pulmonary edema and multiple organ failure [49]. These two trials were not designed to distinguish between the actions of ascorbate and vitamin E. However, a third randomized trial observed decreased morbidity for severely burned patients who received a very high dose of ascorbate (1,584 mg/kg/day) parenterally [50]. Of particular relevance to microvascular barrier function, ascorbate treatment was associated with significant reductions in edema formation, fluid resuscitation volume, and respiratory dysfunction [50].

2) http://www.ncbi.nlm.nih.gov/pubmed/15333422

Beneficial Effects Antioxidant Supplementation 2004 Anesth Analg CrimiThe Beneficial Effects of Antioxidant Supplementation in Enteral Feeding in Critically Ill Patients: A Prospective, Randomized, Double-Blind, Placebo-Controlled Trial. Anesth Analg. 2004 Sep;99(3):857-63. Ettore Crimi, MD*, Antonio Liguori, MD†, Mario Condorelli, MD‡, Michele Cioffi, MD§, Marinella Astuto, MD||, Paola Bontempo, MD PhD§, Orlando Pignalosa, MD§, Maria Teresa Vietri, MD§, Anna Maria Molinari, MD§, Vincenzo Sica, MD§, Francesco Della Corte, MD* and Claudio Napoli, MD PhD

Department of Anesthesiology and Intensive Care, University of Eastern Piedmont, Novara, Italy; †Coronary Care Unit, Pellegrini Hospital, Naples, Italy; ‡Department of Medicine, University of Naples, Naples, Italy; \$Division of Clinical Pathology, II University of Naples, Naples, Italy; and ||Department of Anesthesiology and Intensive Care, University of Catania, Catania, Italy

We investigated whether intervention with **antioxidant vitamins C and E** in enteral feeding influenced oxidative stress and clinical outcome in **critically ill patients**. Two-hundred-sixteen patients expected to require at least 10 days of enteral feeding completed the study. One-hundred-five patients received enteral feeding supplemented with antioxidants, and 111

control patients received an isocaloric formula. Plasma lipoperoxidation (by thiobarbituric acid reactive substances [TBARS] and prostaglandin F2 α isoprostane levels), low-density lipoprotein (LDL) oxidizability, and LDL tocopherol content were determined at baseline and at the end of the 10-day period. The clinical 28-day outcome was also assessed. Plasma TBARS and isoprostanes were 5.33 \pm 1.26 nM/mL and 312 \pm 68 pg/mL, respectively, before treatment and 2.42 \pm 0.61 nM/mL and 198 \pm 42 pg/mL after intervention (P < 0.01 for both comparisons). Antioxidants improved LDL resistance to oxidative stress by approximately 30% (the lag time before treatment was 87 \pm 23 min and was 118 \pm 20 min after treatment; P < 0.04). There was a significantly reduced 28-day mortality after antioxidant intervention (45.7% in the antioxidant group and 67.5% in the regular-feeding group; P < 0.05). Isoprostanes may provide a sensitive biochemical marker for dose selection in studies involving antioxidants.

In summary, we show that AOX intervention with proper doses of **vitamin E and C supplemental** to enteral feeding prevents lipid peroxidation and oxidative stress in vivo. AOX intervention also significantly influenced the 28-day outcome in critically ill patients. In absolute terms, mortality was frequent, but this was expected because this condition is relatively common in elderly patients with frequent comorbidities (28,29). Among patients older than 65 years of age, Knaus et al. (28) reported hospital mortality rates of 60% with 1 organ system failure, 90% with 2 organ system failures, and 100% with 3 or more organ system failures.

Our findings are in agreement with those of a large clinical study (595 patients) showing that AOX supplementation reduces the incidence of organ failure and shortens the length of stay in a cohort of critically ill surgical patients (30). The lack of adverse effects, coupled with the minimal expense, supports the use of AOX in critically ill patients. Interestingly, there is growing interest in superoxide dismutase mimetics in critical care medicine (31).

(3) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1422648/?tool=pubmed

Ann Surg. 2002 Dec;236(6):814-22.

Randomized, prospective trial of **antioxidant supplementation in critically ill surgical patients**. Nathens AB, Neff MJ, Jurkovich GJ, Klotz P, Farver K, Ruzinski JT, Radella F, Garcia I, Maier RV. Division of Trauma and General Surgery, Harborview Medical Center and the Department of Surgery, University of Washington, Seattle, Washington, USA.

Abstract

OBJECTIVE: To determine the effectiveness of early, routine antioxidant supplementation using alpha-tocopherol and ascorbic acid in reducing the rate of pulmonary morbidity and organ dysfunction in critically ill surgical patients.

SUMMARY BACKGROUND DATA: Oxidative stress has been associated with the development of the acute respiratory distress syndrome (ARDS) and organ failure through direct tissue injury and activation of genes integral to the inflammatory response. In addition, depletion of endogenous antioxidants has been associated with an increased risk of nosocomial infections. The authors postulated that antioxidant supplementation in critically ill surgical patients may reduce the incidence of ARDS, pneumonia, and organ dysfunction. METHODS: This randomized, prospective study was conducted to compare outcomes in patients receiving antioxidant supplementation (alpha-tocopherol and ascorbate) versus those receiving standard care. The primary endpoint for analysis was pulmonary morbidity (a composite measure of ARDS and nosocomial pneumonia). Secondary endpoints included the

development of multiple organ failure, duration of mechanical ventilation, length of ICU stay, and mortality.

RESULTS: Five hundred ninety-five patients were enrolled and analyzed, 91% of whom were victims of trauma. The relative risk of pulmonary morbidity was 0.81 (95% confidence interval 0.60-1.1) in patients receiving antioxidant supplementation. Multiple organ failure was significantly less likely to occur in patients receiving antioxidants than in patients receiving standard care, with a relative risk of 0.43 (95% confidence interval 0.19-0.96). Patients randomized to antioxidant supplementation also had a shorter duration of mechanical ventilation and length of ICU stay.

CONCLUSIONS: The early administration of antioxidant supplementation using alphatocopherol and ascorbic acid reduces the incidence of organ failure and shortens ICU length of stay in this cohort of critically ill surgical patients.

Following treatment assignment, patients randomized to antioxidant supplementation received α-tocopherol (dl-α-tocopheryl acetate; **Aquasol E, Astra USA, Westborough, MA) 1,000 IU** (20 mL) q8h per naso- or orogastric tube and 1,000 mg ascorbic acid given intravenously (American Reagent Labs, Shirley, NY) in 100 mL D5W q8h for the shorter of the duration of admission to the ICU or 28 days.

(4) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2575590/?tool=pubmedCrit Care. 2008; 12(4): R101.

Published online 2008 August 7. doi: 10.1186/cc6981. PMCID: PMC2575590

Influence of early antioxidant supplements on clinical evolution and organ function in critically ill cardiac surgery, major trauma, and subarachnoid hemorrhage patients Mette M Berger,1 Ludivine Soguel,1 Alan Shenkin,2 Jean-Pierre Revelly,1 Christophe Pinget,3 Malcolm Baines,2 and René L Chioléro1

The intervention was intravenous supplements for 5 days (selenium 270 μ g, zinc 30 mg, vitamin C 1.1 g, and vitamin B1 100 mg) with a double-loading dose on days 1 and 2 or placebo.

ICU Study on ventilator dependency

(5) http://www.ncbi.nlm.nih.gov/pubmed/20149369 Injury. 2010 Jul;41(7):857-61. Epub 2010 Feb 10.

High-dose antioxidant administration is associated with a reduction in post-injury complications in critically ill trauma patients. Giladi AM, Dossett LA, Fleming SB, Abumrad NN, Cotton BA. Department of Surgery, University of Michigan, Ann Arbor, MI, United States. Abstract BACKGROUND: We recently demonstrated a high-dose antioxidant (AO) protocol was associated with reduction in mortality. The purpose of this study was to evaluate the impact of AO on organ dysfunction and infectious complications following injury.

PATIENTS AND METHODS: High-dose AO protocol: ascorbic acid 1000 mg q 8 h, alphatocopherol 1000 IU q 8 h, and selenium 200 mcg qd for 7-day course. Retrospective cohort study evaluating all patients admitted after protocol implementation (AO+), October 1, 2005

to September 30, 2006. Comparison cohort (AO-): all patients admitted in the year prior to implementation, October 1, 2004 to September 30, 2005.

RESULTS: 2272 patients included in the AO+ group, 2022 patients in the AO- group. Demographics and injury severity were similar. Abdominal compartment syndrome (ACS) (2.9% vs. 0.7%, <0.001), surgical site infections (2.7% vs. 1.3%, p=0.002), pulmonary failure (27.6% vs. 17.4%, p<0.001), and ventilator-dependent respiratory failure (10.8% vs. 7.1%, p<0.001) were significantly less in the AO+ group. Multivariate regression showed 53% odds reduction in abdominal wall complications and 38% odds reduction in respiratory failure in the AO+ group.

CONCLUSIONS: Implementation of a high-dose AO protocol was associated with a reduction in respiratory failure and ventilator-dependence. In addition, AO were associated with a marked decrease in abdominal wall complications, including ACS and surgical site infections.

(6) http://www.ajcn.org/cgi/reprint/63/5/760.pdf

Am J Clin Nutr. 1996 May;63(5):760-5.

Total vitamin C, ascorbic acid, and dehydroascorbic acid concentrations in plasma of critically ill patients. Schorah CJ, Downing C, Piripitsi A, Gallivan L, Al-Hazaa AH, Sanderson MJ, Bodenham A. Division of Clinical Sciences, University of Leeds, United Kingdom.

Plasma concentrations of the antioxidant vitamin ascorbic acid were measured by high-performance liquid chromatography in critically ill patients in whom the excessive generation of reactive oxygen species could compromise antioxidant defense mechanisms. Median concentrations of both total vitamin C (ascorbic acid and dehydroascorbic acid) and ascorbic acid in these patients were < 25% (P < 0.001) of the values found in healthy control subjects and in subjects in two other disease groups (diabetes, gastritis) in which reactive oxygen species are reported to be increased. The low values could not be explained by age, sex, intake, or treatment differences, but were associated with the severity of the illness and were not prevented by the use of parenteral nutrition containing ascorbic acid. In addition, the vitamin was less stable in blood samples taken from critically ill patients than in similar samples from subjects in the other groups. The findings indicate that antioxidant defenses could be considerably compromised in these very sick patients. If this reduces the patient's capacity to scavenge reactive species, then the potential of these species to damage DNA and lipid membranes could be increased and compromise recovery.

(7) http://www.journalofsurgicalresearch.com/article/S0022-4804(02)00083-5/abstract JSR Volume 109, Issue 2, Pages 144-148 (February 2003) Ascorbic acid dynamics in the seriously ill and injured C.L Long, Ph.D., K.I Maull, M.D., R.S Krishnan, M.D., H.L Laws, M.D., J.W Geiger, B.S., L Borghesi, M.D., W Franks, R.Ph., MBA†, T.C Lawson, M.D., H.E Sauberlich, Ph.D.† Received 3 July 2002

Abstract Background. In addition to the known beneficial effects of ascorbic acid on wound healing and the immune response, it is also a potent extracellular antioxidant. Recent work in septic rats suggests that high-dose ascorbic acid total parenteral nutrition (TPN) supplementation may protect cells from free radical injury and improve survival. In this study, we determined ascorbic acid levels in the immediate post-injury/illness period and evaluated the ability of early short-term high levels of ascorbic acid in TPN to normalize plasma levels. Materials and Methods. Ascorbic acid levels were determined in 12 critically injured patients

and 2 patients with severe surgical infections. Each patient received TPN supplemented with increasing doses of ascorbic acid over a 6-day period. Therapeutic responses were determined by plasma and urine measurements using high-pressure liquid chromatography. Results. The initial mean \pm SEM baseline plasma ascorbic acid concentration was depressed (0.11 \pm 0.03 mg/dl) and unresponsive following 2 days on 300 mg/day supplementation (0.14 \pm 0.03; P = 1.0) and only approached low normal plasma levels following 2 days on 1000 mg/day (0.32 \pm 0.08; P = 0.36). A significant increase was noted following 2 days on 3000 mg/day (1.2 \pm 0.03; P = 0.005).

Conclusion. We confirmed extremely low plasma levels of ascorbic acid following trauma and infection. Maximal early repletion of this vitamin requires rapid pool filling early in the post-injury period using supraphysiologic doses for 3 or more days.

(8) http://www.ncbi.nlm.nih.gov/pubmed/20689415

Current Opinion in Clinical Nutrition & Metabolic Care: Vitamin C requirement in surgical patients Fukushima, Ryoji; Yamazaki, Eriko

Recent findings: Blood vitamin C concentration falls after uncomplicated surgery and further decreases in surgical intensive care unit patients. The decline may be owing to increased demand caused by increased oxidative stress. To normalize plasma vitamin C concentration, much higher doses than the recommended daily allowance or doses recommended in parenteral nutrition guidelines are needed in these patients. In uncomplicated surgical patients, more than 500 mg/day of vitamin C may be required, with much higher doses in surgical intensive care unit patients. In uncomplicated gastrointestinal surgery, continuous parenteral administration of 500 mg/day of vitamin C reduced postoperative oxidative stress as manifested by reduced urinary excretion of isoprostane. In some studies, postoperative atrial fibrillation was prevented after cardiac surgery by perioperative vitamin C supplementation. In critically ill patients, some prospective randomized controlled trials support parenteral supplementation of high doses of vitamin C, E and trace elements.Summary: Vitamin C requirement is increased in surgical patients, and the potential advantage of supplementation is to increase the plasma and tissue levels of vitamin C and thereby reduce oxidative stress. Although some clinical benefits of high-dose vitamin C supplementation have been shown in the critically ill, the optimal dose for supplementation and the clinical benefits remain to be investigated in surgical patients.

Low Vitamin C levels in Hospitalized patients

(9) http://www.ncbi.nlm.nih.gov/pubmed/20018480>Nutrition. 2009 Dec 15. [Epub ahead of print]

Metabolic origin of hypovitaminosis C in acutely hospitalized patients. Evans-Olders R, Eintracht S, John Hoffer L. Lady Davis Institute for Medical Research, McGill University and Jewish General Hospital, Montreal, Quebec, Canada.

RESULTS: Vitamin C administration increased plasma and mononuclear leukocyte vitamin C concentrations from subnormal ($16.3 \pm 12.4 \pm 1$

(10) Eur J Intern Med. 2003 Nov;14(7):419-425. <u>Hypovitaminosis C in hospitalized patients</u>. Fain O, Pariés J, Jacquart B, Le Moël G, Kettaneh A, Stirnemann J, Héron C, Sitbon M, Taleb C, Letellier E, Bétari B, Gattegno L, Thomas M.

RESULTS: The prevalence of **hypovitaminosis** C (depletion: SAAL<5 mg/l or deficiency: SAAL<2 mg/l) was 47.3%. Some 16.9% of the patients had vitamin C deficiency. There was a strong association between hypovitaminosis C and the presence of an acute phase response (p=0.002). Other univariate risk factors for vitamin C depletion were male sex (p=0.02), being retired (p=0.037), and infectious diseases (p=0.002). For vitamin C deficiency, the significant univariate risk factors included the same ones found for vitamin C depletion, plus being unemployed (p=0.003) and concomitant excessive alcohol and tobacco consumption (p<0.0001). Logistic regression showed that being retired (p=0.015) and concomitant excessive alcohol and tobacco consumption (p=0.0003) were significant independent risk factors. Hemorrhagic syndrome and edema were described more often in patients with vitamin C deficiency than in those with vitamin C depletion or without hypovitaminosis. Clinical signs were more frequent for an ascorbic acid level below 2.5 mg/l.

CONCLUSION: **Hypovitaminosis** C **is frequent in hospitalized patients** but should be interpreted according to the presence or absence of an acute phase response. The main risk factors are living conditions and excessive alcohol and tobacco consumption.

- (11) http://www.jacn.org/cgi/content/abstract/27/3/428
 Journal of the American College of Nutrition, Vol. 27, No. 3, 428-433 (2008) Published by the American College of Nutrition Vitamin C Deficiency in a University Teaching Hospital Runye Gan, Shaun Eintracht, MD and L. John Hoffer, MD, PhD
- (12) 2006 American Society for Nutrition J. Nutr. 136:2611-2616, October 2006 Nutritional Immunology. <u>Vitamin C Deficiency Increases the Lung Pathology of Influenza</u> Virus–Infected Gulo–/– Micel Wei Li2, Nobuyo Maeda3 and Melinda A. Beck2,*

This study was designed to determine the effects of vitamin C deficiency on the immune response to infection with influenza virus. L-Gulono–lactone oxidase gene-inactivated mice (gulo-/- mice) require vitamin C supplementation for survival. Five-wk-old male and female gulo-/- mice were provided water or water containing 1.67 mmol/L vitamin C for 3 wk before inoculation with influenza A/Bangkok/1/79. There were no differences in lung influenza virus titers between vitamin C-adequate and -deficient mice; however, lung pathology in the vitamin C-deficient mice was greater at 1 and 3 d after infection but less at d 7 compared with vitamin C-adequate mice. Male vitamin C-deficient mice had higher expression of mRNA for regulated upon activation normal T expressed and secreted (RANTES), IL-1B, and TNF- in the lungs at d 1 after infection compared with male controls. However, at d 3 after infection, male vitamin C-deficient mice had less expression of mRNA for RANTES, monocyte chemotactic protein-1 (MCP-1), and IL-12 compared with male controls. None of these differences were observed in female mice. Vitamin C-deficient male mice also had greater nuclear factor-B activation as early as 1 d after infection compared with male controls. These data suggest that vitamin C is required for an adequate immune response in limiting lung pathology after influenza virus infection.

Paul Marek

13) Marik, Paul E., et al. "<u>Hydrocortisone, Vitamin C and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study.</u>" *CHEST Journal* (2016).

The global burden of sepsis is estimated as 15 to 19 million cases annually with a mortality rate approaching 60% in low income countries. METHODS: In this retrospective before-after clinical study, we compared the outcome and clinical course of consecutive septic patients treated with intravenous vitamin C, hydrocortisone and thiamine during a 7-month period (treatment group) compared to a control group treated in our ICU during the preceding 7 months. The primary outcome was hospital survival. A propensity score was generated to adjust the primary outcome.

FINDINGS: There were 47 patients in both treatment and control groups with no significant differences in baseline characteristics between the two groups. The hospital mortality was 8.5% (4 of 47) in the treatment group compared to 40.4% (19 of 47) in the control group (p < 0.001). The propensity adjusted odds of mortality in the patients treated with the vitamin C protocol was 0.13 (95% CI 0.04-0.48, p=002). The SOFA score decreased in all patients in the treatment group with none developing progressive organ failure. Vasopressors were weaned off all patients in the treatment group, a mean of 18.3 \pm 9.8 hours after starting treatment with vitamin C protocol. The mean duration of vasopressor use was 54.9 \pm 28.4 hours in the control group (p<0.001).

CONCLUSION: Our results suggest that the early use of intravenous vitamin C, together with corticosteroids and thiamine may prove to be effective in preventing progressive organ dysfunction including acute kidney injury and reducing the mortality of patients with severe sepsis and septic shock.

Dr Fred Klenner

14) http://www.ltdk.helsinki.fi/users/hemila/CP/Klenner_1948_ch.pdf

http://www.seanet.com/~alexs/ascorbate/194x/klenner-fr-southern med surg-1948-v110-n2-p36.htm

Virus Pneumonia and Its Treatment With Vitamin C . Fred R. Klenner, M.D., Reidsville, North Carolina – Read by Title to the Tri-State Medical Association of the Carolinas and Virginia, meeting at Charleston, February 9th and 10th

15) http://www.ncbi.nlm.nih.gov/pubmed/18147027

South Med Surg. 1949 Jul;111(7):209-14.

The treatment of poliomyelitis and other virus diseases with vitamin C. KLENNER FR

16) http://www.seanet.com/~alexs/ascorbate/194x/klenner-fr-southern_med_surg-1949-v111-n7-p209.htm
The Treatment of Poliomyelitis and Other Virus Diseases with Vitamin C
From Southern Medicine & Surgery, Volume 111, Number 7, July, 1949, pp. 209-214

Fred R. Klenner, M.D., Reidsville, North Carolina

17) http://www.doctoryourself.com/klennerbio.html

HIDDEN IN PLAIN SIGHT: The Pioneering Work of FREDERICK ROBERT KLENNER, M.D. by Andrew W. Saul Assistant Editor, Journal of Orthomolecular Medicine J Orthomolecular Med, 2007. Vol 22, No 1, p 31-38.

18) http://www.seanet.com/~alexs/ascorbate/198x/smith-lh-clinical_guide_1988.htm
Clinical Guide to the Use of Vitamin C The Clinical Experiences of Frederick R. Klenner, M.D., abbreviated, sumarized and annotated by Lendon H. Smith, M.D.
2233 SW Market Street, Portland, Oregon 97201

19) http://www.seleneriverpress.com/media/pdf_docs/
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ARCHIVES OF PEDIATRICS, New York The Practical Monthly on the Diseases of Infants and Children 69: 151-155, April 1952

20) http://www.orthomolecular.org/library/jom/1991/pdf/1991-v06n02-p099.pdf

The Origin of the 42-Year Stonewall of Vitamin C Robert Landwehr1

21)

 $\underline{\text{http://www.indiaenvironmentportal.org.in/files/Vitamin\%20C\%20Intravenous\%20Use\%20by\%20Complementary.pdf}\\$

Vitamin C: Intravenous Use by Complementary and Alternative Medicine Practitioners and Adverse Effects Sebastian J. Padayatty1., Andrew Y. Sun1., Qi Chen2, Michael Graham Espey1, Jeanne Drisko2, Mark Levine1* 1 Molecular and Clinical Nutrition Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland, United States of America, 2 Program in Integrative Medicine, University of Kansas Medical Center, Kansas City, Kansas, United States of America

22) Injectable Vitamin C, an e-book on Amazon by Robert McCracken PhD

23) http://www.ncbi.nlm.nih.gov/pubmed/17253561

Cochrane Database Syst Rev. 2007 Jan 24;(1):CD005532. Vitamin C for preventing and treating pneumonia. Hemilä H, Louhiala P. University of Helsinki, Department of Public Health, POB 41, Mannerheimintie 172, Helsinki, Finland, FIN-00014.

AUTHORS' CONCLUSIONS: The prophylactic use of vitamin C to prevent pneumonia should be further investigated in populations who have high incidence of pneumonia, especially if dietary vitamin C intake is low. Similarly, the therapeutic effects of vitamin C should be studied especially in patients with low plasma vitamin C levels. The current evidence is too weak to advocate widespread prophylactic use of vitamin C to prevent pneumonia in the general population. However, therapeutic vitamin C supplementation may be reasonable for pneumonia patients who have low vitamin C plasma levels because its cost and risks are low.

Vitamin C Prevents Flu

24) Exp. Biol. Med. 2007;232:847-851 <u>Ascorbic Acid Role in Containment of the World Avian Flu Pandemic</u> John T. A. Ely1 Radiation Studies, University of Washington, Seattle, Washington 98195 (i) ascorbic acid is not being administered to humans infected or at risk for influenza, and (ii) ascorbic acid is (mistakenly) believed to be a vitamin ("vitamin C"). Proper use of ascorbic acid as described here could provide effective containment for the flu pandemic.

Vitamin C Can Cure – Web Site

25) http://www.vitaminccancure.org/events

quote: In response to the Auckland DHB 14th September press release, visiting Vitamin C expert, Dr Thomas Levy said today, "to assert that there is 'no evidence' that high-dose vitamin C is either safe or effective is to ignore the results of thousands of such IV administrations by doctors around the world, as well as to ignore tens of thousands of articles in the medical literature, in the most esteemed medical institutions in the world, that have been published over the last 70 years." The DHB decision was made in the wake of mounting demand for high-dose vitamin C after news broke out of Waikato Dairy farmer Alan Smith's complete recovery from what the hospital classed as a terminal case of Swine flu. Mr Smith is the hospital's only Swine Flu patient on life support to have survived. He is also the only one to have received the high-dose intravenous vitamin C, which was administered at the family's request after being advise that life support, and therefore his life, were about to be terminated. Introduced by Alan Smith himself, Dr Levy, cardiologist, associate professor, lawyer and author, spoke about Vitamin C, use, myths, safety and efficacy on Friday 17th September, at Auckland Girls Grammar School, New Zealand. end quote

Thomas Levy MD JD Book Curing the Incurable

26) http://www.livonlabs.com/cgi-bin/start.cgi/LV/apps/curing-the-incurable.html

27) http://www.amazon.com/review/R1H1ZW20OC44I7/

<u>Curing the Incurable, Vitamin C, Infectious Disease and Toxins by Thomas E Levy MD JD</u> A Remarkable Medicine Has Been Overlooked, December 15, 2007 By Jeffrey Dach MD

28) http://www.livonlabs.com/

Lypo-SphericTM Vitamin C proven many times more powerful than all other oral forms of Vitamin C Recent clinical trials by world-renowned Vitamin C expert and pharmacologist, Steve Hickey, PhD, show that Lypo-SphericTM Vitamin C is able to produce serum levels of Vitamin C nearly double those thought theoretically possible with any oral form of Vitamin C.*

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29) http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0050012

Combined Impact of Health Behaviours and Mortality in Men and Women: The EPIC-Norfolk Prospective Population Study Kay-Tee Khaw1*, Nicholas Wareham2, Sheila Bingham3, Ailsa Welch1, Robert Luben1, Nicholas Day1

population study of 20,244 men and women with no known cardiovascular disease or cancerat baseline survey in 1993–1997, living in the general community in the United Kingdom, and followed up to 2006. Participants scored one point for each health behaviour: currentnon-smoking, not physically inactive, moderate alcohol intake (1–14 units a week) and **plasma vitamin C >50 mmol/l** indicating fruit and vegetable intake of at least five servings a day, for a total score ranging from zero to four.

Higher Vitamin C Levels mean reduced all cause mortality

30) http://www.ncbi.nlm.nih.gov/pubmed/11247548

Lancet. 2001 Mar 3;357(9257):657-63. Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study. European Prospective Investigation into Cancer and Nutrition. Khaw KT, Bingham S, Welch A, Luben R, Wareham N, Oakes S, Day N. Department of Public Health and Primary Care, Institute of Public Health, University of Cambridge School of Clinical Medicine, UK. lasma ascorbic acid concentration was inversely related to mortality from all-causes, and from cardiovascular disease, and ischaemic heart disease in men and women. Risk of mortality in the top ascorbic acid quintile was about half the risk in the lowest quintile (p<0.0001).

31) http://www.ajcn.org/cgi/content/full/87/1/64

American Journal of Clinical Nutrition, Vol. 87, No. 1, 64-69, January 2008

Plasma vitamin C concentrations predict risk of incident stroke over 10 y in 20 649 participants of the European Prospective Investigation into Cancer–Norfolk prospective population study 1,2,3Phyo K Myint, Robert N Luben, Ailsa A Welch, Sheila A Bingham, Nicholas J Wareham and Kay-Tee Khaw

top quartiles of baseline plasma vitamin C concentrations had a 42% lower risk (relative risk: 0.58; 95% CI: 0.43, 0.78) than did those in the bottom quartile,

32) http://www.ncbi.nlm.nih.gov/pubmed/10488881?dopt=Abstract

Int J Tuberc Lung Dis. 1999 Sep;3(9):756-61. Vitamin C and acute respiratory infections. Hemilä H, Douglas RM. Department of Public Health, University of Helsinki, Finland. Abstract

So far over **60 studies** have examined the effects of **vitamin C on the common cold**. No effect on common cold incidence was observed in the six largest studies, indicating that vitamin C has no preventive effects in normally nourished subjects in the Western countries.

There are, however, smaller studies reporting benefit. In three trials of subjects under heavy acute physical stress, common cold incidence decreased by on average 50%, and in four trials of British males common cold incidence decreased by on average 30% in the vitamin C groups. The dietary vitamin C intake in the UK is low, and consequently the benefit may be due to the correction of marginal deficiency, rather than high vitamin doses. Regular vitamin C supplementation (> or =1 g/day) has quite consistently reduced the duration of colds, but the size of the benefit has varied greatly. In the four largest studies the duration of colds was reduced only by 5%. In two of these studies, however, absence from school and work was reduced by 14-21% per episode, which may have practical importance. Three controlled studies recorded a reduction of at least 80% in the incidence of pneumonia in the vitamin C group, and one randomised trial reported substantial treatment benefit from vitamin C in elderly UK patients hospitalized with pneumonia or bronchitis. It seems that the preventive effects of supplementation are mainly limited to subjects with low dietary vitamin C intake, but therapeutic effects may occur in wider population groups. Further carefully designed trials are needed to explore the effects of vitamin C.

33) http://www.ncbi.nlm.nih.gov/pubmed/10543583?dopt=Abstract

The effectiveness of vitamin C in preventing and relieving the symptoms of virus-induced respiratory infections. Gorton HC, Jarvis K. Abstract

BACKGROUND: An ever increasing demand to evaluate the effect of dietary supplements on specific health conditions by use of a "significant scientific" standard has prompted the publication of this study.

OBJECTIVE: To study the effect of megadose Vitamin C in preventing and relieving cold and flu symptoms in a test group compared with a control group.

DESIGN: Prospective, controlled study of students in a technical training facility.

SUBJECTS: A total of 463 students ranging in age from 18 to 32 years made up the control group. A total of 252 students ranging in age from 18 to 30 years made up the experimental or test group.

METHOD: Investigators tracked the number of reports of cold and flu symptoms among the 1991 test population of the facility compared with the reports of like symptoms among the 1990 control population. Those in the control population reporting symptoms were treated with pain relievers and decongestants, whereas those in the test population reporting symptoms were treated with hourly doses of 1000 mg of Vitamin C for the first 6 hours and then 3 times daily thereafter. Those not reporting symptoms in the test group were also administered **1000-mg doses 3 times daily.**

RESULTS: Overall, reported flu and cold symptoms in the test group decreased 85% compared with the control group after the administration of megadose Vitamin C.

CONCLUSION: Vitamin C in megadoses administered before or after the appearance of cold and flu symptoms relieved and prevented the symptoms in the test population compared with the control group.

Allan Smith Story from Brad Weeks MD

34) <u>http://weeksmd.com/?p=4191</u>

Posted by Brad Weeks, MD on September 2, 2010

I want to make it clear that adequately dosed vitamin C, to my knowledge, has never failed to cure an acute viral syndrome. Specifically, all these doctors should now realized that H1N1, the swine flu virus, while perhaps proving to be more potent than a host of other flu viruses, need not be a feared bogeyman with vitamin C in their arsenal.

While I intend to assemble a more substantial case report from the hospital chart in the future, here are the words of my colleague in **New Zealand**, **John Appleton**:

"The short story is: Waikato farmer goes to Fiji for holiday, Starts developing flu like symptoms—decides to tough it out Arrives back in NZ very sick—swine flu Tauranga Hospital not able to treat him (what was not known at the time is that he has leukemia—he didn't know either) Sent him to Auckland Hospital—continues to

deteriorate—Tamiflu—antibiotics etc. (usual stuff) Brother-in-law (knows a bit about vitamin C) contacts Thomas Levy in the US who refers him to me I provided a lot of info on vitamin C etc and referred family to CAM (Centre for Advanced Medicine) www.camltd.co.nz in Auckland Family pushes to get him some IVC—hospital refuses CAM doctors encourages hospital then to try vitamin C Patient deteriorates further and is on life support—family told nothing more can be done and life support will be switched off on Monday. Lungs not functioning.

Family says NO-until everything has been tried-they won't agree to life support being 'switched off'. Hospital is pushed hard to give him IVC and reluctantly they agree. (50 grams twice a day I think) saying if no improvement by Friday that's it Patient shows signs of improvement by Wednesday–hospital very surprised Concerns expressed about kidneys (which we anticipated) New specialist wants to stop vitamin C-family is told liver is failing 'caused by vitamin C'. I give them lots of data to say liver is more likely to be affected by antibiotics. Patient recovery continues to the point where he can be transferred to Waikato (closer to home); on ventilator and NG tube feeding Doctors there more receptive to vitamin C but won't agree to continue as per Auckland Family gets (name deleted) high profile lawyer involved who writes letter about patient rights and rings hospital to recommend that they can either sort it out with the family or.....? Hospital continues with VC albeit at a much lower dose. CAM doctor travels to Waikato to endorse and recommend IVC at higher doses. I have heard that the lawyer was shocked at what she learned about hospital system Patient continues to recover–now conscious (thinks he has only been in hospital 3 days)–now 8 weeks in total Hospital staff stunned—never seen anything like this Patient is told by brotherin-law that VC has saved him Family absolutely blown away at what has gone on. Wife has not lost her husband and children have their father. Patient now fully 'with it' and is talking normally with family and taking Lypospheric vitamin C (6 grams daily)"

For those doctors wondering about doses, I communicated directly with the brother-in-law. He informed me that on the Tuesday following the initial "deadline" 25 grams was given intravenously. On Wednesday, 25 gram infusions were again repeated twice. Thursday the patient received 75 grams, and starting on Friday he received 100 grams intravenously and stayed at this dose daily for another 4 to 6 days. Then the new consultant had the vitamin C discontinued completely. One week later, the IVC was restarted at only one gram twice daily.

Please resend this case history to any and all who you think could benefit, including your friends and contacts in our government. The latest info on the swine flu indicates it certainly has the potential capacity to become a great killer. This does not have to be the case. Obviously, a reasonable daily dose of vitamin C could be expected to do an even better job at preventing H1N1 while having no downside relative to the mass vaccinations getting ready to take place.

Below find the link to the New Zealand 60 Minutes show on the "terminal" advanced swine flu patient cured with intravenous vitamin C. Also note toward the end of the clip that the patient's hairy cell leukemia "disappeared" as well. The abilities of properly utilized vitamin C are slowly but surely beginning to be recognized.

35) http://drculik.blogspot.com/2008/07/lypospheric-vitamin-c.html

36) Nutrients 2017, 9(4), 339; <u>Vitamin C and Infections</u> Harri Hemilä Department of Public Health, University of Helsinki Published: 29 March 2017 In the early literature, vitamin C deficiency was associated with pneumonia. After its identification, a number of studies investigated the effects of vitamin C on diverse infections. A total of 148 animal studies indicated that vitamin C may alleviate or prevent infections caused by bacteria, viruses, and protozoa. The most extensively studied human infection is the common cold. Vitamin C administration does not decrease the average incidence of colds in the general population, **yet it halved the number of colds in physically active people.** Regularly administered vitamin C has **shortened the duration of colds**, indicating a biological effect. However, the role of vitamin C in common cold treatment is unclear. Two

controlled trials found a statistically significant dose—response, for the duration of common cold symptoms, with up to 6–8 g/day of vitamin C. Thus, the negative findings of some therapeutic common cold studies might be explained by the low doses of 3–4 g/day of vitamin C. Three controlled trials found that vitamin C prevented pneumonia. Two controlled trials found a treatment benefit of vitamin C for pneumonia patients. One controlled trial reported treatment benefits for tetanus patients. The effects of vitamin C against infections should be investigated further.

Books: Steve Hickey Book The Science of Vitamin C

Financial Disclosure: The author has no financial ties to disclose, nor financial ties to any vitamin C manufacturer or products mentioned in this article. However, I do have an amazon affiliate link to a vitamin C product, where I earn a commission.

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Intravenous Vitamin C as Cancer Chemotherapy

Posted on June 4, 2017



Intravenous Vitamin C as Cancer Chemotherapy

by Jeffrey Dach MD

Susan is a new patient who wants hormone replacement for relief of menopausal symptoms. While chatting during her first visit, Susan mentioned that her OB/Gyne doctor has been following her for a "pelvic mass" which was noted on a pelvic sonogram 6 months ago for fullness and discomfort in her lower abdomen. So, before doing anything else, we sent Susan for a follow up sonogram. Sure enough, the mass had increased in size over the last 6 months. This is highly suspicious, so Susan was sent back to her OB/Gyne for laparoscopic surgery which revealed Susan has ovarian cancer which had already spread to the peritoneal cavity. The surgeon then did a complete hysterectomy and debulked the peritoneal metastatic deposits. Susan recovered quickly from surgery and was then scheduled for chemotherapy with an oncologist.

Sister Recommends IV Vitamin C For Susan

Susan's sister told her about Intravenous vitamin C for cancer patients. So, Susan called one of my colleagues in Boca Raton who offers IV vitamin C for cancer patients. However, when she mentioned the IV vitamin C to her oncologist, he blew up in front of her face and practically hit the ceiling. He was very opposed to it, saying the Iv vitamin C would reduce the effectiveness of the chemotherapy.

IV Vitamin C Makes Ovarian Cancer More Chemo-Sensitive and Reduces Adverse effects of Chemo.(26-28)

Susan's oncologist is quite wrong about this. This question has been studied over the last 20 years, revealing that quite the opposite is true. High dose intravenous IV vitamin C actually synergies and augments conventional chemotherapy, making the chemo drugs more

effective. This is especially true for ovarian cancer chemotherapy. A study by Jeanne Drisko in the 2003 Journal of the American College of Nutrition (27) and a more recent study by Yan Ma in 2014 Science Translational Medicine (28) are to this point. They state:

"High-dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer and reduced toxicity of chemotherapy." (27-28)

Intravenous High Dose Vitamin C: Safest and Most Valuable

After reviewing the medical literature on high dose IV vitamin C for cancer patients, Dr Michael J González and Hugh D. Riordan state in their 2005 article (29):

"AA Ascorbic Acid (Vitamin C) is one of the safest and most valuable substances available to the physician for treating cancer." (29)

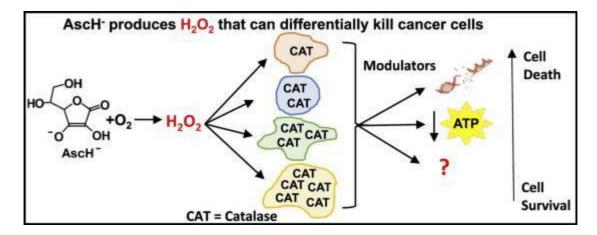
Overwhelming Evidence

In this article we will pull together a huge volume of published studies on high dose intravenous vitamin C for the cancer patient, and demonstrate the overwhelming evidence that not only is this safe and effective along with conventional chemotherapy, IV Vitamin C may also be regarded as an effective stand alone chemotherapy agent , killing cancer cells through a well described pro-oxidative mechanism.

Lymphoma Cells are especially sensitive to IV Vitamin C at low serum concentrations (**LD50** ~ **0.5 mmol/l**) .(83-84) Downregulating the dual anti-oxidant system with **Auranofin** (which inhibits thioredoxin reductase system) and a second agent such as celecoxib(87) which attenuates glutathione levels, potentiates the cytotoxic effects.(85-86)(87)

Vitamin C Mechanism Deferentially Kills Cancer Cells

The mechanism by which high dose vitamin C kills cancer cells selectively while leaving normal cells unharmed has been extensively studied. (see below diagram by Beuttner)(7)



Above figure from Beuttner Garry Redox Biol 2016. (7) Fig 8(7)

Vitamin C is a pro-oxidant which produces hydrogen peroxide toxic to cancer cells which have reduced levels of the catalase enzyme needed for degradation of hydrogen peroxide.(7-

8) Extracellular spaces and normal cells contain plenty of catalase enzyme which promptly degrade the hydrogen peroxide, explaining why normal cells are unharmed.

Vitamin C Targets Cancer Stem Cells

The cancer stem cell problem is the inability of conventional cancer chemotherapy to kill cancer stem cells which are not actively replicating. This explains the transient remissions after chemotherapy with relapse at frequent intervals after completing treatment. Unlike conventional chemotherapy, Vitamin C actually attacks cancer stem cells which may result in complete cure with no further relapse.(45) Dr. Bonucelli studied the effect of Vitamin C on Breast Cancer cell cultures and states in a 2017 article in Oncotarget:(45)

"Vitamin C has two mechanisms of action. First, it is a potent pro-oxidant, that actively depletes the reduced glutathione pool, leading to cellular oxidative stress and apoptosis in cancer cells. Moreover, it also behaves as an inhibitor of glycolysis, by targeting the activity of GAPDH, a key glycolytic enzyme.

Here, we show that Vitamin C can also be used to target the CSC Cancer Stem Cell population, as it is an inhibitor of energy metabolism that feeds into the mitochondrial TCA cycle and OXPHOS.

A breast cancer based clinical study has already shown that the use of Vitamin C, concurrent with or within 6 months of chemotherapy, significantly reduces both tumor recurrence and patient mortality." (45)

Cancer Cells Have Large Amounts of Iron – Artemisinin

In addition to lacking catalase, cancer cells contain larger amounts of iron which react with the peroxide to produce damaging ROS (Reactive Oxygen Species).(3)(46-49) This is called Ferroptosis and is augmented with concomitant use of Artemisinin which contains an endoperoxide bridge also delivering oxidative therapy to the cancer cells.(3)

The IV version of artemisinin is Artesunate, widely available and recommended by WHO (world Health Organization) for first line treatment for severe malaria treatment of malaria. See this <u>poster</u> for preparation and dosing of IV Artesunate, courtesy of <u>Medicines</u> for Malaria Venture (MMV).(73-74) Artesunate IV Dose is 2.4 mg per kg for adults.

Watch video: Artesunate for Injection Video courtesy of MMV

See my previous article on artemisinin as highly effective anti-cancer agent.

Hyperbaric Oxygen or Ozone Sauna

Concomitant use of <u>Hyperbaric oxygen</u> or <u>Ozone Sauna therapy</u> augments the Pro-Oxidative Effect of IV vitamin C. (2)(54-57)

Alpha Lipoic Acid Augments Killing Effect of Vitamin C

As mentioned in my previous <u>article</u>, the addition of Alpha Lipoic Acid (*left image*) to the IV vitamin C augments the cancer cell killing effect at lower serum concentrations of vitamin C. Alpha Lipoic Acid increases the electron flux through the mitochondria of the cancer cell, an intolerable state of affairs which triggers mitochondrial induced apoptosis of the cancer cell.(51-52)

The <u>alpha lipoic acid</u> (for injection) is usually given in a chaser bag to follow the IV Vitamin C infusion. Dr Zeigler reports that daily IV infusions of 600 mg Alpha Lipoic Acid for three weeks is safe.(71-72) Drs Casciari and Riordan studied the combination of high dose IV vitamin C with alpha lipoic acid, and they write in 2001 (51):

Lipoic acid synergistically enhanced ascorbate cytotoxicity, reducing the 2-day LC 50 in hollow fibre tumours from 34 mM to 4 mM. Lipoic acid, unlike ascorbate, was equally effective against proliferating and non-proliferating cells. Ascorbate levels in human blood plasma were measured during and after intravenous ascorbate infusions. Infusions of 60 g produced peak plasma concentrations exceeding 20 mM with an area under the curve (24 h) of 76 mM h. Thus, tumoricidal concentrations may be achievable in vivo." (51)

Another source for the IV Alpha Lipoic Acid and Vitamin C is McGuff Compounding Pharmacy in Santa Ana, Ca.

Menadione vitamin K3, Ubiquinol, PQQ

Agents like Alpha Lipoic Acid which also increase electron flux through the mitochondrial electron transport chain include Vitamin K3 (39-43), CoQ10, PQQ, etc.(29)(60) As expected, these all synergize and augment the cancer cell killing effects of IV vitamin C. These are all very safe vitamins, so they can be added to the IV vitamin C program.(39-44)

Chinese Skullcap Oroxylin A

Baicalin

The botanical plant, Chinese Skull Cap, contains oroxylin A
(Baicailin see left diagram) which acts as a glycolysis inhibitor in cancer cells, and is
recommended as a safe treatment for the cancer patent. Researchers found Oroxylin A
inhibits glycolysis and the binding of hexokinase II (HK II) with mitochondria in human
breast carcinoma cell lines, thus inducing apoptosis. Chinese skullcap was also effective as an
anti-cancer agent in lung cancer, AML leukemia, and glioblastoma cell models. See my
previous article on this topic for references. Scientific Name for Chinese skullcap is:
Scutellaria baicalensis Georgi available on at Elk Mountain Herbs.

Mebendazole and Ivermectin.

One may safely add add FDA approved anti-parasitic drugs Mebendazole and Ivermectin to the anti-cancer program, as they have been studied, found safe and effective as anticancer agents. See my previous <u>article</u> on this topic for references.

Doxycyxline and High Dose IV Vitamin C -Lethal Combination for Cancer Stem Cells

The common antibiotic Doxycycline works by blocking bacterial ribosomal protein production. Mammalian mitochondria are remarkably similar to bacteria. The famous cell biologist, Lynn Margulis originated the endo-symbiotic theory, the idea that mitochondria evolved when bacteria where incorporated into eukaryotic single celled organisms in a symbiotic relationship. If so, then many of the routine antibiotics which target bacteria can be expected to also target mitochondrial functions in cancer cells with an added bonus of targeting cancer stem cells. This has been found to be the case by Michal Lisanti's goup in an elegant 2015 study entitled, "Antibiotics that target mitochondria effectively eradicate cancer stem cells, across multiple tumor types: treating cancer like an infectious disease." Oncotarget 6.7 (2015): 4569-4584.

This explains the ability of Doxycycline antibiotics to induce <u>clinical remission in many cases</u> of periorbital and gastric MALT lymphomas treated with Doxycycline. Dr. Michael Lisanti's group published a <u>study</u> using in vitro breast cancer cell model showing Doxycycline and High Dose IV Vitamin C is a lethal combination for eradication of cancer stem cells.(70)

Intravenous Vitamin C For Septic Shock

44 critically ill patients in the ICU were studied by Dr Carr in 2017, and found to be vitamin C deficient, similar to scurvy.(89-90) Dr Paul Marik reported in CHEST 2016 that IV vitamin C is curative for septic shock patients in the ICU. (75-80) Hydrocortisone and Thiamine was also given. See: Marik, Paul E., et al. "Hydrocortisone, Vitamin C and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study." CHEST Journal (2016). Hydrocortisone Vitamin C and Thiamine for Sepsis Marik Paul E CHEST 2016

Vitamin C Prevents Pneumonia: Nutrients 2017, 9(4), 339; <u>Vitamin C and Infections</u> Harri Hemilä Department of Public Health, University of Helsinki Published: 29 March 2017

Safety of High Dose IV Vitamin C

Safety of IV vitamin C has been evaluated in Phase One Clinical trials in three patients with B cell lymphoma (75 grams IV) with serum ascorbate level of greater than 15 with no adverse events.(8). A second Clinical Trial in 35 lung cancer patients with high dose IV vitamin C, three times a week for 4 weeks, likewise showed no adverse effects. Ascorbate serum levels were recorded in the range of 15-20 mMoles/L.(88) Both trials showed excellent safety profile with no adverse effects.

Conclusion:

It is quite obvious high dose intravenous vitamin C is an extremely safe and beneficial therapy for cancer patients which selectively kills cancer cells while leaving normal cells unharmed. In fact, it should be offered routinely on all hospital oncology wards along with the chemo

infusions. The fact that main stream oncology has rejected and ignored this inexpensive, safe and effective therapy that should be a routine therapy on all oncology wards is simply astounding. You can change things by giving your doctor a copy of this article.

Articles with related interest:

Doxycycline and IV vitamin C Anti-Cancer Synergy

Targeting Cancer Stem Cells with Non Toxic Therapies

Artemisinin Anti-Cancer Weapon From China

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Links and References

vitamin C IV for Cancer

1) Mastrangelo, Domenico, et al. "Cytotoxic effects of high concentrations of sodium ascorbate on human myeloid cell lines." Annals of hematology 94.11 (2015): 1807-1816.

The effect of high doses of intravenous (sodium) ascorbate (ASC) in the treatment of cancer has been controversial although there is growing evidence that ASC in high (pharmacologic) concentrations induces dose-dependent pro-apoptotic death of tumor cells, in vitro. Very few data are available on the role of ASC in the treatment of acute myeloid leukemia (AML). Ascorbate behaves as an antioxidant at low (physiologic), and as pro-oxidant at pharmacologic, concentrations, and this may account for the differences reported in different experimental settings, when human myeloid cell lines, such as HL60, were treated with ASC. Considering the myeloid origin of HL60 cells, and previous literature reports showing that some cell lines belonging to the myeloid lineage could be sensitive to the pro-apoptotic effects of high concentrations of ASC, we investigated in more details the effects of high doses (0.5 to 7 mM) of ASC in vitro, on a variety of human myeloid cell lines including the following: HL60, U937, NB4, NB4-R4 (retinoic acid [RA]-resistant), NB4/AsR (ATOresistant) acute promyelocytic leukemia (APL)-derived cell lines, and K562 as well as on normal CD34+ progenitors derived from human cord blood. Our results indicate that all analyzed cell lines including all-trans retinoic acid (ATRA)- and arsenic trioxide (ATO)resistant ones are **highly sensitive** to the cytotoxic, pro-oxidant effects of high doses of ASC, with an average 50 % lethal concentration (LC50) of 3 mM, depending on cell type, ASC concentration, and time of exposure. Conversely, high doses of ASC neitherdid exert significant cytotoxic effects nor impaired the differentiation potential in cord blood (CB) CD34+ normal cells. Since plasma ASC concentrations within the millimolar (mM) range can be easily and safely reached by intravenous administration, we conclude that phase I/II clinical trials using high doses of ASC should be designed for patients with advanced/refractory AML and APL. free pdf

2) Goodman, Annekathryn. "Vitamin C and cancer." AIMS Medical Science 3.1 (2016): 41-51. <u>Vitamin C and cancer Goodman AIMS Medical Science 2016</u>

Venturelli et al have suggested combining hyperbaric oxygen or O2 sensitizers with the use of vitamin C.

Vitamin C AND D3 Augment Effects of ARTEMISININ

3) Gerhardt, Thomas, et al. "Effects of antioxidants and pro-oxidants on cytotoxicity of dihydroartemisinin to Molt-4 human leukemia cells." Anticancer research 35.4 (2015): 1867-1871. Antioxidants and Pro oxidants cytotoxicity of dihydroartemisinin to leukemia cells Gerhardt Anticancer Res 2015

Compared to control, ascorbate and H2O2 both caused a significant decrease in cell count both at 24-h (p<0.05 and p<0.0001 for ascorbate and H2O2, respectively) and 48-h (p<0.0001 for both ascorbate and H2O2) time points. It may be possible to improve therapeutic outcomes by compounding the oxidizing effect of artemisinin and certain supplements, pushing cancer cells toward oxidative overload (14). We hypothesize that ascorbate acts more like a pro-oxidant in cancer cells due to their higher cytoplasmic iron levels.

regression of Pulmonary Mets

4) Seo, Min-Seok, Ja-Kyung Kim, and Jae-Yong Shim. "<u>High-dose vitamin C promotes regression of multiple pulmonary metastases originating from hepatocellular carcinoma.</u>" Yonsei medical journal 56.5 (2015): 1449-1452.

We report a case of regression of multiple pulmonary metastases, which originated from hepatocellular carcinoma after treatment with intravenous administration of high-dose vitamin C. A 74-year-old woman presented to the clinic for her cancer-related symptoms such as general weakness and anorexia. After undergoing initial transarterial chemoembolization (TACE), local recurrence with multiple pulmonary metastases was found. She refused further conventional therapy, including sorafenib tosylate (Nexavar). She did receive high doses of vitamin C (70 g), which were administered into a peripheral vein twice a week for 10 months, and multiple pulmonary metastases were observed to have completely regressed. She then underwent subsequent TACE, resulting in remission of her primary hepatocellular carcinoma.

5) Mastrangelo, D. "<u>The Cure from Nature: The Extraordinary Anticancer Properties of</u> Ascorbate (Vitamin C)." J Integr Oncol 5 (2016): 157.

ascorbate seems to behave differently not just according to its dose, but rather according to the target cell, being an antioxidant for normal cells, and pro- oxidant for cancer cells. Almost a hundred years ago, Paul Erlich, the founder of modern chemotherapy, who received the Nobel Prize for Physiology and Medicine, hypothesized the creation of the "magic bullet" for use in the fight against human disease, thus inspiring generations of scientists to devise new powerful anticancer agents: today we know that the "magic bullet" is here; **ascorbate, in vitro is extremely effective and selective, as we have demonstrated in leukemic cells lines and their normal counterpart** [36] ... to the clinical oncologists the endeavor and responsibility to translate these wonderful data in a clinical (revolutionary) reality!.

Ron Hunninghake

6) http://orthomolecular.org/library/ivccancerpt.shtml INTRAVENOUS VITAMIN C and CANCER Ron Hunninghake

Integrative Cancer Therapies, titled "Orthomolecular Oncology Review: Ascorbic Acid and Cancer 25 Years Later." RECNAC data has shown that vitamin C is toxic to tumor cells without sacrificing the performance of chemotherapy.

Garry Beuttner Figure 1 Cancer Cells have less Catalase for degradation of H202

7) Doskey, Claire M., et al. "<u>Tumor cells have decreased ability to metabolize H 2 O 2</u>: Implications for pharmacological ascorbate in cancer therapy." Redox Biology 10 (2016): 274-284.

We have previously shown that the extracellular flux of H_2O_2 generated by the P-AscH $^-$ in the medium will increase the intracellular steady-state levels of H_2O_2 . Kinetic models indicate that **catalase** is the major antioxidant enzyme involved in the removal of H_2O_2 at concentrations greater than 10 μ M, leading us to investigate the catalase activity in the tumor cell lines

7a) Olney KE, Du J, van 't Erve TJ, et al. <u>INHIBITORS OF HYDROPEROXIDE</u> <u>METABOLISM ENHANCE ASCORBATE-INDUCED CYTOTOXICITY</u>. Free radical research. 2013;47(3):154-163.

IV Vitamin C for Relapsed Refractory B cell lymphoma

8) https://www.ncbi.nlm.nih.gov/pubmed/25248425

KAWADA, Hiroshi, et al. "Phase I Clinical Trial of Intravenous L-ascorbic Acid Following Salvage Chemotherapy for **Relapsed B-cell non-Hodgkin's Lymphoma.**" The Tokai journal of experimental and clinical medicine 39.3 (2014): 111-115.

PURPOSE:To determine the safety and the appropriate dose of intravenous l-ascorbic acid (AA) in conjunction with chemotherapy for patients with relapsed lymphoma.

PATIENTS AND METHODS:Patients with relapsed CD20-positive B-cell non-Hodgkin's lymphoma, who were going to receive the CHASER regimen as salvage therapy, were enrolled and treated with escalating doses of AA administered by drip infusion after the 2nd course of the CHASER regimen. The target plasma concentration immediately after AA administration was >15 mM (264 mg/dl).

RESULTS: A serum AA concentration of >15 mM was achieved in 3 sequentially registered patients, all of whom had received a 75 g whole body dose. No obvious adverse drug reaction was observed in the patients. The trial was therefore successfully completed. CONCLUSION:Intravenous AA at a whole body dose of 75 g appears to be safe and sufficient to achieve an effective serum concentration. A phase II trial to evaluate the efficacy of intravenous AA in relapsed/refractory lymphoma patients will now be initiated.

- 9) Levine, Mark, Sebastian J. Padayatty, and Michael Graham Espey. "<u>Vitamin C: a concentration-function approach yields pharmacology and therapeutic discoveries.</u>" Advances in Nutrition: An International Review Journal 2.2 (2011): 78-88.
- 10) Frömberg, Anja, et al. "<u>Ascorbate exerts anti-proliferative effects through cell cycle inhibition and sensitizes tumor cells towards cytostatic drugs.</u>" Cancer chemotherapy and pharmacology 67.5 (2011): 1157-1166.

- 11) Du, Juan, et al. "Mechanisms of ascorbate-induced cytotoxicity in pancreatic cancer." Clinical Cancer Research 16.2 (2010): 509-520.
- 12) Verrax, Julien, and Pedro Buc Calderon. "Pharmacologic concentrations of ascorbate are achieved by parenteral administration and exhibit antitumoral effects." Free Radical Biology and Medicine 47.1 (2009): 32-40. <u>Pharmacologic concentrations ascorbate achieved parenteral administration antitumoral effects Verra Julien Free Radical Biology Med 2009</u>

Riordan Clinic Research Institute February 2013

13) The Riordan IVC Protocol for Adjunctive Cancer Care
Intravenous Ascorbate as a Chemotherapeutic and Biological Response Modifying Agent
Riordan IVC Protocol Adjunctive Cancer Care IV Vitamin C Ascorbate Feb 2013

IV site irritation may occur at the infusion site when given in a vein and not a port. This can be caused by an infusion rate exceeding 1.0 gram/minute. The protocol suggests adding magnesium to reduce the incidence of vein irritation and spasm.

Eating before the IVC infusion is recommended to help reduce blood sugar fluctuations.

IVC should only be given by slow intravenous drip at a rate of 0.5 grams per minute. (Rates up to 1.0 gram/minute are generally tolerable, but close observation is warranted. Patients can develop nausea, shakes, and chills.

We presently use a sodium ascorbate solution, MEGA-C-PLUS®, 500 mg/mL, pH range 5.5-7.0 from Merit Pharmaceuticals, Los Angeles, CA, 90065.

We advise patients to orally supplement with at least 4 grams of vitamin C daily, especially on the days when no infusions are given, to help prevent a possible vitamin C "rebound effect." Oral alpha lipoic acid is also recommended on a case by case basis.

Vitamin C as anti-viral agent

14) MIkirova, Nina, and Ronald Hunninghake. "Effect of high dose vitamin C on Epstein-Barr viral infection." Medical Science Monitor 20 (2014): 725-732. <u>High dose vitamin C Epstein-Barr viral infection MIkirova Nina Ronald Hunninghake Medical Science Monitor</u> 2014

Background: Many natural compounds were tested for the ability to suppress viral replication. The present manuscript details an analysis of high dose vitamin C therapy on patients with EBV infection.

Material and Methods: The data were obtained from the patient history database at the Riordan Clinic. Among people in our database who were treated with **intravenous vitamin C** (7.5 g to 50 g infusions) between 1997 and 2006, 178 patients showed **elevated levels of EBV EA IgG (range 25 to 211 AU) and 40 showed elevated levels of EBV VCA IgM (range 25 to 140 AU).** Most of these patients had a diagnosis of chronic fatigue syndrome, with the rest being diagnosed as having mononucleosis, fatigue, or EBV infection. Results: Our data provide evidence that high dose intravenous vitamin C therapy has a positive effect on disease duration and reduction of viral antibody levels. Plasma levels of ascorbic acid and vitamin D were correlated with levels of antibodies to EBV. We found an inverse correlation between EBV VCA IgM and vitamin C in plasma in

patients with mononucleosis and CFS meaning that patients with high levels of vitamin C tended to have lower levels of antigens in the acute state of disease.

In addition, a relation was found between vitamin D levels and EBV EA IgG with lower levels of EBV early antigen IgG for higher levels of vitamin D.

Conclusions: The clinical study of ascorbic acid and EBV infection showed the reduction in EBV EA IgG and EBV VCA IgM antibody levels over time during IVC therapy that is consistent with observations from the literature that millimolar levels of ascorbate hinder viral infection and replication in vitro.

Chen 2005

15) Chen, Qi, et al. "Pharmacologic ascorbic acid concentrations selectively kill cancer cells: action as a pro-drug to deliver hydrogen peroxide to tissues." Proceedings of the national academy of sciences of the United States of America 102.38 (2005): 13604-13609. Human pharmacokinetics data indicate that i.v. ascorbic acid (ascorbate) in pharmacologic concentrations could have an unanticipated role in cancer treatment. Our goals here were to test whether ascorbate killed cancer cells selectively, and if so, to determine mechanisms, using clinically relevant conditions. Cell death in 10 cancer and 4 normal cell types was measured by using 1-h exposures. Normal cells were unaffected by 20 mM ascorbate, whereas 5 cancer lines had EC50 values of <4 mM, a concentration easily achievable i.v. Human lymphoma cells were studied in detail because of their sensitivity to ascorbate (EC50 of 0.5 mM) and suitability for addressing mechanisms. Extracellular but not intracellular ascorbate mediated cell death, which occurred by apoptosis and pyknosis/necrosis. Cell death was independent of metal chelators and absolutely dependent on H2O2 formation. Cell death from H2O2 added to cells was identical to that found when H2O2 was generated by ascorbate treatment. H2O2 generation was dependent on ascorbate concentration, incubation time, and the presence of 0.5-10% serum, and displayed a linear relationship with ascorbate radical formation. Although ascorbate addition to medium generated H2O2, ascorbate addition to blood generated no detectable H2O2 and only trace detectable ascorbate radical. Taken together, these data indicate that ascorbate at concentrations achieved only by i.v. administration may be a pro-drug for formation of **H2O2**, and that blood can be a delivery system of the pro-drug to tissues. These findings give plausibility to i.v. ascorbic acid in cancer treatment, and have unexpected implications for treatment of infections where H2O2 may be beneficial.

see fig 4 good illustration of H2O2 formation

Chen – glioblastoma xenografts

16) Chen, Qi, et al. "<u>Pharmacologic doses of ascorbate act as a prooxidant and decrease growth of aggressive tumor xenografts in mice.</u>" Proceedings of the National Academy of Sciences 105.32 (2008): 11105-11109.

Ascorbic acid is an essential nutrient commonly regarded as an antioxidant. In this study, we showed that ascorbate at pharmacologic concentrations was a prooxidant, generating hydrogen-peroxide-dependent cytotoxicity toward a variety of cancer cells in vitro without adversely affecting normal cells. To test this action in vivo, normal oral tight control was bypassed by parenteral ascorbate administration. Real-time microdialysis sampling in mice bearing glioblastoma xenografts showed that a single pharmacologic dose of ascorbate produced sustained ascorbate radical and hydrogen peroxide formation selectively within interstitial fluids of tumors but not in blood. Moreover, a regimen of daily pharmacologic ascorbate treatment significantly decreased growth rates of ovarian (P < 0.005),

pancreatic (P < 0.05), and glioblastoma (P < 0.001) tumors established in mice. Similar pharmacologic concentrations were readily achieved in humans given ascorbate intravenously. These data suggest that ascorbate as a prodrug may have benefits in cancers with poor prognosis and limited therapeutic options.

17) Chen, Qi, et al. "Ascorbate in pharmacologic concentrations selectively generates ascorbate radical and hydrogen peroxide in extracellular fluid in vivo." Proceedings of the National Academy of Sciences 104.21 (2007): 8749-8754.

Hugh D. Riordan, Stephen M. Hewitt, Arie Katz, L. John Hoffer, Mark Levine

18) Padayatty, Sebastian J., et al. "<u>Intravenously administered vitamin C as cancer therapy: three cases.</u>" Canadian Medical Association Journal 174.7 (2006): 937-942.

Early clinical studies showed that high-dose vitamin C, given by intravenous and oral routes, may improve symptoms and prolong life in patients with terminal cancer. Double-blind placebo-controlled studies of oral vitamin C therapy showed no benefit. Recent evidence shows that oral administration of the maximum tolerated dose of vitamin C (18 g/d) produces peak plasma concentrations of only 220 µmol/L, whereas intravenous administration of the same dose produces plasma concentrations about 25-fold higher. Larger doses (50–100 g) given intravenously may result in plasma concentrations of about 14 000 μmol/L. At concentrations above 1000 µmol/L, vitamin C is toxic to some cancer cells but not to normal cells in vitro. We found 3 well-documented cases of advanced cancers, confirmed by histopathologic review, where patients had unexpectedly long survival times after receiving high-dose intravenous vitamin C therapy. We examined clinical details of each case in accordance with National Cancer Institute (NCI) Best Case Series guidelines. Tumour pathology was verified by pathologists at the NCI who were unaware of diagnosis or treatment. In light of recent clinical pharmacokinetic findings and in vitro evidence of antitumour mechanisms, these case reports indicate that the role of high-dose intravenous vitamin C therapy in cancer treatment should be reassessed.

John Hoffer MD – Lymphoma Remission with Vit C IV

19) The Journal of Orthomolecular Medicine Vol. 15, 4th Quarter 2000 Vitamin C: A Case History of an Alternative Cancer Therapy John Hoffer, M.D., Ph.D.

Also striking was the report, in a subsequent paper by Cameron, Campbell and Jack, of **two vitamin C-induced complete remissions in the same patient of a stage IVB non-Hodgkins lymphoma**.12 The patient was a 42 year-old truck driver who developed fever and constitutional symptoms in 1973, and was found to have a right pulmonary infiltrate. Two months later the infiltrate had evolved into mediastinal and hilar enlargement, and a pleural effusion was present. The clinical diagnosis of lung cancer was made and no treatment offered. However, when the patient then developed hepatosplenomegaly and extensive peripheral lymphadenopathy, a lymph node biopsy was carried out and the diagnosis of non-Hodgkin's lymphoma was made. The accuracy of this diagnosis was later confirmed by expert pathologists.5,10 Although the plan at that time was for radiotherapy and cytotoxic chemotherapy, an administrative delay in obtaining the patient's transfer to a referral center and his poor clinical condition motivated his physicians to administer **intravenous vitamin** C. The response was so strikingly favorable that all indications for standard lymphoma therapy promptly disappeared. **Within a few days the patient experienced a return of well-**

being associated with complete regression of lymphadenopathy and hepatosplenomegaly. The pleural effusion resolved and the chest x-ray became normal. After three months vitamin C therapy was tapered and stopped. Four weeks after stopping vitamin C, the patient's constitutional symptoms returned and a repeat chest x-ray again showed right hilar enlargement and a pleural effusion. The patient was started on oral ascorbic acid, but it was ineffective in preventing further clinical deterioration, so he was admitted to hospital for an intravenous ascorbic acid infusion (20 g/day for 14 days) followed by oral ascorbic acid. A slow but sustained clinical improvement resulted. As of 1979, the patient, still on vitamin C, remained in complete remission.5

20) Hoffer, L. John, et al. "<u>High-dose intravenous vitamin C combined with cytotoxic chemotherapy in patients with advanced cancer: a phase I-II clinical trial.</u>" PloS one 10.4 (2015): e0120228.

Mercola

- 21) <u>Vitamin C: The Supplement Almost Everyone Should Take When They Are Sick</u> November 20, 2010 Mercola
- 22) Vitamin C May Be a Potent Adjunct to Cancer Treatment March 06, 2017 Mercola
- 23) Why high-dose vitamin C kills cancer cells, Low levels of catalase enzyme make cancer cells vulnerable to ascorbate

By: Jennifer Brown 2017.01.10

Ron Hunninghake, MD

24) https://riordanclinic.org/our-locations/
Ron Hunninghake, MD Chief Medical Officer
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316-682-3100 | 3100 N Hillside Ave • Wichita, KS 67219
MORE ABOUT THIS LOCATION
Hays Kansas
785-628-3215 | 1010 E 17th St.• Hays, KS 67601
MORE ABOUT THIS LOCATION
Kansas City
913.745.4757 | 21620 Midland Drive Suite B, Shawnee, KS 66218

25) How Vitamin C Fights Cancer by Ron Hunninghake (Transcript)

Vitamin C Synergy with Chemotherapy

- 26) Kurbacher, Christian M., et al. "<u>Ascorbic acid (vitamin C) improves the antineoplastic activity of doxorubicin, cisplatin, and paclitaxel in human breast carcinoma cells in vitro.</u>" Cancer letters 103.2 (1996): 183-189.
- 27) Drisko, Jeanne A., Julia Chapman, and Verda J. Hunter. "The use of antioxidants with first-line chemotherapy in two cases of ovarian cancer." Journal of the American College of Nutrition 22.2 (2003): 118-123.

28) Ma, Yan, et al. "High-dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer and reduced toxicity of chemotherapy." *Science translational medicine* 6.222 (2014): 222ra18-222ra18. High dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer reduced toxicity chemotherapy Ma Yan Mark Levine Sci trans med 2014

Ascorbate (vitamin C) was an early, unorthodox therapy for cancer, with an outstanding safety profile and anecdotal clinical benefit. Because oral ascorbate was ineffective in two cancer clinical trials, ascorbate was abandoned by conventional oncology but continued to be used in complementary and alternative medicine. Recent studies provide rationale for reexamining ascorbate treatment. Because of marked pharmacokinetic differences, intravenous, but not oral, ascorbate produces millimolar concentrations both in blood and in tissues, killing cancer cells without harming normal tissues. In the interstitial fluid surrounding tumor cells, millimolar concentrations of ascorbate exert local pro-oxidant effects by mediating hydrogen peroxide (H(2)O(2)) formation, which kills cancer cells. We investigated downstream mechanisms of ascorbate-induced cell death. Data show that millimolar ascorbate, acting as a pro-oxidant, induced DNA damage and depleted cellular adenosine triphosphate (ATP), activated the ataxia telangiectasia mutated (ATM)/adenosine monophosphate-activated protein kinase (AMPK) pathway, and resulted in mammalian target of rapamycin (mTOR) inhibition and death in ovarian cancer cells. The combination of parenteral ascorbate with the conventional chemotherapeutic agents carboplatin and paclitaxel synergistically inhibited ovarian cancer in mouse models and reduced chemotherapy-associated toxicity in patients with ovarian cancer. On the basis of its potential benefit and minimal toxicity, examination of intravenous ascorbate in combination with standard chemotherapy is justified in larger clinical trials.

Riordan Clinic Hugh D. Riordan

29) González, Michael J., et al. "Orthomolecular oncology review: ascorbic acid and cancer 25 years later." Integrative cancer therapies 4.1 (2005): 32-44. **Hugh D. Riordan** Orthomolecular oncology rev ascorbic acid cancer 25 years later González Michael Hugh D Riordan Int cancer ther 2005

"AA Ascorbic Acid (Vit C) is one of the safest and most valuable substances available to the physician for treating cancer."

new body of data that evidences the chemotherapeutic potential of ascorbic acid

Hydrogen peroxide is most likely generated intracellularly during ascorbate's metabolic oxidation dehydroascorbate. Hydrogen peroxide reduces cel-lular levels of thiols and can initiate membrane lipidperoxidation.

There is a 10- to 100-fold greater content of catalase in normal cells than in tumor cells.

the combination of megadoses of IV ascorbate togetherwith oxygen, vitamin K, lipoic acid, coenzyme Q10, and small doses of copper may seem logical as part of anontoxic treatment protocol for cancer. To ascorbate's advantage, tumor cells have an increased requirement for glucose. 104To compensate for this increased need for glucose, tumor cells increase their quantity of glucose transporters. 105 This action greatly enhances the entrance of either ascorbate or its oxidized form,

dehydroascorbate, into the cancer cell. This facilitates the action of ascorbate as a selective, nontoxic (to normal cells) chemotherapeutic agent. Since AA and glucose have similar molecular structures, cellular intake of vitamin C is favored in malignant cells.

Lipoic acid (thioctic acid), an aqueous and lipid-soluble antioxidant that recycles vitamin C, decreased the dose of vitamin C required to kill 50% of tumor cells from 700 mg/dL to 120 mg/dL.

- "AA Ascorbic Acid (Vit C) is one of the safest and most valuable substances available to the physician for treating cancer."
- 31) http://ar.iiarjournals.org/content/29/3/809.long Ohno, Satoshi, et al. "High-dose vitamin C (ascorbic acid) therapy in the treatment of patients with advanced cancer." Anticancer research 29.3 (2009): 809-815.
- 32) http://www.pnas.org/content/105/32/11037.long

Frei, Balz, and Stephen Lawson. "Vitamin C and cancer revisited." Proceedings of the National Academy of Sciences 105.32 (2008): 11037-11038.

Older literature

33) http://www.pnas.org/content/73/10/3685.full.pdf?

Cameron, Ewan, and Linus Pauling. "Supplemental ascorbate in the supportive treatment of cancer: Prolongation of survival times in terminal human cancer." Proceedings of the National Academy of Sciences 73.10 (1976): 3685-3689.

- 34) Cameron, Ewan, and Linus Pauling. "<u>Supplemental ascorbate in the supportive treatment of cancer: reevaluation of prolongation of survival times in terminal human cancer."</u>
 Proceedings of the National Academy of Sciences 75.9 (1978): 4538-4542.
- 35) https://www.ncbi.nlm.nih.gov/pubmed/7609676

Riordan, N. H., et al. "Intravenous ascorbate as a tumor cytotoxic chemotherapeutic agent." Medical hypotheses 44.3 (1995): 207-213.

36) http://www.doctoryourself.com/ckorea2008.html

High-Dose Vitamin C Therapy for Major Diseases (Seoul, Korea. September 25, 2008) Andrew W. Saul Editor-in-Chief, Orthomolecular Medicine News Service; Assistant Editor, Journal of Orthomolecular Medicine.

- 37) Pollard, Harvey B., et al. "Pharmacological ascorbic acid suppresses syngeneic tumor growth and metastases in hormone-refractory prostate cancer." in vivo 24.3 (2010): 249-255. We report here that ascorbic acid treatment does lead to both the suppression of the primary tumor mass, and also to the reduction in the incidence of lung metastases. Additionally, we found that ascorbic acid treatment changes the quantitative relationship between primary tumor weight and the number of lung metastases from random to essentially linear. This is the first report of ascorbic acid effects on tumor biology in a syngeneic, immune-competent rodent system.
- 38) Mayland, Catriona R., Michael I. Bennett, and Keith Allan. "<u>Vitamin C deficiency in cancer patients.</u>" Palliative medicine 19.1 (2005): 17-20. To assess the prevalence of vitamin C deficiency within a group of hospice patients. To assess the relationship between plasma

vitamin C, dietary intake and subsequent survival.

METHODS:Patients with advanced cancer were recruited from a large hospice. Data were collected on demographic details, physical functioning and smoking history. An estimate was obtained of the number of weekly dietary portions consumed equivalent to 40 mg of vitamin C, the recommended daily intake. Plasma vitamin C was measured by a single blood sample. The study had local ethical approval.

RESULTS:Fifty patients were recruited (mean age 65.2 years, 28 female). Plasma vitamin C deficiency was found in 15 (30%). Dietary intake of vitamin C was correlated to plasma vitamin C (r=0.518, P<0.0001). Low dietary intake, low albumin, high platelet count, high CRP level and shorter survival were all significantly associated with low plasma vitamin C concentrations (<11 micromol/L). There was no correlation between plasma vitamin C, smoking history or physical functioning.

CONCLUSION: Vitamin C deficiency is common in patients with advanced cancer and the most important factors determining plasma levels are dietary intake and markers of the inflammatory response. Patients with low plasma concentrations of vitamin C have a shorter survival.

IV vit C synergy with vitamin K3

39) Verrax, Julien, et al. "Redox-active quinones and ascorbate: an innovative cancer therapy that exploits the vulnerability of cancer cells to oxidative stress." *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents)* 11.2 (2011): 213-221. Quinones and ascorbate exploits vulnerability cancer cells to oxidative stress Verrax Julien Anti Cancer 2011

40) Apatone Vit C and Menadione (VK3)

subjects in need thereof.

Tareen, Basir, et al. "A 12 week, open label, phase I/IIa study using apatone for the treatment of prostate cancer patients who have failed standard therapy." *Int J Med Sci* 5.2 (2008): 62-67. Tareen Basir Apatone for prostate cancer Ascorbate K3 Int J Med Sci 2008

When VC and VK3 were combined in a ratio of 100:1(Apatone) and administered to human tumor cell lines, including androgen independent prostate cancer cells(DU145), they exhibited a synergistic inhibition of cellgrowth and induced cell death by apoptosis at concentrations that were 10 to 50 times lower than for the individual vitamins

- 41) Ascorbate, vitamin K3 and hydroxytolans in the treatment of cancer
 US 8680142 B2 Abstract The combination of compounds of the hydroxytolan family with
 ascorbate plus naphthoquinone (Vitamin K3; VK3), or a quinone or semiquinone analogue
 of VK3, kill tumor cells, inhibit tumor growth and development, and treat cancer in
- 42) Gilloteaux, Jacques, et al. "Synergistic antitumor cytotoxic actions of ascorbate and menadione on human prostate (DU145) cancer cells in vitro: nucleus and other injuries preceding cell death by autoschizis." Ultrastructural pathology 38.2 (2014): 116-140. ascorbate and menadione on human prostate cancer death by autoschizis Gilloteaux Jacques Ultrastruct path 2014
- 42A) Lamson, Davis W., et al. "The vitamin C: vitamin K3 system-enhancers and inhibitors of the anticancer effect." Altern Med Rev 15.4 (2010): 345-351. Vitamin C and K3 Anticancer Effect Lamson Davis Altern Med Rev 2010

- 43) Bonilla-Porras, Angelica R., Marlene Jimenez-Del-Rio, and Carlos Velez-Pardo. "Vitamin K3 and vitamin C alone or in combination induced apoptosis in leukemia cells by a similar oxidative stress signalling mechanism." Cancer cell international 11.1 (2011): 19.
- 44) Ma, Wei-Dong, et al. "<u>Chimaphilin induces apoptosis in human breast cancer MCF-7</u> cells through a ROS-mediated mitochondrial pathway." Food and Chemical Toxicology 70 (2014): 1-8.

IV Vitamin C targets Cancer stem cells

45) Bonuccelli G, De Francesco EM, de Boer R, Tanowitz HB, Lisanti MP. <u>NADH</u> autofluorescence, a new metabolic biomarker for cancer stem cells: <u>Identification of Vitamin C and CAPE as natural products targeting "stemness.</u>" Oncotarget. 2017;8(13):20667-20678. doi:10.18632/oncotarget.15400.

Increased Iron in Cancer Cells reacts with H202 from Ascorbate to kill cells

- 46) <u>Vitamin C puts the pedal to the metal</u> Monica Venere Increased iron in cancer cells drives selective sensitization of tumors to ascorbate treatment to prolong survival.
- 47) O2:— and H2O2-Mediated Disruption of **Fe Metabolism** Causes the Differential Susceptibility of NSCLC and GBM Cancer Cells to Pharmacological Ascorbate, Schoenfeld, Joshua D. et al. Cancer Cell Volume 31, Issue 4, p487–500.e8, 10 April 2017

High-dose ascorbate sensitizes NSCLC and GBM cells to radio-chemotherapy

- •O2:— and H2O2 increase labile iron causing cancer cell-selective ascorbate toxicity
- •Therapeutic levels of ascorbate are achievable and well tolerated in GBM and NSCLC
- •Cancer cell oxidative metabolism can be targeted with ascorbate for cancer therapy

Pharmacological ascorbate has been proposed as a potential anti-cancer agent when combined with radiation and chemotherapy. The anti-cancer effects of ascorbate are hypothesized to involve the autoxidation of ascorbate leading to increased steady-state levels of H2O2; however, the mechanism(s) for cancer cell-selective toxicity remain unknown. The current study shows that alterations in cancer cell mitochondrial oxidative metabolism resulting in increased levels of O2— and H2O2 are capable of **disrupting intracellular iron metabolism**, thereby selectively sensitizing non-small-cell lung cancer (NSCLC) and glioblastoma (GBM) cells to ascorbate through pro-oxidant chemistry involving redox-active labile iron and H2O2. In addition, preclinical studies and clinical trials demonstrate the feasibility, selective toxicity, tolerability, and potential efficacy of pharmacological ascorbate in GBM and NSCLC therapy.

- 48) Toyokuni, Shinya, et al. "<u>Iron and thiol redox signaling in cancer: an exquisite balance to escape ferroptosis.</u>" Free Radical Biology and Medicine (2017). Cancer cells are under persistent oxidative stress with a **delicate balance between catalytic iron and thiols**, **thereby escaping ferroptosis**. Thus, **high-dose** *L*-ascorbate and non-thermal plasma as well as glucose/glutamine deprivation may provide additional benefits as cancer therapies over preexisting therapeutics.
- 49) McCarty, Mark Frederick, and Francisco Contreras. "<u>Increasing superoxide production</u> and the labile iron pool in tumor cells may sensitize them to extracellular ascorbate." *Frontiers in oncology* 4 (2014).

50) Mata, Ana Maria Oliveira Ferreira da, et al. "Ascorbic acid in the prevention and treatment of cancer." *Revista da Associação Médica Brasileira* 62.7 (2016): 680-686.

Ascorbate synergy with alpha lipoic acid – Riordan Clinic

- 51) Casciari, J. J., Riordan et al. "Cytotoxicity of ascorbate, lipoic acid, and other antioxidants in hollow fibre in vitro tumours." British journal of cancer 84.11 (2001): 1544.
 88) Cytotoxicity of ascorbate and alpha lipoic acid in vitro tumours Casciari Brit J Cancer
- 88) Cytotoxicity of ascorbate and alpha lipoic acid in vitro tumours Casciari Brit J Cancer 2001
- 52) Patented by Riordan Clinic –<u>Treatment of cancer using lipoic acid in combination with</u> ascorbic acid US 6448287 B1

Lipoic acid and/or its water soluble salt is used to treat cancer, alone or in combination with ascorbic acid (vitamin C). Alone or in combination, it was shown to be effective on in vitro tumors and mouse tumors. The agents can be administered safely, and have been used effectively in case studies.

Electron Microscopy of Mitochondria in cancer cells

53) Xia, Jiliang, et al. "Multiple myeloma tumor cells are selectively killed by pharmacologically-dosed ascorbic acid." EBioMedicine 18 (2017): 41-49.

High-dose chemotherapies to treat multiple myeloma (MM) can be life-threatening due to toxicities to normal cells and there is a need to target only tumor cells and/or lower standard drug dosage without losing efficacy. We show that pharmacologically-dosed ascorbic acid (PAA), in the presence of iron, leads to the formation of highly reactive oxygen species (ROS) resulting in cell death. PAA selectively kills CD138+ MM tumor cells derived from MM and smoldering MM (SMM) but not from monoclonal gammopathy undetermined significance (MGUS) patients. PAA alone or in combination with melphalan inhibits tumor formation in MM xenograft mice. This study shows PAA efficacy on primary cancer cells and cell lines in vitro and in vivo.

Hyperbaric 02 augments IV vitamin C

54) <u>Increasing the Effectiveness of Intravenous Vitamin C as an Anticancer Agent.</u> Journal of Orthomolecular Medicine Volume 32, Number 1, 2017. JOM Archives, Volume 30, Number 1, 2015

We propose the utilization of **hyperbaric oxygen immediately after IV vitamin C therapy** to increase its effectiveness as an anticancer agent, in order to increase the formation of hydrogen peroxide, and therefore enhance the anticancer effect of IV vitamin C.

- 55) Research Links Oceanside Hyperbaric
- 56) <u>Pharmacological Ascorbic Acid and Hyperbaric Oxygen Therapy Target Tumor Cell Metabolism via an Oxidative Stress Mechanism</u>

Submitted on 08 Feb 2017

Janine M. DeBlasi, Nathan P. Ward, PhD, Angela M. Poff, PhD, Andrew P. Koutnik, BS, Christopher Q. Rogers, PhD, David M. Diamond, PhD, Dominic P. D'Agostino, PhD Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL

High-dose ascorbic acid (AA) is an anti-carcinogenic, minimally toxic, metabolic therapy that targets tumor cell metabolism via an oxidative stress (OxS) mechanism. At pharmacological levels (achieved i.v.), AA delivers H2O2 to tumorous tissue upon oxidation, initiating cell death. High-dose AA has shown significant anticancer effects in vitro, in vivo, and in small-scale human reports at concentrations nontoxic to normal cells, thus having great potential as an adjuvant to the standard of care. Hyperbaric oxygen therapy (HBOT) is another non-toxic, pro-oxidative, metabolic therapy that delivers 100% oxygen at elevated barometric pressure, elevating tissue pO2 and oxygenating hypoxic tumor cells, which, when coupled with high levels of reactive oxygen and nitrogen species present in cancer cells, can further augment OxS and lead to cell death. We hypothesized that AA would induce ROS-dependent OxS and that this would be further augmented with HBOT. This study's aims were as follows (1) to examine the anticancer effect of AA in vitro, (2) to evaluate the mechanism of AA-induced OxS, (3) to determine if HBOT and AA are synergistic.

To characterize the anticancer effects of AA in vitro, we measured cell viability and proliferation following treatment with graded concentrations of AA in mouse brain tumorderived VM-M3 cells. We found that AA mediates cell death in a concentration-dependent manner, and that concentrations great than or equal to 0.5mM AA significantly induced cell death compared to control. We also found that concentrations > 0.05mM AA inhibit cell proliferation compared to control and 0.01mM AA at 72 and 96 hours of growth. To investigate the role of OxS in AA-induced cytotoxicity, we measured VM-M3 cell viability in the presence of AA and antioxidant N-Acetylcysteine (NAC), and found that treatment with 0.5 and 5mM NAC attenuates the OxS-induced cytotoxic effect of AA. To determine if HBOT can enhance the therapeutic effect of AA, we measured VM-M3 cell viability following treatment with HBOT and AA. We found that HBOT significantly enhanced the cytotoxic effect of 0.3mM AA.

This data indicates that AA exhibits anti-cancer effects in vitro through an OxS mechanism and that **HBOT** can enhance this therapeutic effect. Evidence supports the use of these minimally toxic, pro-oxidative, metabolic therapies as adjuvants to the current standard of care.

57) <u>Anti-Cancer Effects of Ascorbic Acid and Hyperbaric Oxygen Therapy in vitro</u> Janine M. DeBlasi, Nathan P. Ward, Angela M. Poff, Andrew P. Koutnik, Christopher Q. Rogers and Dominic P. D'Agostino

Author Affiliations Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL

To determine if HBOT can enhance the therapeutic effect of AA, we measured measure VM-M3 cell viability following treatment with HBOT and AA. We found that HBOT significantly enhanced the cytotoxic effect of 0.3mM AA (p<0.001). To complete this aim, we will measure VM-M3 cell proliferation following treatment with HBOT, HBOT pre-treatment, and AA.

This data indicates that AA exhibits anti-cancer effect in vitro through an OxS mechanism and that HBOT can enhance this therapeutic effect. These non-toxic, pro-oxidant metabolic therapies should be further investigated as adjuvants to the current standard of care.

58) Neil Riordan IVC

A comprehensive collection on IVC Literature and Therapies

Weill Cornell Vitamin C Study in Science 2015

59) Yun, Jihye, et al. <u>Vitamin C selectively kills KRAS and BRAF mutant colorectal cancer cells by targeting GAPDH</u>. *Science* 350.6266 (2015): 1391-1396.

60) Buy Paperback on Amazon 2014

Gonzalez, Michael J., and Jorge R. Miranda-Massari. New insights on vitamin C and cancer. Springer New York, 2014. New Insights vitamin C and Cancer Gonzalez Michael Springer 2014

the combination of megadoses of IV ascorbate together with **oxygen**, **vitamin K**, **lipoic acid**, **carnitine**, **magnesium**, **Coenzyme Q10**, and small doses of copper may seem logical as part of a non-toxic treatment protocol for cancer.

61) Pharmacologic ascorbic acid concentrations selectively kill cancer cells: Action as a prodrug to deliver hydrogen peroxide to tissues Qi Chen*†, Michael Graham Espey‡, Murali C. Krishna‡, James B. Mitchell‡, Christopher P. Corpe*, Garry R. Buettner, Emily Shacter, and Mark Levine*

Effects of Ascorbic Acid on Death of Human Lymphoma Cells.

Human lymphoma cells (JLP-119) were studied in detail to determine the effects of ascorbate on cell death. Lymphoma cells were selected because of their sensitivity to ascorbate (Fig. 1A), the suitability of these cells for nuclear staining to characterize the mode of cell

death (16, 19, 28), and the **report of a positive clinical response of lymphoma to i.v. ascorbate** (14) (unpublished work). Cells were incubated for 1 hwith 0.1–5 mM ascorbate and washed, and Hoechst

PI nuclear staining was performed 18 h later to determine the amount and type of cell death (Fig. 2 A). Ascorbate induced concentration-dependent cell death, which was **nearly 100% at 2 mM.** As ascorbate concentration increased, the pattern of death changed from apoptosis to pyknosis necrosis, a pattern suggestive of H2O2-mediated cell death (19). We determined the time nec-essary for cell death after exposure to 2 mM ascorbate for 1 h (Fig.2B). Apoptosis occurred by 6 h after exposure, and cell death by pyknosis was

90% at 14 h after exposure. In contrast to lymphoma cells, there was little or no killing of normal lymphocytes and monocytes by ascorbate (Fig. 2 C)

vitamin C for Prostate cancer

62) Garcia, Keishla M., et al. "Intravenous Vitamin C and Metabolic Correction as Adjuvant Therapy for prostate Cancer: a Case Report." (2016). Intravenous Vitamin C for prostate Cancer Case Report Garcia Keishla 2016

Vitamin K3 Menadione Augments IV Vitamin C

63) Autoschizis: a new word in cancer treatment

Subject: A combination of vitamin C and **vitamin K-3 in a 100:1 ratio** causes a unique form of cancer cell destruction that has been named autoschizis.

64) Bonilla-Porras, Angelica R., Marlene Jimenez-Del-Rio, and Carlos Velez-Pardo. "Vitamin K3 and vitamin C alone or in combination induced apoptosis in leukemia cells by a similar oxidative stress signalling mechanism." Cancer cell international 11.1 (2011): 19.

We provide evidence that VK3 and VC alone or in combination induces apoptosis in leukemia cells by a sequential cascade of molecular events involving the production of ROS, simultaneous activation of NF-κB/p53/c-Jun transcription factors, mitochondrial depolarization and caspase-3 activation pathway. These data confirm our hypothesis that VK3 and VC kill leukemia cells by oxidative stress mechanism. Most importantly, VK3 and VC are **harmless to lymphocytes**, at least under the present *in vitro* conditions. T

65) High dose intravenous vitamin c treatment in a patient with lung cancer: A case report Michael J. González

School of public health, Medical Sciences Campus, University of Puerto Rico, Ponce PR.

Vitamin C Iv for Ovarian CA – enhances chemo, reduces toxicity

66) (see 28) Ma, Yan, et al. "High-dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer and reduced toxicity of chemotherapy." Science translational medicine 6.222 (2014): 222ra18-222ra18. High Dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer reduced toxicity of chemo Ma Yan Science translational medicine 2014.

Stem Cell Transplant Pts have Low Vitamin C. Low Serum Vit C in Leukemia /Lymphoma Patients

67) Ascorbic acid serum levels are reduced in patients with hematological malignancies. Mirelle J.A.J. Huijskens,a Will K.W.H. Wodzig,b Mateusz Walczak,a Wilfred T.V. Germeraad, a,? and Gerard M.J. Bosa

In this paper we demonstrate that patients treated with chemotherapy and/or hematopoietic stem cell transplantation (HSCT) have highly significant reduced serum ascorbic acid (AA) levels compared to healthy controls. We recently observed in in vitro experiments that growth of both T and NK cells from hematopoietic stem cells is positively influenced by AA. It might be of clinical relevance to study the function and recovery of immune cells after intensive treatment, its correlation to AA serum levels and the possible effect of AA supplementation.

Vitamin C or ascorbic acid (AA), an essential water-soluble vitamin with many functions [1], [2], has a crucial role in cellular immune responses [3]. Patients treated with intensive chemotherapy and/or hematopoietic stem cell transplantation (HSCT) have low immune cell counts for weeks to months [4]. Meanwhile, patients are highly susceptible to infections resulting in morbidity and mortality. We recently observed that in the presence of AA, early hematopoietic progenitors commit and mature into T cells and proliferate faster [5]. Moreover, we showed that AA enhances proliferation and maturation of NK cells [6]. As AA has a major influence on (re)generation of immune cells in vitro, we executed an observational study in which AA serum values of patients with hematological malignancies treated with and without HSCT were compared with those of healthy volunteers to see if low AA levels should be considered of importance regarding immune recovery of these patients.

68) High-dose Vitamin C (Ascorbic Acid) Therapy in the Treatment of Patients with **Advanced Cancer**

SATOSHI OHNO1,2, YUMIKO OHNO2, NOBUTAKA SUZUKI1,2, GEN-ICHIRO

SOMA3,4,5 and MASAKI INOUE2

Vitamin C (ascorbic acid, ascorbate) has a controversial history in cancer treatment. Emerging evidence indicates that ascorbate in cancer treatment deserves re-examination. As research results concerning ascorbate pharmacokinetics and its mechanisms of action against tumor cells have been published, and as evidence from case studies has continued to mount that ascorbate therapy could be effective if the right protocols were used, interest among physicians and scientists has increased. In this review, high-dose vitamin C therapy in cancer treatment is re-evaluated.

- 69) Levine, Mark, Michael Graham Espey, and Qi Chen. "Losing and finding a way at C: new promise for pharmacologic ascorbate in cancer treatment." Free radical biology & medicine 47.1 (2009): 27.
- 70) Ernestina Marianna De Francesco, Gloria Bonuccelli, Marcello Maggiolini, Federica Sotgia, Michael P. Lisanti. <u>Vitamin C and Doxycycline: A synthetic lethal combination therapy targeting metabolic flexibility in cancer stem cells (CSCs)</u>. Oncotarget, 2015; DOI: 10.18632/oncotarget.18428

Alpha Lipoic acid Dosage 600 mg/day IV is safe

- 71) Ziegler, Dan, and F. Arnold Gries. "<u>Alpha-lipoic acid in the treatment of diabetic peripheral and cardiac autonomic neuropathy</u>" *Diabetes* 46. Supplement 2 (1997): S62-S66. In conclusion, *intravenous treatment with alpha-lipoic acid (600 mg/day) over 3 weeks is safe and effective* in reducing symptoms of diabetic peripheral neuropathy, and oral treatment with 800 mg/day for 4 months may improve cardiac autonomic dysfunction in NIDDM.
- 72) Treatment of symptomatic diabetic polyneuropathy with the antioxidant alpha-lipoic acid: a 7-month multicenter randomized controlled trial (ALADIN III Study). ALADIN III Study Group. Alpha-Lipoic Acid in Diabetic Neuropathy. D Ziegler, M Hanefeld, K J Ruhnau, H Hasche, M Lobisch, K Schütte, G Kerum and R Malessa 509 outpatients were randomly assigned to sequential treatment with 600 mg alpha-lipoic acid once daily intravenously for 3 weeks, followed by 600 mg alpha-lipoic acid three times a day orally for 6 months

Artesenuate for Injection

73) <u>Artesunat Injection 2009 Artesunat Injection Product Sheet</u> (Artesunate 60mg/ml) 2009 Neros Pharmaceticals.

Each vial contains 60mg of Artesunate Each ampoule contains 1 ml of 5% Sodium bicarbonate solution.

Slow IV injection: Dissolve 60mg of Artesunate with 1ml of 5% sodium bicarbonate solution for injection and add 5ml of 0.9% sodium chloride solution for injection before use to make 1ml contains 10mg of Artesunate. Injection must follow immediately soon after dissolution, if the solution appears cloudy or sediment occurs, it should be rejected.

The usual injection dosage for each time: Adult: 1.2mg/kg. Give 1 dose daily for the 5 consecutive days.

74) POSTER on preparation and Dosing Artesunate: <u>Injectable_Artesunate_poster_guidelines</u> for administration

guidelines for administration of injectable artesunate for severe malaria 6 ml. 3 ml. Artesunate 60 mg solution concentration. 10 mg/ml 20 mg/ml. Withdraw all the air. from the vial. Artesunate. 60mg.

IV Vitamin C for sepsis

- 75) Marik, Paul E., et al. "Hydrocortisone, Vitamin C and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study." CHEST Journal (2016). Hydrocortisone Vitamin C and Thiamine for Sepsis Marik Paul E CHEST 2016
- 76) <u>Vitamin C and sepsis: The genie is now out of the bottle</u> Posted by: Thomas E. Levy, MD, JD in Vitamin C Benefits May 22, 2017 naturalhealth365
- 77) <u>Doctor used vitamin C to save almost 150 patients from certain death of sepsis</u>. Posted by: Dena Schmidt, staff writer in Vitamin C Benefits April 12, 2017
- 78) <u>Doctor Turns Up Possible Treatment For Deadly Sepsis</u> March 23, 201712:01 AM ET Heard on Morning Edition
- 79) <u>Has sepsis met its match? New treatment may save millions around the world</u> EVMS Magazine Eastern Virginia Medical School
- 80) Sepsis treatment protocol

Vitamin C: 1.5 g IV q 6 hourly for 4 days

Hydrocortisone: 50mg IV push q 6 hourly for 6 days

Thiamine: 200mg IV q 12 hourly for 4 days

Vitamin K3 Sources

- 81) Global Vitamin K3 (Menadione) Market 2017: Competitive Study and Key Sellers
- 1 Oxyvit
- 2 Dirox
- 3 Brother Enterprises
- 4 Haining Peace Chemical
- 5 Mianyang Vanetta Chemical
- 6 Huasheng Chemical Technology
- 82) Lee, Min Ho, et al. "Menadione induces G2/M arrest in gastric cancer cells by down-regulation of CDC25C and proteasome mediated degradation of CDK1 and cyclin B1." American Journal of Translational Research 8.12 (2016): 5246.

B lymphoma sensitive to ascorbate

83) New insights into redox homeostasis as a therapeutic target in B-cell malignancies Graczyk-Jarzynka, Agnieszkaa; Zagozdzon, Radoslawb,c; Muchowicz,

Angelikaa; Siernicka, Martaa,d; Juszczynski, Przemyslawe,*; Firczuk, Malgorzataa,*Current Opinion in Hematology: July 2017 – Volume 24 – Issue 4 – p 393–401

As published by Chen et al.[51], lymphoma cells are much more sensitive to direct exposure to exogenous H2O2 as compared to normal B cells. Accordingly, **lymphoma cells are among the most sensitive to L-ascorbate (LD50 ~ 0.5 mmol/l)**, which generates exogenous H2O2[51]. Despite the high sensitivity in vitro, the antilymphoma activity of high dose parenteral L-ascorbate in vivo is limited [54].

84) Chen, Qi, et al. "<u>Pharmacologic ascorbic acid concentrations selectively kill cancer cells: action as a pro-drug to deliver hydrogen peroxide to tissues.</u>" Proceedings of the national academy of sciences of the United States of America 102.38 (2005): 13604-13609.

Human pharmacokinetics data indicate that i.v. ascorbic acid (ascorbate) in pharmacologic concentrations could have an unanticipated role in cancer treatment. Our goals here were to test whether ascorbate killed cancer cells selectively, and if so, to determine mechanisms, using clinically relevant conditions. Cell death in 10 cancer and 4 normal cell types was measured by using 1-h exposures. Normal cells were unaffected by 20 mM ascorbate, whereas 5 cancer lines had EC50 values of <4 mM, a concentration easily achievable i.v. Human lymphoma cells were studied in detail because of their sensitivity to ascorbate (EC50 of 0.5 mM) and suitability for addressing mechanisms. Extracellular but not intracellular ascorbate mediated cell death, which occurred by apoptosis and pyknosis/necrosis. Cell death was independent of metal chelators and absolutely dependent on H2O2 formation. Cell death from H2O2 added to cells was identical to that found when H2O2 was generated by ascorbate treatment. H2O2 generation was dependent on ascorbate concentration, incubation time, and the presence of 0.5-10% serum, and displayed a linear relationship with ascorbate radical formation. Although ascorbate addition to medium generated H2O2, ascorbate addition to blood generated no detectable H2O2 and only trace detectable ascorbate radical. Taken together, these data indicate that ascorbate at concentrations achieved only by i.v. administration may be a pro-drug for formation of H2O2, and that blood can be a delivery system of the pro-drug to tissues. These findings give plausibility to i.v. ascorbic acid in cancer treatment, and have unexpected implications for treatment of infections where H2O2 may be beneficial.

85) Cancer Res. 2010 Nov 15;70(22):9505-14. Loss of thioredoxin reductase 1 renders tumors highly susceptible to pharmacologic glutathione deprivation. Mandal PK1, Schneider M, Kölle P, Kuhlencordt P, Förster H, Beck H, Bornkamm GW, Conrad M.

Tumor cells generate substantial amounts of reactive oxygen species (ROS), engendering the need to maintain high levels of antioxidants such as **thioredoxin** (**Trx**)- **and glutathione** (**GSH**)-**dependent enzymes.** Exacerbating oxidative stress by specifically inhibiting these types of ROS-scavenging enzymes has emerged as a promising chemotherapeutic strategy to kill tumor cells. However, potential redundancies among the various antioxidant systems may constrain this simple approach. Trx1 and thioredoxin reductase 1 (Txnrd1) are upregulated in numerous cancers, and Txnrd1 has been reported to be indispensable for tumorigenesis. However, we report here that genetic ablation of Txnrd1 has no apparent effect on tumor cell behavior based on similar proliferative, clonogenic, and tumorigenic potential. This finding reflects widespread **redundancies between the Trx- and GSH-dependent systems** based on evidence of a bypass to Txnrd1 deficiency by compensatory upregulation of GSH-metabolizing enzymes. Because the survival and growth of Txnrd1-deficient tumors were strictly dependent on a functional GSH system, Txnrd1-/- tumors were highly susceptible to

experimental GSH depletion in vitro and in vivo. Thus, our findings establish for the first time that a concomitant inhibition of the two major antioxidant systems is highly effective in killing tumor, highlighting a promising strategy to combat cancer.

This unique feature of tumor cells can be exploited for "selective toxicity" using the redox modifiers like l-buthionine sulfoximine (BSO), **ascorbic acid**, arsenic trioxide, imexon, phenethyl isothiocyanate, and motexafin gadolinium that selectively kill the tumor cells by perturbing the redox homeostasis (10).

86) Kiebala, Michelle, et al. "<u>Dual targeting of the thioredoxin and glutathione</u> <u>antioxidant systems in malignant B cells: a novel synergistic therapeutic approach.</u>" Experimental hematology 43.2 (2015): 89-99.

B-cell malignancies are a common type of cancer. One approach to cancer therapy is to either increase oxidative stress or inhibit the stress response systems on which cancer cells rely. In this study, we combined **non-toxic concentrations of Auranofin (AUR), an inhibitor of the thioredoxin (Trx) system,** with **non-toxic concentrations of buthionine-sulfoximine (BSO), a compound that reduces intracellular glutathione (GSH) levels,** and investigated the effect of this drug combination on multiple pathways critical for malignant B-cell survival.

AUR interacted synergistically with BSO at low concentrations to trigger death in multiple malignant B-cell lines and primary mantle cell lymphoma (MCL) cells. Additionally, there was less toxicity toward normal B-cells. Low AUR concentrations inhibited Trx reductase (TrxR) activity, an effect significantly increased by BSO co-treatment. TrxR over-expression partially reversed AUR+BSO toxicity. Interestingly, the combination of AUR+BSO inhibited NF-κB signaling. Moreover, synergistic cell death induced by this regimen was attenuated in cells over-expressing NF-κB proteins, arguing for a functional role for NF-κB inhibition in AUR+BSO-mediated cell death.

Together, these findings suggest that AUR+BSO synergistically induce malignant B-cell death, a process mediated by dual inhibition of TrxR and NF-κB, and such an approach warrants further investigation in B-cell malignancies.

Here we show that mantle cell lymphoma (MCL) cells exhibit dramatically reduced viability following combined exposure to AUR and BSO, even at low concentrations of both agents.

87) Bernard, M. P., et al. <u>"Targeting cyclooxygenase-2 in hematological malignancies: rationale and promise."</u> Current pharmaceutical design 14.21 (2008): 2051-2060.—

There is much interest in the potential use of Cox-2 selective inhibitors in combination with other cancer therapeutics. Malignancies of hematopoietic and non-hematopoietic origin often have increased expression of cyclooxygenase-2 (Cox-2), a key modulator of inflammation. For example, hematological malignancies such as chronic lymphocytic leukemia, chronic myeloid leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma and multiple myeloma often highly express Cox-2, which correlates with poor patient prognosis. Expression of Cox-2 enhances survival and proliferation of malignant cells, while negatively influencing anti-tumor immunity. Hematological malignancies expressing elevated levels of Cox-2 potentially avoid immune responses by producing factors that enhance angiogenesis and metastases. Cellular immune responses regulated by natural killer cells, cytotoxic T lymphocytes, and T

regulatory cells are also influenced by Cox-2 expression. Therefore, Cox-2 selective inhibitors have promising therapeutic potential in patients suffering from certain hematological malignancies. Cox-2 selective inhibitor **celecoxib**, at a dose of 400 mg/day. More recently, our laboratory has examined the effects of both **celecoxib** and OSU03012 on B-CLL, as well as B cell lymphomas [21]. **Treatment with either drug significantly attenuated glutathione levels.** Glutathione controls damaging reactive oxygen species (ROS) production and low levels of glutathione were associated with decreased malignant B cell viability.

88) Ou, Junwen, et al. "The safety and pharmacokinetics of high dose intravenous ascorbic acid synergy with modulated electrohyperthermia in Chinese patients with stage III-IV non-small cell lung cancer." European Journal of Pharmaceutical Sciences 109 (2017): 412-418.

Ascorbic acid (AA) infusion and modulated electrohyperthermia (mEHT) are widely used by integrative cancer practitioners for many years. However, there are no safety and pharmacokinetics data in Chinese cancer patients. We carried out a clinical trial to evaluate the safety and pharmacokinetics of those methods in patients with stage III-IV non-small cell lung cancer (NSCLC). Blood ascorbic acid in the fasting state was obtained from 35 NSCLC patients; selecting from them 15 patients with stage III-IV entered the phase I study. They were randomized allocated into 3 groups, and received doses 1.0, 1.2, 1.5 g/kg AA infusions. Participants in the first group received intravenous AA (IVAA) when mEHT was finished, in the second group IVAA was administered simultaneously with mEHT and in the third group IVAA was applied first, and followed with mEHT. Pharmacokinetic profiles were obtained when they received solely IVAA and when IVAA in combination with mEHT. The process was applied 3 times a week (every other day, weekend days off) for 4 weeks. We found that fasting plasma AA levels were significantly correlated with stage of the disease. Peak concentration of AA was significantly higher in the simultaneous treatments than in other combinations with mEHT or in solely IVAA-managed groups. IVAA synergy with simultaneous mEHT is safe and the concomitant application significantly increases the plasma AA level for NSCLC patients.

89)
Carr, Anitra C., et al. "Hypovitaminosis C and vitamin C deficiency in critically ill patients despite recommended enteral and parenteral intakes." Critical Care 21 (2017).

Vitamin C is an essential water-soluble nutrient which cannot be synthesised or stored by humans. It is a potent antioxidant with anti-inflammatory and immune-supportive roles. Previous research has indicated that vitamin C levels are depleted in critically ill patients. In this study we have assessed plasma vitamin C concentrations in critically ill patients relative to infection status (septic shock or non-septic) and level of inflammation (C-reactive protein concentrations). Vitamin C status was also assessed relative to daily enteral and parenteral intakes to determine if standard intensive care unit (ICU) nutritional support is adequate to meet the vitamin C needs of critically ill patients.

Methods

Forty-four critically ill patients (24 with septic shock, 17 non-septic, 3 uncategorised) were recruited from the Christchurch Hospital Intensive Care Unit. We measured concentrations of plasma vitamin C and a pro-inflammatory biomarker (C-reactive protein) daily over 4 days and calculated patients' daily vitamin C intake from the enteral or total parenteral nutrition they received. We compared plasma vitamin C and C-reactive protein concentrations between septic shock and non-septic patients over 4 days using a mixed effects statistical model, and

we compared the vitamin C status of the critically ill patients with known vitamin C bioavailability data using a four-parameter log-logistic response model. Results

Overall, the critically ill patients exhibited hypovitaminosis C (i.e., <23 μ mol/L), with a mean plasma vitamin C concentration of 17.8 ± 8.7 μ mol/L; of these, one-third had vitamin C deficiency (i.e., <11 μ mol/L). Patients with hypovitaminosis C had elevated inflammation (C-reactive protein levels; P < 0.05). The patients with septic shock had lower vitamin C concentrations and higher C-reactive protein concentrations than the non-septic patients (P < 0.05). Nearly 40% of the septic shock patients were deficient in vitamin C, compared with 25% of the non-septic patients. These low vitamin C levels were apparent despite receiving recommended intakes via enteral and/or parenteral nutritional therapy (mean 125 mg/d).

Conclusions

Critically ill patients have low vitamin C concentrations despite receiving standard ICU nutrition. Septic shock patients have significantly depleted vitamin C levels compared with non-septic patients, likely resulting from increased metabolism due to the enhanced inflammatory response observed in septic shock.

90) Marik, Paul E., and Michael H. Hooper. "<u>Doctor—your septic patients have scurvy!.</u>" (2018): 23.

Attachments area

IVC, Chemotherapy, & Radiation - Are They Compatible?

http://d.mp3vhs.de/RobertCathcart/6.mp4

The Scientific Basis of IVC for Cancer

http://d.mp3vhs.de/RobertCathcart/7.mp4

Vitamin C Is Taking The Fight To The Big "C" – Dr. Ron Hunninghake

http://d.mp3vhs.de/RobertCathcart/8.mp4

Von: Hoppenstedt Hendrik [mailto:hendrik.hoppenstedt@bundestag.de]

Gesendet: Donnerstag, 29. März 2018 14:24

An: Volker H. Schendel

Betreff: AW: Anfrage an die Bundesregierung?

Sehr geehrter Herr Schendel,

vielen Dank für Ihre E-Mail. Eine Anfrage an die Bundesregierung halte ich nicht für sinnvoll, da die Bundesregierung nicht der richtige Adressat für Ihr Anliegen ist. Die Bundesregierung, namentlich das Bundesgesundheitsministerium und der Deutsche Bundestag als Gesetzgeber setzen den gesetzlichen und politischen Rahmen, in dem die Partner im Gesundheitswesen ihre Entscheidungen treffen können. Die gesetzlichen Grundlagen für das Thema Arzneimittel finden sich insbesondere im fünften Sozialgesetzbuch (SGB V).

Danach entscheidet in unserem Gesundheitssystem nicht die Bundesregierung, sondern der Gemeinsame Bundesausschuss als oberstes Beschlussgremium der gemeinsamen Selbstverwaltung der Ärzte, Krankenhäuser und Krankenkassen über den Leistungskatalog der gesetzlichen Krankenversicherung. Er legt fest, welche Leistungen der medizinischen Versorgung von der GKV erstattet werden.

Ich rege daher an, dass Sie sich direkt an den Gemeinsamen Bundesausschuss wenden (https://www.g-ba.de/).

Mit freundlichen Grüßen

Hendrik Hoppenstedt

Dr. Hendrik Hoppenstedt

Mitglied des Deutschen Bundestages

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Von: Volker H. Schendel [mailto:volker@vonabisw.de]

Gesendet: Montag, 26. März 2018 11:09

An: Hoppenstedt Hendrik < hendrik.hoppenstedt@bundestag.de >

Betreff: WG: Anfrage an die Bundesregierung?

Gesundheitspolitische Bedeutung der Wirkung und Wirksamkeit von Vitamin C in Hochdosis bis zu 250.000 mg täglich

Sehr geehrter Herr Dr. Hoppenstedt,

seit Jahrzehnten gibt es frei verfügbare wissenschaftliche Informationen zur therapeutischen Wirkung und Wirksamkeit von Vitamin C in Hochdosis bis zu 250.000 mg täglich, ohne daß dies sich in Deutschland in gesundheitspolitischen Aktivitäten niedergeschlagen hätte.

Als Beispiel mag dieses frei verfügbare Pdf dienen:

80 Years of High-Dose-Vitamin C Research

http://d.mp3vhs.de/RobertCathcart/1.pdf

Meine Frage an Sie:

Sind Sie bereit, eine diesbezügliche Anfrage an die Bundesregierung zu richten?

Mit freundlichen Grüßen

Volker H. Schendel

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Sehr geehrter Herr Dr. Hoppenstedt.

Wir haben Ihre Antwort im Kreis der BOAI-Mitglieder diskutiert im Hinblick darauf, daß der "Bundesausschuß" wegen der dort eingeforderten Randomisierten Doppelblindstudien und damit wissenschaftstheoretisch im Widerspruch stehend zu Dr. habil. Gerhard Kienle: Arzneimittelsicherheit und Gesellschaft. Eine kritische Untersuchung, keine zielführende Option darstellt.

https://www.amazon.de/Arzneimittelsicherheit-Gesellschaft-Eine-kritische-Untersuchung/dp/3794503732/ref=sr 1 3?s=books&ie=UTF8&qid=1522687261&sr=1-3

Ein weibliches Mitglied fühlt sich beim "Bundesausschuß" an den Arzt in ihrer Nachbarschaft erinnert. Zitat: "Ein Arschloch, das gequirlte Scheisse zum Frühstück verzehrt – mit Genuß".

Mit freundlichen Grüßen

Volker H. Schendel

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