# Oral vs. Intravenous Vitamin C

Ronald Hunninghake, MD

## Oral vs. Intravenous Vitamin C

Optimizing the Use of Vitamin C in the Care of Cancer Patients

*Cancer is a word, not a sentence.*

*- John Diamond*

Ron Hunninghake, MD
Chief Medical Officer
The Olive W. Garvey Center for Healing Arts

## My Objectives

- Redefine Orthomolecular Oncology
- Introduce The Riordan Approach
- Clarify How Vitamin C Fights Cancer
  - IVC as a Biological Response Modifier
  - The Pro-oxidant Effect of IVC – ***Redox Cycling***
  - ***The Antiangiogenesis Effect* of IVC**
- Discuss 'Ortho-dosing' of Vitamin C
- Illustrate Objectives with Two Case Studies

"The Doctor" painting

## *The Doctor* (1891)

**Sir Samuel Luke Fildes**

- one of the best known of all late-Victorian paintings (partly because reproductions hung in many doctor's offices)
- now in the National Gallery of British Art

(Image courtesy of Wikipedia)

- depicts a pensive physician watching a gravely ill child
- inspired by the death of Sir Fildes' own son

## What **message** was Sir Fildes trying to convey with this painting?

The compassion of the physician
The hopeless feelings of the family
The medical helplessness of that time period
The devastation of life-threatening disease

## Clinical Oncology Paradigms

| Conventional | ????? |
|---|---|
| Treat the Disease | |
| Determine Grade and Stage of Tumor | |
| Kill Cancer Cells | |
| More Oxidative Stress | |
| Quantity of Survival | |

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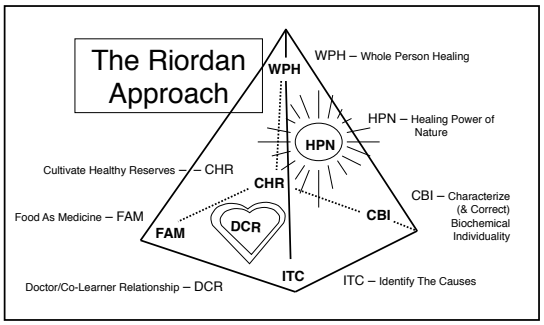
## Allopathic Oncology

- '*Relating to or being a system of medicine that aims to* combat disease ***by using remedies*** *(as drugs or surgery) which produce effects that are different from those of the disease being treated*.' -- Webster's
- 'The Silver Bullet' mentality
  - the latest chemotherapeutic "breakthrough"
  - the newest and hottest technology…i.e. "the cyberknife"
  - the cancer surgery that is or will be the "standard of care"
- DANGER: the broader clinical context of the patient's illness is lost in the rush to implement "***the therapy***"

## Orthomolecular Oncology

| Allo-pathic | Ortho-pathic |
|---|---|
| Treat the Disease | Care for the Patient |
| Determine Grade and Stage of Tumor | Search for and Correct Underlying Causes |
| Kill Cancer Cells | Strengthen Healthy Cells |
| More Oxidative Stress | Lessen Oxidative Stress |
| | Quality of Life |
| Quantity of Survival | |

"We don't treat cancer here.
-
We treat patients who have cancer."
.
-Dr. Hugh Riordan
1932-2005


## The Riordan Approach

| Riordan Approach<br>Doctor-Colearner Relationship | Ortho-pathic |
|---|---|
| Identify the Causes | |
| Characterize (& Correct) Biochemical Individuality | |
| Care for the Whole Person | |
| Food as Medicine | |
| Cultivate Healthy Reserves | |
| Healing Power of Nature | |

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## Greek '*Orthos*-' defined…

| *Orthos-* | Modern Usage | Defined… |
|---|---|---|
| *Right* | orthogonal | A ***right*** angle |
| *Correct* | orthodontics | ***correct*** the bite |
| *Straight* | orthopedist | ***straighten*** the fracture |
| *True* | orthodox | a ***true, correct*** belief |
| *Akin to* | orthochromatic | Colors ***akin to*** nature |
| *Right* | orthomolecular | The ***right*** molecule |
| | orthopathic | _____ approach to illness |

***Summation***

## Orthomolecular Medicine **Bridges** Allopathic and Alternative

| Riordan Approach | Ortho-pathic |
|---|---|
| Doctor-Colearner Relationship | Ortho-relational<br>Ortho-cellular |
| Identify the Causes | Ortho-molecular |
| Characterize (& Correct) Biochemical Individuality | Ortho-personal |
| Care for the Whole Person | Ortho-nutritional |
| Food as Medicine | Ortho-dosing |
| Build Healthy Reserves | Ortho-natural |
| Healing Power of Nature | |

## First Cancer Case at The Center*

- George Williams, friend and patient of Dr. Hugh
- 1980 – Adenocarcinoma of right kidney
- Underwent nephrectomy → mets to lung, liver
- IVC 30 grams twice weekly…felt well
- **After 15 months of therapy, mets were gone**
- 14 yrs later, at age 84, George died of CHF

***J Orthomol Med** 1990; 5:5-7

## medpage TODAY

PUTTING BREAKING MEDICAL NEWS INTO PRACTICE

Medical News: Other Cancers

**Re-Assessment Urged for Intravenous Vitamin C and Cancer***

Published: March 27, 2006

- acceptable for CME

*Sebastian J. Padayatty, et al

"Intravenously administered vitamin C as cancer therapy: three cases" CMAJ 2006;174(7):937-42.

## IVC – a '*Natural*' Silver Bullet?

- IVC therapy for cancer is in danger of being viewed as a *natural* "silver bullet"
- We best **NOT FORGET** the unique "birthing ground" of IVC in our quest for scientific proof of its therapeutic efficacy
- Ideally, the emerging field of orthomolecular oncology can serve to **COMPLETE and HEAL** the field of conventional, allopathic oncology

## Orthomolecular Oncology – *the difference between soft & hard*

| Riordan Approach | Ortho-pathic |
|---|---|
| Doctor-Colearner Relationship | Ortho-relational |
| Identify the Causes | Ortho-cellular |
| **Characterize (& Correct) Biochemical Individuality** | **Ortho-molecular** |
| Care for the Whole Person | Ortho-personal |
| Food as Medicine | Ortho-nutritional |
| **Build Healthy Reserves** | **Ortho-dosing** |
| Healing Power of Nature | Ortho-natural |

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## Riordan Approach to Cancer

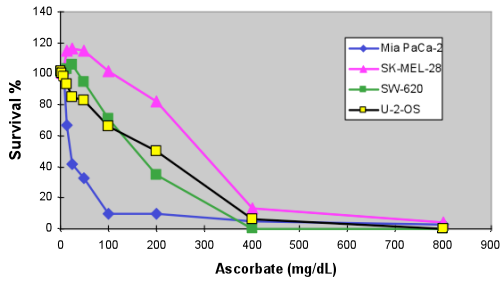
- Apply **all aspects** of the Riordan Approach, **plus…**
- Use the **right dose** of vitamin C - "**ortho-dosing**"
  1. **biological response modifier**
  2. **nontoxic chemotherapeutic agent**
  3. **natural antiangiogenesis treatment**
- ***The Art & Science of Orthomolecular Oncology***
  'Spontaneous Remission Induction'

## Orthomolecular Oncology Pioneers

- James Lind
- Albert Szent-Gyorgyi
- Irwin Stone
- Abram Hoffer
- Linus Pauling
- Fredrick Klenner
- Lendon Smith
- Claus Jungeblut
- William McCormick
- Ewan Cameron
- Robert Cathcart
- Hugh Riordan

RECNAC Research Team

## Key RECNAC Research Finding



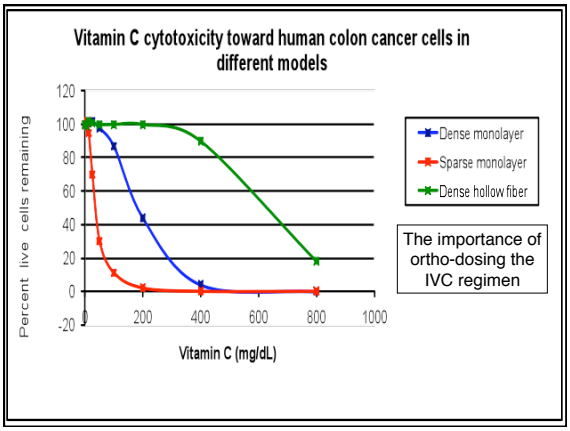

## Validation of RECNAC's Pioneering Work

Sept. 20, 2005 – National Institutes of Health

"Pharmacologic ascorbic acid concentrations selectively kill cancer cells: action as a pro-drug to deliver hydrogen peroxide to tissues"

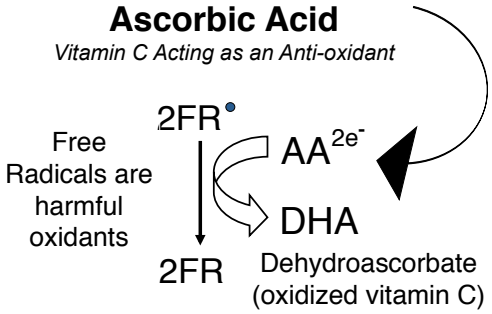
- ***Proceedings of National Academy of Science***
- Chen, Espey, Krishna, Mitchell, Corpe, Buettner, Shacter, **Levine**

*Sept 20; 102: 13604, 2005*




## Ascorbic Acid

*Vitamin C Acting as an Anti-oxidant*



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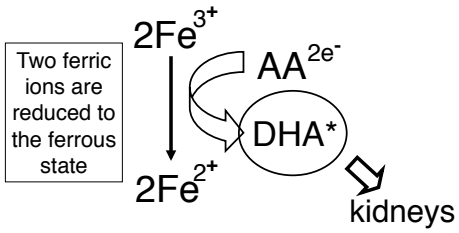
## Dehydroascorbic Acid

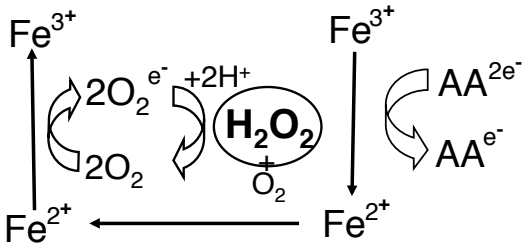
*Oxidized Vitamin C (DHA) Is Not Reabsorbed*




*Misguided Sloan Kettering Study

## The Pro-oxidant Effect of Vitamin C

in the Presence of Iron and Oxygen




National Institutes of Health
May 14, 2007

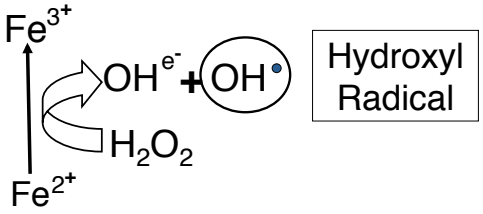
"Ascorbate in pharmacologic concentrations selectively generates ascorbate radical and hydrogen peroxide in extracellular fluid *in vivo*"

- ***Proceedings of National Academy of Science***
- Chen, Espey, Krishna, Mitchell, Corpe, Buettner, Shacter, **Levine**

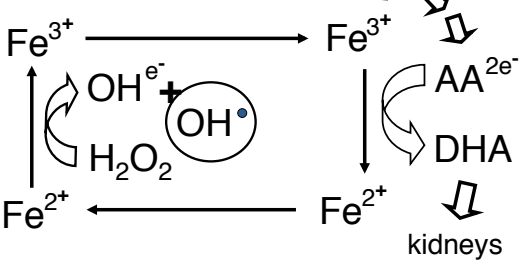
*May 14, 2007* I vol. 104 I no. 21 I **8749-8754**

## Fenton's Reaction

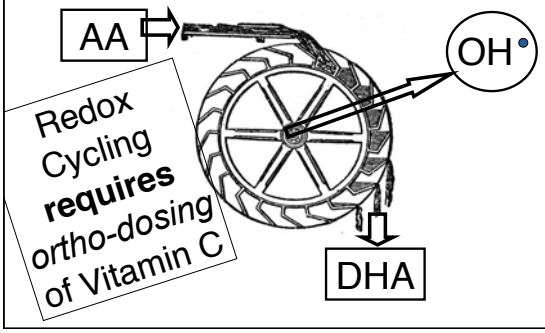
*Ferrous Iron is Oxidized Back to Ferric State*




## Redox Cycling with IVC




Water Wheel Analogy –
*Vitamin C Generating a Pro-oxidant*



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## The Riordan IVC Protocol

Intravenous Ascorbate (IVC) as a Chemotherapeutic and Biologic Response Modifier

- BCRI: Bio-Communication Research Institute
- Introduction
- Treatment rationale and biological response
- Inclusion criteria and candidates
- Precautions and side effects
- Administration of IVC
- Concurrent Therapy
- Conclusions

## IVC Relieves the Classic Picture of **Scurvy** in Cancer Patients.

- The Unrecognized Symptoms of Scurvy
  - Tired and listless
  - Sallow skin color with easy bruising
  - Poor appetite and poor sleep
  - Low threshold for pain
- IVC relieves the scurvy of cancer rapidly

## IVC – A Biological Response Modifier

- relieves scurvy
- boosts immunity
- stimulate collagen formation
- inhibits hyaluronidase
- induces apoptosis

- antiangiogenic

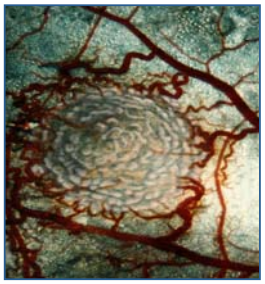
## BCRI ***Anti*-angiogenesis** Research*

Dr. Judah Folkman
The first to investigate angiogenesis in cancer in the early 1980's

Angiogenesis means "new blood vessel growth"

Tumor cells produce **growth factors**

Most important → **VEGF**



Reference: Anti-angiogenic Effect of High Doses of Ascorbic Acid
Mikirova, Ichim, Riordan; J Transl Med. 2008; 6: 50. published 9-12-08
http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2562367

## **VEGF** – Vascular Endothelial Growth Factor

1. VEGF causes **cellular proliferation**
   - stimulates mature endothelial cells
   - recruits bone marrow endothelial stem cells to the tumor site
2. VEGF stimulates **secretion of MMPs**
   - proteinases that break down extracellular matrix
   - allow new blood vessel growth toward tumor

## Angiogenesis: New Blood Vessel Growth

**Tumor cells produce…**

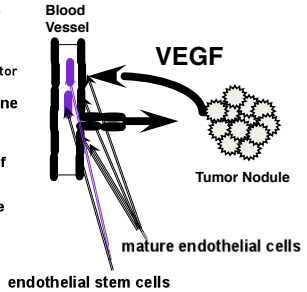
**VEGF**

Vascular Endothelial Growth Factor

**a tumor angiogenesis cytokine**

**VEGF → cellular proliferation**

1. **stimulates proliferation of mature endothelial cells**
2. **endothelial stem cells are recruited from the bone marrow**

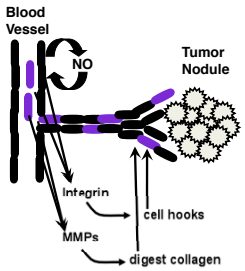


## New Endothelial Cell Actions

Endothelial cells produce MMPs proteinases that digest collagen.

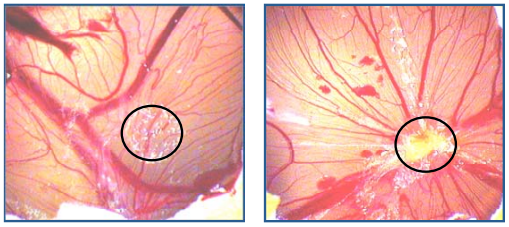
Endothelial cells produce nitric oxide

1. angiogenesis regulator
2. stimulates formation of
   a. integrins
   b. VE-adherins
3. act as "grapple hooks" for migration and adhesion of endothelial cells through extracellular matrix




## Tumor Angiogenesis

**Effect of Tumor Conditioned Medium (TCM) on Angiogenesis**



Control TCM

## VEGF Feedback Loops

- Positive local feedback
  - New blood vessel growth brings more nutrients to the tumor cells
  - As the tumor cell population grows, more VEGF is made
- Negative distant feedback
  - Tumor cells also make **angiostatin and endostatin**
  - These cytokines inhibit angiogenesis at sites of metastasis

## Beware of "I think we got it all!"

- Resection of primary tumors results in sudden vascularization and growth of mets!
- This is due to loss of feedback inhibition from angiostatin and endostatin
- Mets are free to stimulate angiogenesis

## Angiogenesis Inhibitors

**FDA Approved**

**Avastin** – Antibody to VEGF
**Increased survival by 5 months in colorectal**
**GI perforation, wound rupture, high BP, kidney, heart**

**Clinical Trials**

**Thalidomide** – Blocks migration (Nitric Oxide effects)
**Neovastat** – Multi-functional (from Shark Cartilage)
**Angiostatin** – Multi-functional
**Endostatin** – Multi-functional

**Natural**

**Foods** – **Pomegranate juice, Red wine.**
**Extracts** – **Green Tea, Horse Chestnut, Butcher's broom**
**Nutrients** – **Lipoic acid, vitamins A and D.** → **Vitamin C**

## Vitamin C and Angiogenesis

**Cell Types studied by BCRI**

- **HUVEC (umbilical cord)**
  - **"Mature" endothelial cells from umbilical cords.**
  - **Grown in the presence of growth factors and heparin.**
  - **Form "Tubules" on Matrigel extracellular matrix material.**
- **Endothelial Progenitor Cells (EPC) are adult stem cells**
  - **Isolated from human peripheral blood mononuclear cells.**
  - **Grown on fibronectin with EGF and VEGF supplemented growth medium.**
  - **Form "Tubules" on extraMatrigel cellular matrix material.**

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## Vitamin C and Angiogenesis

**Cell Type Characterization**

- Cells have characteristic surface markers.

- Fluorescence-labeled antibodies to these markers can be used to distinguish cell types

**Endothelial Cell Markers**

**HUVEC** (mature umbilical)
- CD31
- CD145
- VEGR-R2
- HLA-ABC

**EPC** (adult stem cells)
- CD34
- VEGF-R2
- CD31
- CD146
- VE-cadherin
- CD105
- CD90
- Negative for CD133

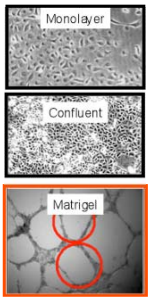
## Assays Used to Study Vitamin C and Angiogenesis

**Angiogenesis Assays**

- Matrigel "Tubule" formation.
- Aorta ring assay.
- Cell migration assays.
- Matrigel plug *in vivo* assay.

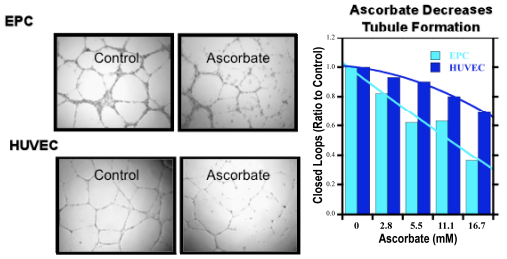
**Cellular Function Assays**

- Nitric Oxide (NO) production rates.
- ATP production rates.



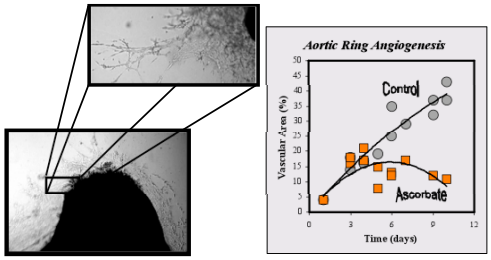

## Vitamin C and Angiogenesis

**Ascorbate and Tubule Formation**




## Vitamin C and Angiogenesis

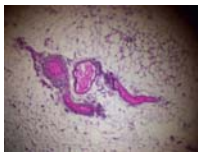
**Aortic Ring Model → Effect of Ascorbate (15 mM) on Vessel Sprouts**




## Vitamin C and Angiogenesis

**Matrigel Plug Assay**

- Insert Matrigel plug under skin
- Control → untreated
- Treated →400 mg/kg ascorbate
- Remove plug
- Detect and quantify vessel growth in histological sections



**Results of Three Experiments**

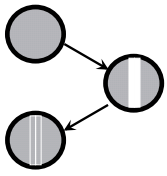
**Plugs from ascorbate treated mice have** less vessel infiltration:

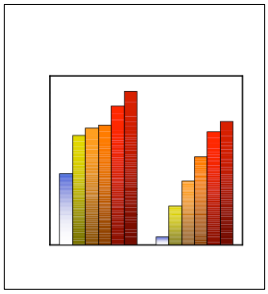
**Expt 1 → 58%** **Expt 2 → 55%** **Expt 3 → 70%**

## Vitamin C and Angiogenesis

**Endothelial Migration Assay**

- Grow Cells
- Scrape a Gap
- Measure Re-growth





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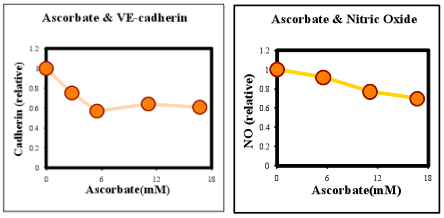
## Vitamin C and Angiogenesis

**Effects of Ascorbate on Endothelial Cells:**

- **Slight Decrease in ATP Production. No Effect on Viability**
- **Decreases VE-adherin Expression and Nitric Oxide Production.**

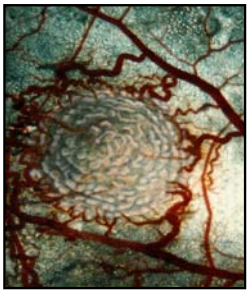



## Summary of the Effect of IVC-Dosages of Vit. C on Angiogenesis

Vitamin C inhibits endothelial cell functions key to angiogenesis

- proliferation
- migration
- nitrous oxide production

without affecting viability of endothelial cells.



## ***IV Ortho-dosing*** required for…

**IVC Antiangiogenesis Effect**

**? IVC Redox generation of the hydroxyl radical ?**

**?? Biological Response Modification ??**

**??? Vitamin C Redox Synergy ???**

What about ***Oral Ortho-dosing***?

## The Hoffer Cancer Regimen

In 1978, Dr. Abram Hoffer started a 15-year test of an **ORAL ortho-dosing** vitamin C redox regimen on 134 advanced cancer patients:

Vitamin C – 12,000 mg (as high as 40,000 mg)
Beta carotene – 30,000 IU
B complex – B100
Selenium – 600 mcg
Vitamin E succinate – 300 IU
Zinc – 60 mg

## Mean Survival (mos.) of Cancer Pts. with Hoffer's Regimen*

| Cancer Type | With Vitamins | Without Vitamins |
|---|---|---|
| Breast | 70 | 3.7 |
| Uterus | 99 | 4.0 |
| Ovary | 16 | 3.6 |
| Lung | 17 | 2.0 |
| Pancreas | 40 | 2.4 |
| All types | 45 | 2.6 |

* J of Orthomolecular Med 1990 and 1993

## Oral 'Ortho-dosing' Redox

1. The frequency and level of dosing of oral C is a critical component of any redox synergy strategy
2. The Riordan IVC Protocol empirically suggests 'off day' gram dosing of vitamin C
3. With the addition of ortho-doses of alpha lipoic acid, vitamin K, selenium, and copper, it may be possible to induce hydroxyl formation with an oral C redox synergy strategy
4. Other antioxidants, such as vitamin E succinate, vitamin $D_3$, Co-Q-10, glutathione, and curcumin, may provide further synergetic benefits

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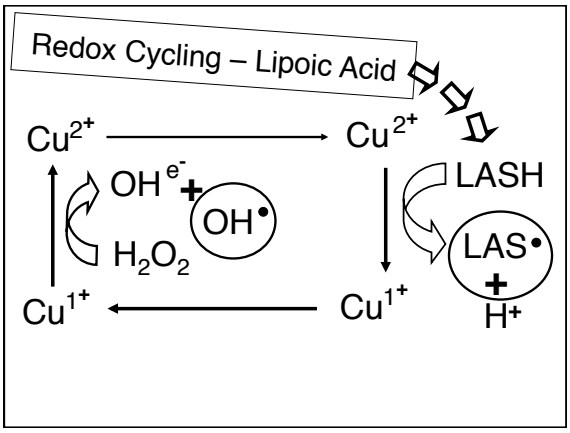
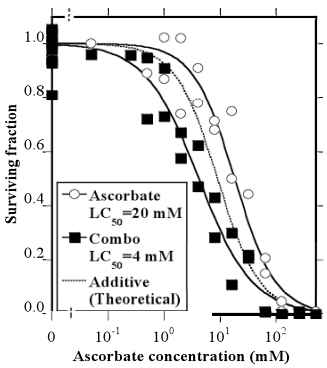
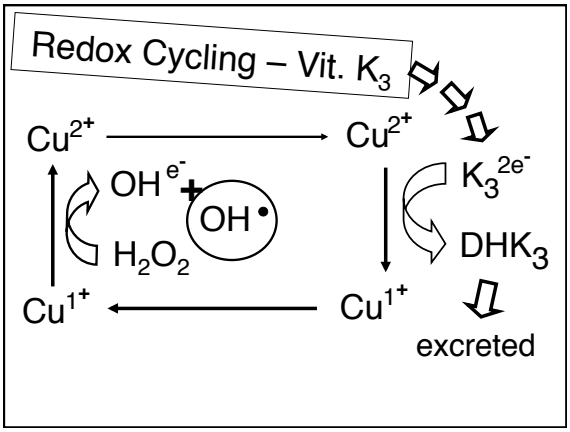



Adding alpha lipoic acid to the ascorbic acid in cell culture shifted the dose response curve to the left.




## Vitamin K3 for Cancer

- March, 2008 study by Summa Health Systems
  - ***Apatone**** granted orphan drug status by FDA
- A phase I/II study using ***Apatone*** at a dose of 5000 mg of vitamin C and 50 mg of vitamin K3
- 17 subjects with end stage prostate cancer who had failed local treatment
  - "two successive rises in PSA post treatment"
- Rise in PSA "velocity" decreased in 13/17
- 15 continued Apatone past 14 months – 1 death

*Also sold under the name "Prostay"

## Reasons to Consider an Oral Ortho-dosing Regimen for Cancer Patients

1. Unavailability of IVC or medical provider of IVC
2. Expense of IVC (especially over the long run)
3. Poor veins/no port-a-cath/oncologist resistance
4. Prevention of "IVC Resistance"
   maintains "oxidative pressure" between IVC infusions
5. Enhancement of Post-IVC serum C levels
6. Enhanced IVC effectiveness in high grade tumors
7. Long term maintenance strategy after successful IVC therapy and cancer remission

## Utilize the Riordan IV-C Protocol (*with the following addendums☺*)

- **Ultra low glycemic/high phytonutrient diet**
- Ortho-dosing Oral-C on the off-days from IV-C
- Ortho-dosing alpha lipoic acid (100 mg/gr of C)
- Ortho-dosing vitamin K3 (published doses)
- Ortho-dosing selenium (monitor for toxicity)
- Ortho-dosing vitamin D3 (monitor 25-OH-D)
- Ortho-dosing of select antioxidants
  (use published research and ortho-physician's guidance)

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## M.C. – Metastatic Breast Ca

- 61 y.o. WF
- Dx – stage II breast Ca
  - at age 47, 4-positive nodes
  - ER positive, PR negative
  - breast conserving surgery
  - BCT chemotherapy
  - tamoxifen for 5 years
  - letrozole started Nov '03
- Sept. '08 – pulm. nodules
  - probable recurrent metastatic breast cancer
- Thoracic CT on 9-18-08
  - Pleural nodules found
  - 3.6 x 2.8 cm L apical nodule
  - 2.1 x 1.8 cm L ant. seg. Nodule
  - L pleural effusion (small)
- PET scan 9-18-08
  - Confirmatory of above
- MRI 9-18-08
  - No other primary found

## M.C. – Appointments and Course

- Sept. 24, 2008 – Dr. GH
- Oct. 9, 2008 – Dr. RK
- Oct. 31, 2008 – Mayo's
- Nov. 19, 2008 – Dr. GH
- Jan. 2, 2009 – Dr. RH
- Jan. 15, 2009 – Mayo's
- Jan19 – Mar2'09 -Mexico
- Mar3 – Apr3 '09 – Colearner
- Apr. 3, 2009 – Dr. RH

- ➡ Intake H & P -The Center
- ➡ Reviewed lab workup "poorly differentiated"
- ➡ **'We have a situation that we cannot cure.'**
- ➡ **Increased IVC dosage to 75 gr 2 x/wk**
- ➡ Adrenal insufficiency – started **cortef & oral C redox – 24gr/d**
- ➡ **"Your tumors have tripled in size and are inoperable."**
- ➡ Daily IVC, IV-H2O2, IV-EDTA
- ➡ Liposomal antioxidants started **1 oz 3 x/d = 10 gr C + 1.2 gr GSH etc**
- ➡ added R lipoic acid – 300 mg TID

## Special Liposomal Formulation M.C. Added 1 oz TID to Regimen

**Supplement Facts**

**Serving Size:** 2 Tablespoons (1oz/29.6mL)
**Servings Per Container:** Approx. 32

| | Amount per serving | %DV |
|---|---|---|
| Calories | 54 | |
| Fat | 6g | 9%* |
| Vitamin C | 3,334mg | 5,557%* |
| Glutathione | 410mg | ** |
| Resveratrol | 120mg | ** |
| Curcumin | 120mg | ** |
| CoQ-10 | 110mg | ** |

*Daily Value (DV) Based on a 2,000 Calorie Diet
**Percent Daily Value Not Established

**Other Ingredients:** Purified Water, Phospholipids, Lecithin, Natural Flavors, Stevia.

## M.C. – Course of Vit. C Treatments

25 IVCs (75 gr. – 2x/wk)
- Oct 10, '08 to Jan 14, '09
- Jan19, '09 to Mar03, '09
  - Daily IVC, etc. in Mexico
- After Mar03, no further IVC due to loss of home nurse

Oral Redox (vitamin C)
- 8 grams 3x/d
- Dec 11, 2008 – to date
- **No bowel intolerance**

Add Liposomal Antioxidants
- Start – Mar 10, 2009 to date
- 1 oz 3x/d → total C = 28 **gr/d**

Post IVC levels
- 127 mg/dl – Oct 6, 08 (15gr.)
- 143 mg/dl – Oct 7, 08 (25gr.)
- 245 mg/dl – Oct 8, 08 (50gr.)
- 288 mg/dl – Oct 10, 08 (75gr.)
- 287 mg/dl – Nov 19, 08 (75gr.)
- 337 mg/dl – Jan 02, 09 (75gr.)

Plasma C levels
- 1.3 mg/dl – Sept 24, 08
- 1.4 mg/dl – Jan 02, 09
- 0.0 mg/dl – Apr 03, 09

## M.C.'s Current Clinical Status

- As of April 03, 2009
  - Stage 4 cancer "clear cell type"
    - vs. intraductal adenocarcinoma recurrence
  - No pain, normal appetite, maintaining normal weight, good color, optimistic, still very engaged!
- As of May 02, 2009
  - Recent CT scan results:

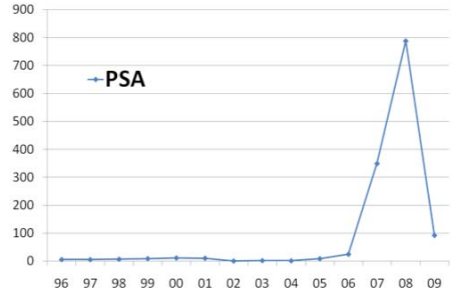
## R.F. – Metastatic Prostate Cancer

- 81 y.o. WM
- Dx – prostate Ca (in 1996)
  - at age 69
  - abnormal DRE
  - PSA – 4.1
  - biopsy –
    - adenocarcinoma
    - well differentiated
    - single focus
    - no Gleason score on path.
  - DVT (Feb '08)
- Bone scan (10-22-1998)
  - Negative
- Bone scan (07-02-2004)
  - Negative
- Pelvic CT (7-25-2007)
  - mets to R seminal vessel and sacrum
- Bone scan (8-01-2007)
  - 20 areas of radiotracer uptake, including spine, ribs, and large area of S1

# Oral vs. Intravenous Vitamin C

Ronald Hunninghake, MD

## R.F.'s Highest PSA Readings by Year




## R.F. – Treatments Through the Years

154 IVCs (30 gr.)
- Oct. 1996 -- Feb. 2000
- Post IVC –
  - 107 mg/dl – April 1998
  - 153 mg/dl – July 1998
  - 245 mg/dl – Feb. 2000

24 IVCs (50-75 gr.)
- Aug. to Nov. 2007
- Post IVC –
  - 201 mg/dl – Aug 13, 2007
  - 258 mg/dl – Aug 30, 2007
  - 349 mg/dl – Oct 2007 (75gr)

Radiation

Lupron/Casadex (14 months)

Beta Glucan and PC SPES (temp.)

Testosterone Troche 16 mg (Jun'05…)

Poly MVA & Zeolite (Mar'07–Jul'07)

Prostay – C:$K_3$ 100:1 ratio
**14,000mg :140mg** (Aug '07…)

PC Hope 2-3/d (Feb '08…)

$D_3$ - 6000 IU
25(OH)D level → 60 ng/dl in Jan'09

## R.F.'s Clinical Status

- Continues to eat a very low glycemic diet
- Appetite is good (wt. recently up 2 lbs.)
- No pain, sleeps well
- Normal skin color
- With recent addition of 6 gr. vitamin C powder, oral C is up the 18 grams a day, no diarrhea
- May 2nd update:

## Take Home Messages

- We can change cancer from a terminal disease to a chronic illness, to an "ortho-remission"
- The allopathic use of IVC is a crucial component of successful cancer therapy… "as an adjunctive Rx"
- The ortho-pathic use of IVC ***with synergistic*** ortho-dosing of oral adjunctive nutrients
  - engages the patient as a colearner
  - empowers the colearner to make and sustain dietary, and lifestyle changes to heal/control cancer
  - provides a scientifically proven biological, redox, and antiangiogenic basis for **orthomolecular** oncologic care

## Parting Thoughts

Never go to a doctor whose office plants have died.

**- Erma Bombeck**

An orgasm a day keeps the doctor away.

**- Mae West**