Research Support for High-Potency Multiple Vitamin and Mineral Supplements

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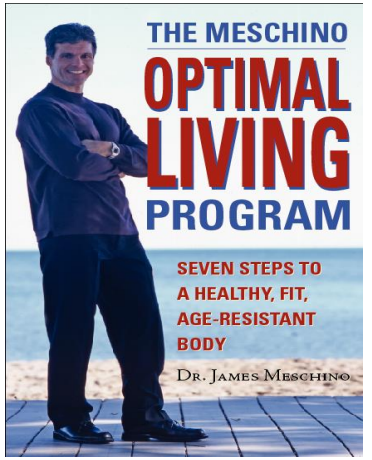


Introduction

Media sometimes reports studies showing no benefit to taking a daily multiple vitamin supplement, but these studies typically look at people taking standard, **drug store-type vitamins, which contain low-doses of antioxidants, vitamin D, calcium, selenium and B-vitamins**.

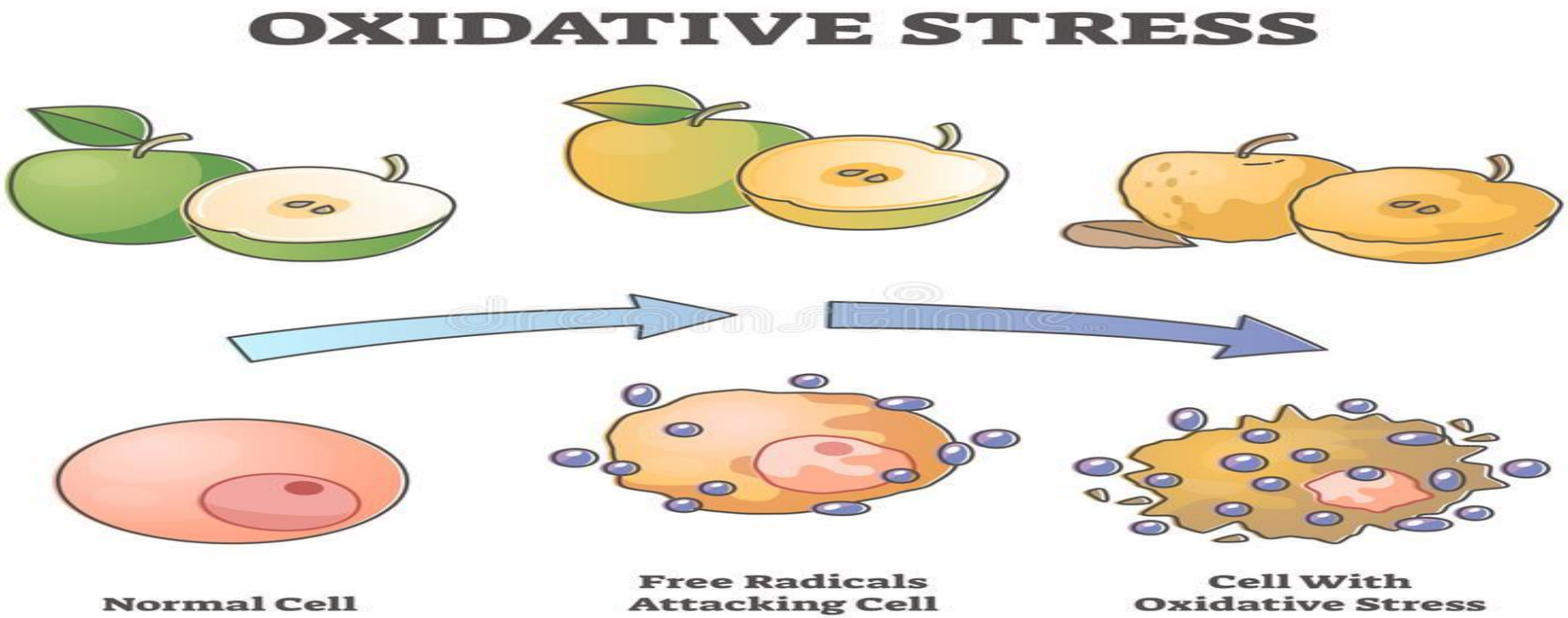
However, the research does support vitamin and mineral supplementation when **meaningful doses** are ingested daily.

This presentation includes peer-reviewed, clinical studies showing the importance of ingesting meaningful doses of key vitamins and minerals via supplementation

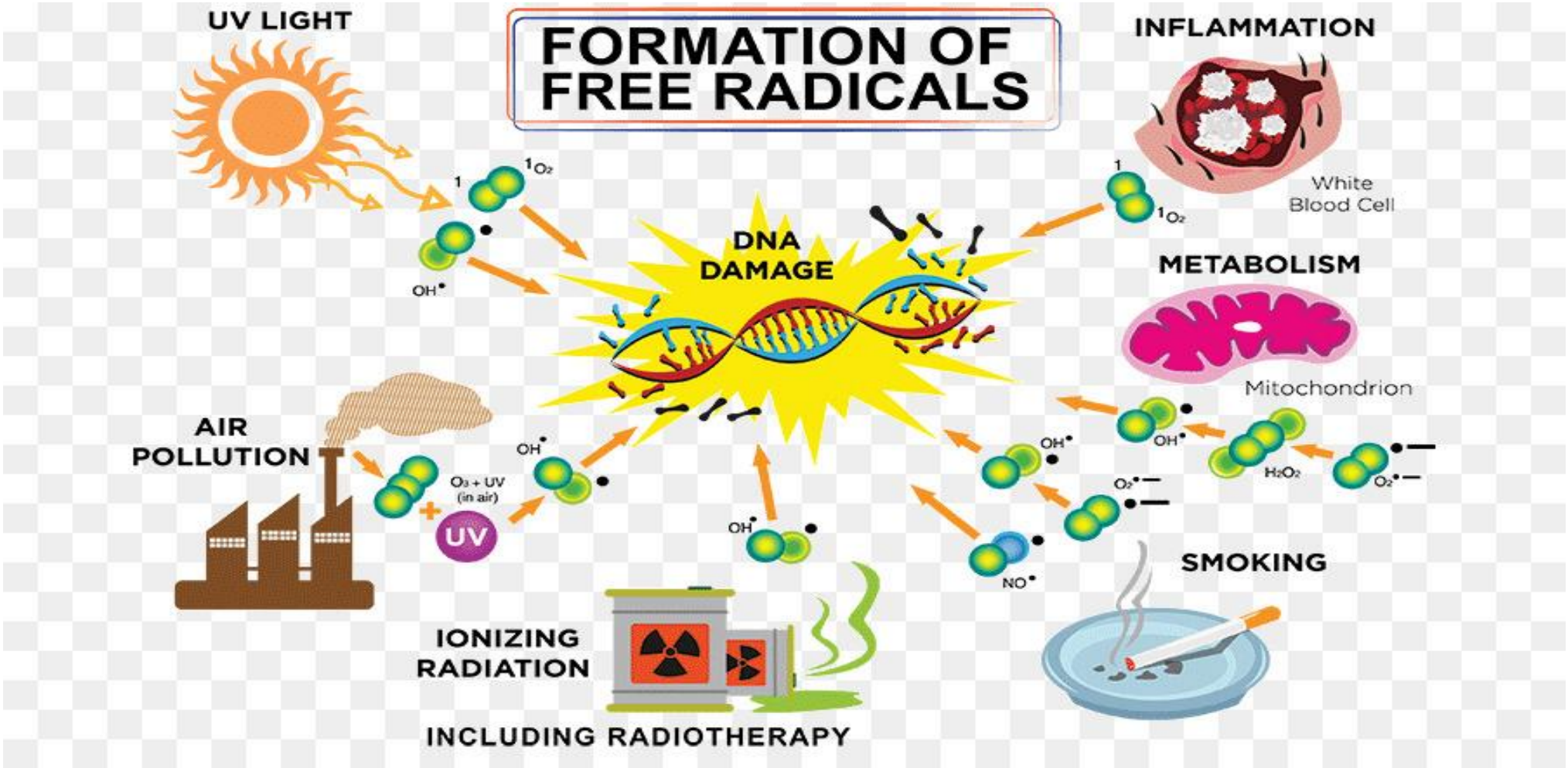
Human Clinical Studies Support Use of a High Potency Multiple Vitamin and Mineral in Applications Related to:

1. Slowing Aging from Free Radical Damage
2. Alzheimer's disease and Parkinson's disease
3. Macular Degeneration – the leading cause of blindness in 55 yr –plus
4. Prevention and Slowing of Cataracts
5. Slowing Age-related Hearing Loss and Reversing Some Genetic Hearing Loss
6. Help Optimize Immunity and Decrease Risk of Serious Infections
7. Improve Recovery From Many Infections (e.g., pneumonia, Covid-19)
8. Decreased Recurrence of Breast Cancer
9. Slowing Age-related Brain Atrophy (Shrinkage) and Memory Loss
10. Adjunct to Mental Health Treatment (e.g., depression, and depression in elderly)
11. Osteoporosis Prevention 1:4 women;1:8 men over 50
12. Child's IQ Dependent on Maternal Stores of Certain Nutrients
13. Wound Healing and Prevention of Age-related Loss of Taste Acuity
14. Night Vision (dark adaptation)
15. Blood Sugar Regulation

1. Free Radical Damage: The same way an apple rots when exposed to oxygen, so do our tissues as we use oxygen to generate energy in our cells (Aging, Cancer, Cataracts, Other).



1. **Free Radicals**: From Oxygen Metabolism and Other Environmental Sources

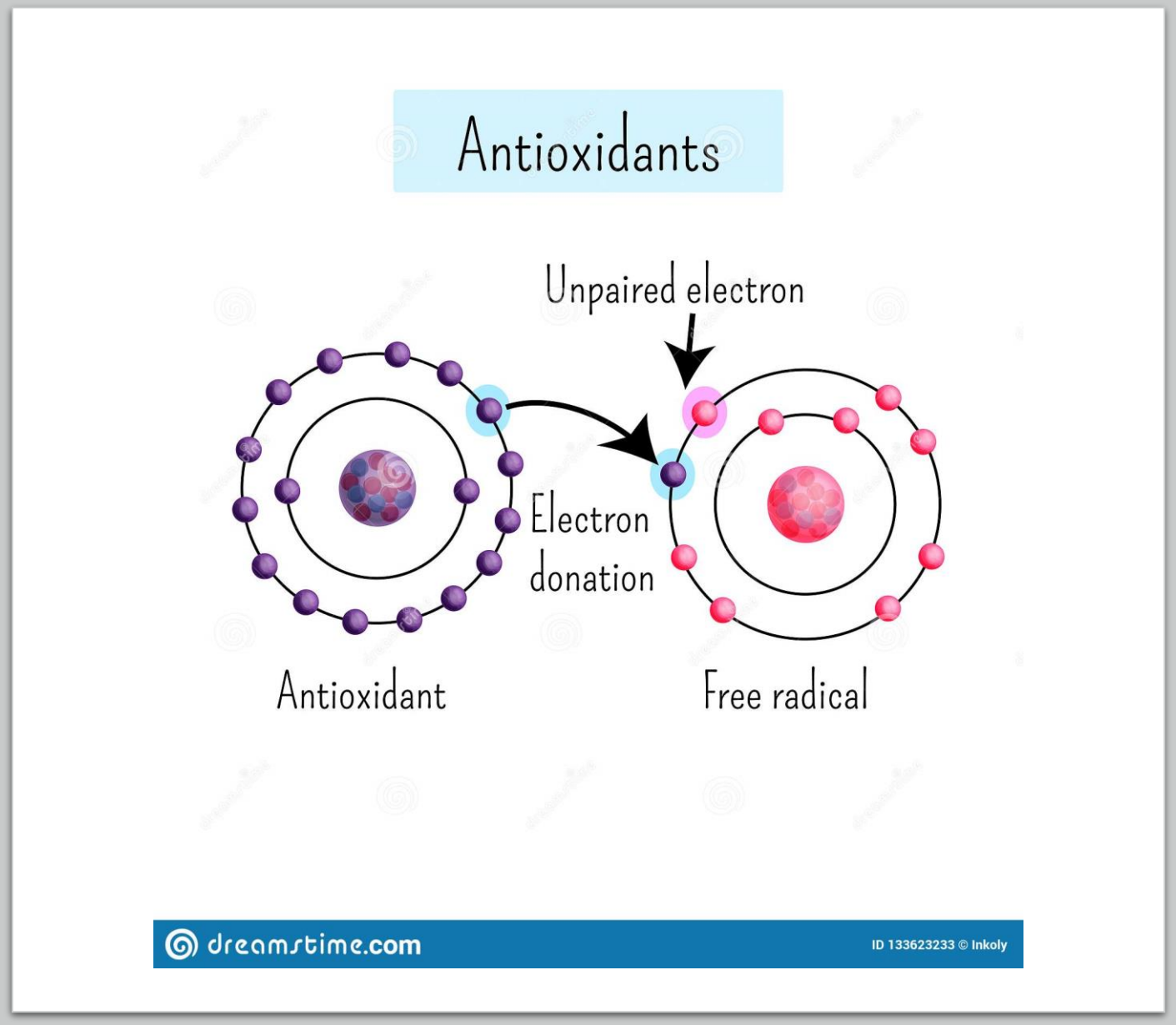


Antioxidants Can Quench Free Radicals:

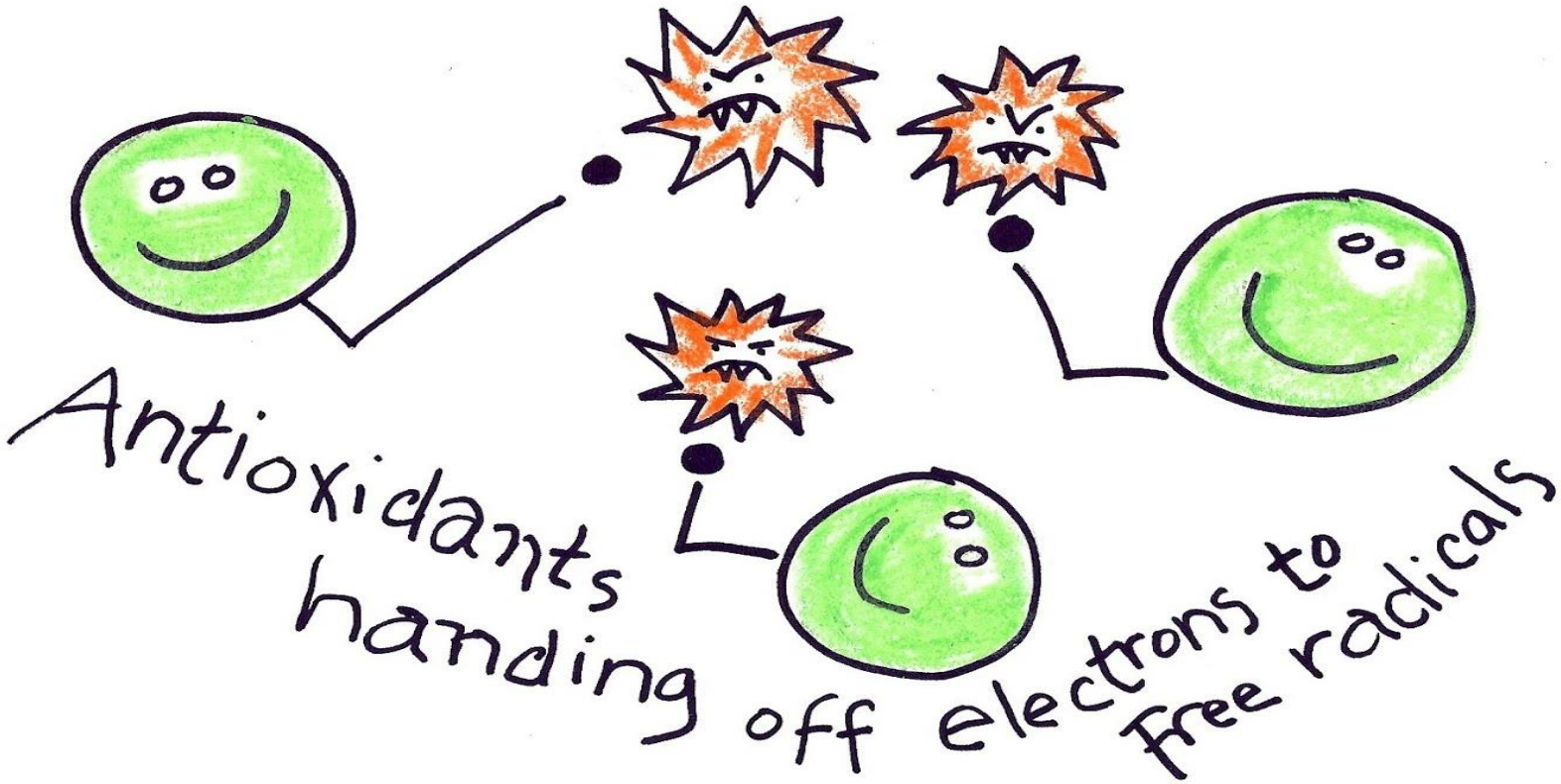
The body makes some antioxidants to protect itself:

- SOD
- Catalase
- Glutathione Peroxidase
- Melatonin etc.

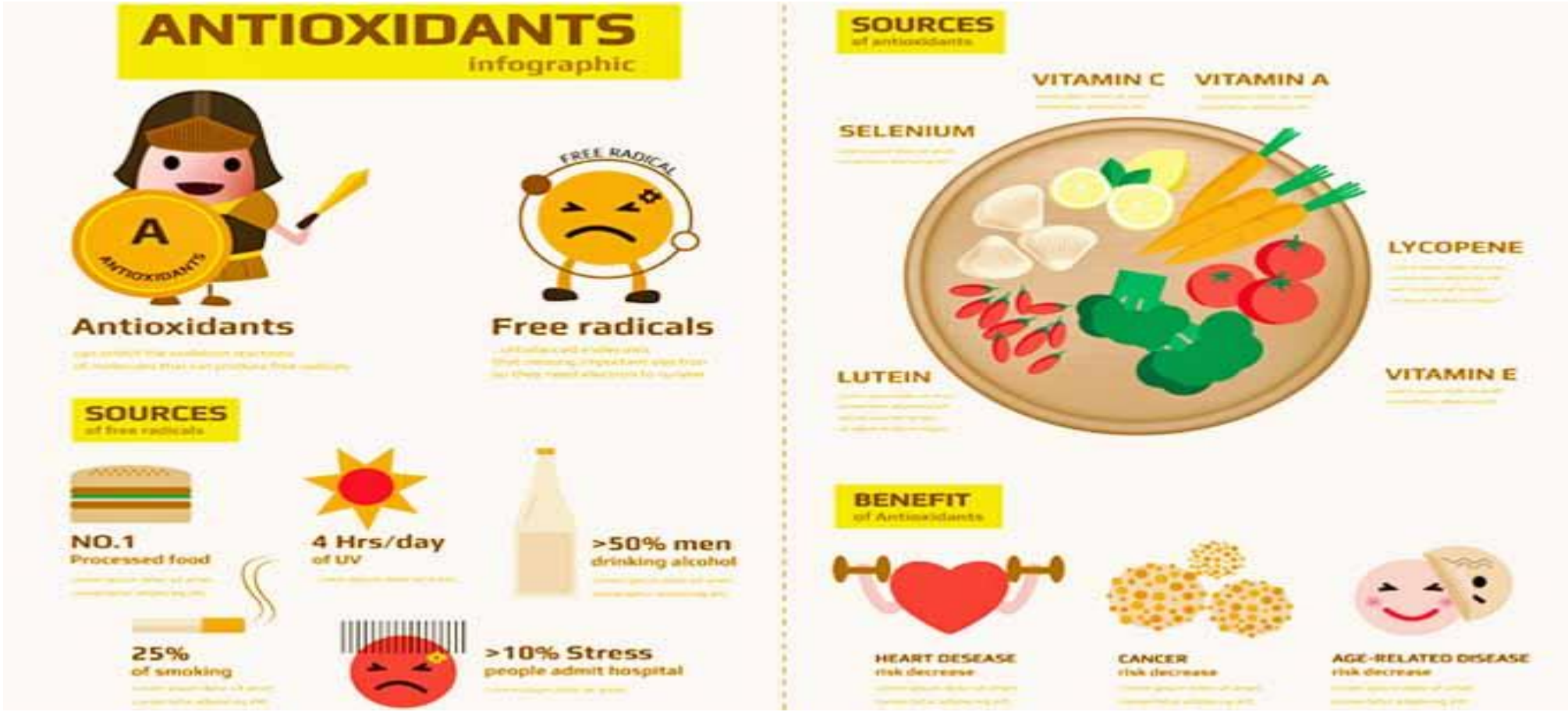
But body also relies on nutritional antioxidants (food and supplements)for more complete protection against oxygen and other free radical sources



Antioxidants Quench and Stabilize Free Radicals, Minimizing Their Damage to the Body



Antioxidants from Food and Supplements: Vits: C,E,A, Selenium, Lycopene, Lutein etc.



Foods with Antioxidants

But Supplements have shown great benefit as well in recent years.

Other Common Sources of Free Radicals Besides Oxygen:

1. Polycyclic Aromatic Hydrocarbons (BBQ smoke, smoked meats & fish)
2. Heterocyclic Amines (charred foods)
3. Nitrosamines (luncheon and deli meats, pepperoni, beef jerky etc.)
4. Alcohol (all sources)- 5-7% of all cancers
5. Cigarette Smoke (30% of all cancer deaths per year)
6. Air Pollution (ozone and sulfur dioxide, sulfur trioxide, hydrazines)
7. Radiation – sun, tanning beds, X-Rays, CT scan

Free Radicals Damage Many Tissues and Organ:

- DNA – mutations - aging and cancer
- Mitochondria – decreased cellular energy
- Enzymes – compromised function
- Cell membrane (outer skin of the cell)
- LDL –cholesterol – increasing heart disease
- Eyes – cataracts and macular degeneration
- Brain – dementia and neurodegenerative dis
- Skin – wrinkles, cancer

Antioxidant Supplementation Studies of Importance

Vitamin E and Alzheimer's disease

Alzheimer's Cooperative Study (2000) - providing early-stage Alzheimer's patients with 2000 IU per day of Vitamin E supplementation **significantly slowed progression of disease compared to placebo group.**

- Vitamin E group did not show increased incidence of heart disease, cancer or any other major disease state.

- Remember: 20% oxygen used by brain – ROS

Grundman M. Vitamin E and Alzheimer disease: the basis for additional clinical trials. Am J Clin Nutr. 2000, 71 (2): 630S-636S.
https://academic.oup.com/ajcn/article/71/2/630S/4729332

Vitamin E and Alzheimer's disease (Study No 2)

Alzheimer's Study (2009) – Vitamin E Supplementation Benefits Alzheimer's Patients

Study Design: 847 Patients with Alzheimer's disease supplemented with **vitamin E (1000 IU, twice/day)**

- ½ Patients in treatment group received Vit E and Alzheimer's Drug
- ½ Patients in treatment group Received only Vit E supp
- Control Group – Received no Vit E or Drug

Results:

- **Vitamin E** on its own **reduced mortality by 23%** compared to patients receiving no therapy

- The **Alzheimer's drug** taken on its own **slightly increased mortality** compared to patients receiving no treatment

- **Vitamin E and Alzheimer's drug** together showed the best overall results (**about 30% reduction in mortality** and improved overall function)

Pavlik VN et al. Vitamin E Use Is Associated with Improved Survival in an Alzheimer's Disease Cohort Dementia and Geriatric Cognitive Disorders 2009, Vol. 28, No. 6: 536-540 https://www.karger.com/Article/Abstract/255105

Antioxidants & Macular Degeneration – leading cause of blindness in those over 55 yr.

Age-Related Eye Disease Study Research Group **(AREDS Study- 2001):**

High Potency Multiple Vitamin and Mineral – A very large double-blind, placebo-controlled trial evaluated the effects of zinc with or without antioxidants on macular degeneration in **3,640 individuals in the early-stage macular degeneration**.

Participants with **best results** were given antioxidants (vitamin C 500 mg, vitamin E 400 IU, and beta-carotene 25,000 IU), zinc (80 mg) and copper (2 mg). **The results indicate that zinc plus antioxidants, significantly slowed the progression of the disease.**

Jampol, L.M., et al. Age-Related Eye Disease Study Research Group (collective name-AREDS**).** A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta-carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no.8. Arch Ophthalmol 2001 Oct; 119 (10): 1417-36)

Antioxidants and Cataracts:

- **Higher blood levels & intake levels** of **Vitamin C, Vitamin E, selenium** associated with **decreased cataract development.**

- One study showed that adults who used **vitamin C and E supplements for more than 10 years decreased the progression of nuclear cataracts.**

American Optometric Association: Diet and Nutrition: https://www.aoa.org/patients-and-public/caring-for-your-vision/nutrition/nutrition-and-cataracts

Antioxidants and Parkinson's Disease:

Antioxidants (Vitamin E and Vitamin C) – free radicals contribute to the progression and, possibly, the cause of Parkinson's disease and other neurodegenerative diseases

- 10-year study of early-stage Parkinson's disease patients given 750 mg of Vitamin C and 800 IU of Vitamin E four times/d (totaling 3,000 mg of Vitamin C and 3,200 IU of Vitamin E per day).

Results – Antioxidant supplementation **significantly delay the need for drug therapy by average of two and half years, compared to placebo group**

Zhao X et al. Benefits of vitamins in the treatment of Parkinson's disease. Oxidative Medicine and Cellular Longevity. 2019. https://www.hindawi.com/journals/omcl/2019/9426867/

Prevention of Parkinson’s Disease with Antioxidants (vitamin C and vitamin E)

Supplementation with Vitamin C and Vitamin E associated with decreased risk of developing Parkinson’s disease, which affects 1:500 Canadians in their lifetime.

References:

https://www.hindawi.com/journals/omcl/2019/9426867/

https://www.researchgate.net/publication/331237523_Benefits_of_Vitamins_in_the_Treatment_of_Parkinson's_Disease

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6399121/

https://www.e-jmd.org/journal/view.php?number=285

Vitamin C: More than Just an Antioxidant (Immunity)

Studies indicate that sub-optimal vitamin C levels (hypovitaminosis C identified as a plasma vitamin C less than 23 umol/L) is relatively common in Western populations, and vitamin C deficiency (less than 11 umol/L) is the fourth leading nutrient deficiency in the U.S.

The 2007-2010 U.S. National Health and Nutrition Examination Survey of approximately **16,000 children and adults found that almost 40% had low levels of vitamin C, while 88% of the U.S. population did not meet the daily requirement for vitamin E (noted to enhance the effects of vitamin C).**

https://www.medpagetoday.com/casestudies/infectiousdisease/87976

Ingestion of 250 mg per day of vitamin C in otherwise healthy people helps to enhance many important aspects of immune function.

The goal is to achieve a vitamin C blood level above **50 umol/L**, which most healthy people can achieve with a daily intake of **100-250 mg of vitamin C per day. (difficult to do from food alone)**

As we get older and immune function declines, some studies suggest that the combination of 1,000 mg vitamin C per day and 200 IU of vitamin E per day improves immune function in people over 60. So higher doses are required as we age.

Studies also show that when **fighting the common cold supplementation with 200 mg per day of vitamin C can help reduce severity and duration**, and the incidence of the common cold if we are also exposed to physical stress.

This level of vitamin C intake may also reduce common cold frequency in those who previously had lower vitamin C blood levels (below 45 umol/L).

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5707683/

- Very importantly, higher levels of intake **(1,000 mg vitamin C per day)** has been shown to **prevent the decline in vitamin C depletion within white blood cells during an infection**.

- Quote from research paper regarding lung infections, pneumonia and vitamin C, “Beneficial effects of vitamin C on recovery have been noted in pneumonia.

- I**n elderly people hospitalized because of pneumonia, who were determined to have very low vitamin C levels, administration of vitamin C reduced the respiratory symptom score in the more severe patients”.**

In other **pneumonia patients**, low-dose vitamin C (**250 – 800 mg/day**) **reduced the hospital stay by 19%** compared with no vitamin C supplementation, whereas the higher-dose group (**500 – 1600 mg/day**) reduced the duration (hospital stay) by **36%.**

Vitamin C supplementation also showed a positive effect on the normalization of chest X-ray, temperature, and erythrocyte sedimentation rate".

2017 Review: Vitamin C and Immune Function https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5707683/

Vitamin E Succinate in Cancer Prevention and Treatment

"The most studied member of these compounds is **RRR-α-tocopheryl succinate** (α-TOS), which has been shown to **induce apoptosis (cell death) in a variety of cancer cell lines**

Studies have demonstrated that α-TOS is a potent growth inhibitor of a wide variety of epithelial cancer cell types including **prostate, breast, lung, colon, cervical and endometrial as well as hematopoietic-lymphoid leukemia, lymphoma and melanoma cells *invitro*.**

In fact, at **least 50 types of cancer cell lines** tested so far have shown a high level of apoptosis (cell death) when challenged with α-TOS except for the osteosarcoma cell line MG63, in which α-TOS causes cell cycle block rather than apoptosis.

Interestingly, α-TOS was shown to have promising anticancer activity against the fatal malignant mesothelioma (when tested experimentally in immunocompromised mice) and the hard-to-treat HER2-positive breast cancer". (1)

“Studies showed that α-TOS targets complex II of the respiratory chain to displace ubiquinone binding. **(Disrupts Energy Factory of Cancer Cells leading to their Death)**

It is therefore possible that disrupting the electron flow of mitochondrial complex II results in generation of ROS in the form of superoxide, triggering **mitochondrial destabilization and initiation of apoptotic pathways**”. (1)

References

1. Papas A et al. Vitamin E and cancer: An insight into the anticancer activities of the vitamin E isomers and analogs. International Journal of Cancer. June 2008, https://onlinelibrary.wiley.com/doi/10.1002/ijc.23689

2. Weber T et al. Vitamin E succinate is a potent novel antineoplastic agent with high selectivity and cooperativity with tumor necrosis factor-related apoptosis-induced ligand (Apo2 Ligand) in vivo. Clinical Cancer Research. March 2002.

3. https://clincancerres.aacrjournals.org/content/8/3/863

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0119549

4.British Journal of Cancer 2003: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2394445/

Human Mesothelioma Case Study

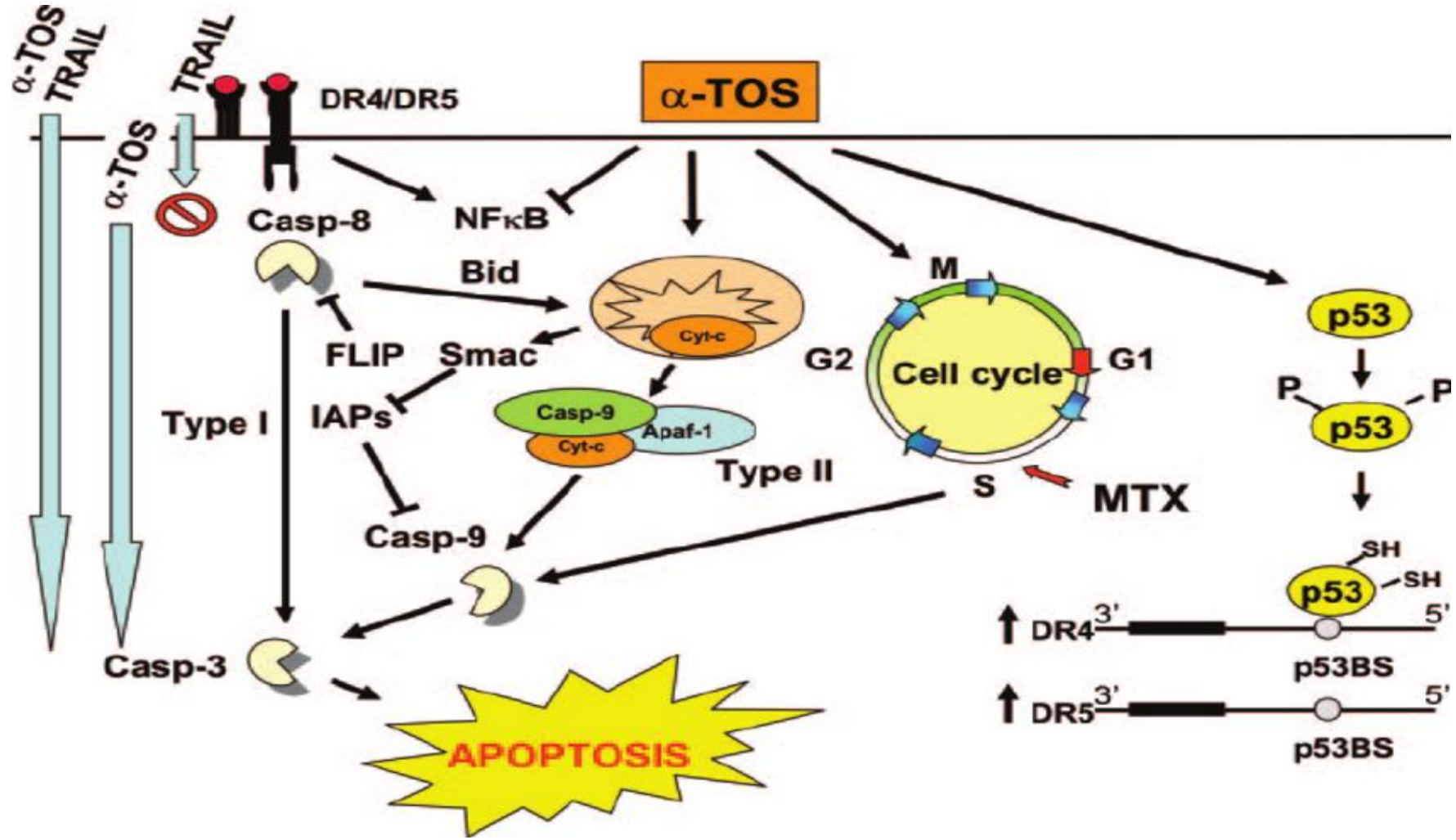
- The data revealed a significant clinical benefit with α-TOS therapy, causing a **reduction in tumor volume and improved the well-being of our subject who had a lethal type of neoplastic pathology** (Robinson *et al.*, 2005).

- We are currently preparing to set up a larger clinical trial in which a cohort of mesothelioma patients will be treated with the mitocan, α-TOS

Dong Lan-Feng et al. Alpha-tocopheryl succinate induces apoptosis by targeting ubiquinone-binding sites in mitochondria respiratory complex II. Oncogene. 2008; 27(31):4324-4335. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2668987/

Vitamin E Succinate (alpha-TOS) and Apoptosis Cell Suicide of Cancer Cells Only

https://www.researchgate.net/figure/Possible-pathways-of-TOS-sensitized-apoptosis-Immunological-ligands-induce-apoptosis_fig2_29466222



Multiple Vitamin and Antioxidant Supplements Reduce Breast Cancer Recurrence

Breast Cancer Research and Therapy (Nov. 2011): Kwan ML, Greenlee H, Lee VS, Castillo EP, Gunderson EP, Habel LA, et al. Multivitamin Use and Breast Cancer Outcomes in Women with Early-Stage Breast Cancer: The Life After Cancer Epidemiology (LACE) Study. Breast Cancer Res Treat. 2011 Nov; 130(1): 195–205.

Study followed women treated for breast cancer looking at their **survival and relapse rates during the 2-yr follow-up period after breast cancer treatment**. Researchers wanted to know if taking a **multiple vitamin supplement had any effect on survival or relapse rates.**

Results: Women in the top 25% of following a healthy lifestyle, who regularly took a multiple vitamin supplement, had a **60-70% reduction in risk of dying from any cause during the study**

A healthy lifestyle was defined as a healthy diet (consuming at least 5.5 servings of fruits and vegetables per day) and being at least moderately physically active (being non-sedentary for 16 hours/week). **For these women, a multiple vitamin and mineral supplement further reduced their risk of dying by 60-70% compared to non-vitamin users.**

2012 J Cancer: Life After Breast Cancer Epidemiology Study:

Greenlee H et al. Antioxidant supplement use after breast cancer diagnosis and mortality in the LACE cohort. Cancer, 2012; 118(8):2048-2058
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3323673/

Study examined antioxidant use after breast cancer (BC) diagnosis and BC outcomes in 2,264 women in the Life After Cancer Epidemiology (LACE) cohort.

Women primarily recruited from the Kaiser Permanente Northern California (KPNC) (83%) and the Utah (12%) cancer registries who were diagnosed with early-stage primary breast cancer between 1997 and 2000

Results: With average 5-yr follow up - Frequent use of vitamin C and vitamin E in the period following BC diagnosis was associated with decreased likelihood of recurrence. "We also observed that frequent use of vitamins C and E after diagnosis was associated with reduced risk of all cause mortality, death from breast cancer, and breast cancer recurrence."

2011 Shanghai Breast Cancer Survival Study (SBCSS):

A Shanghai China study followed **4,877 breast cancer** survivors **and examined antioxidant supplement use (vitamin C, vitamin E, and/or multivitamins**)

Results – with average 4-yr follow - Women who used antioxidants **(vitamin E, vitamin C, multivitamins) had 18% reduced mortality risk and 22% reduced recurrence risk.** The inverse association was found regardless of whether vitamin use was concurrent or nonconcurrent with chemotherapy, but was present only among patients who did not receive radiotherapy.

"Our results do not support the current recommendation that breast cancer patients should avoid use of vitamin supplements."

Nechuta S et a. Vitamin supplement use during breast cancer treatment and survival: A prospective cohort study. *Cancer Epidemiol Biomarkers Prev; 2011; 20(2); 262–71.*
https://cebp.aacrjournals.org/content/20/2/262

Free Radicals, Antioxidant Supplements in **Age-Related Hearing Loss** (ARHL)

- "The research to date suggests that oxidative stress **(free radicals)** and mitochondrial DNA deletion (mtDNA) play a major role in pathophysiology of ARHL. Therefore, similar to other otological conditions, several studies have also showed **that antioxidants can slow ARHL**. https://pubmed.ncbi.nlm.nih.gov/27858145/

- **Animal Studies:** Dietary supplements consisting of beta-carotene (precursor to vitamin A), vitamins C and E and the mineral magnesium (ACEMg) can be beneficial for reducing hearing loss due to aminoglycosides and overstimulation https://pubmed.ncbi.nlm.nih.gov/24439969/

- **Human Trials:** Human trials have shown that antioxidant supplements mitigate hearing loss from chemotherapy drugs, aging, tinnitus, noise-damage and other free radical causes of hearing loss

Reference: 2008 Review: https://www.hearingreview.com/hearing-loss/hearing-disorders/the-case-for-using-multiple-antioxidants-in-hearing-disorders

Even Genetic Hearing Loss Connexin 26

"**Mutations** in the gene encoding **Connexin 26** are the **most common cause of genetic hearing loss.** The hearing loss is typically stable but may be progressive. The reason for progression is unknown.

Antioxidants have been associated with attenuation of hearing loss from other insults. One antioxidant regimen consists of **beta-carotene (metabolized to vitamin A), vitamin C, vitamin E, and magnesium (ACEMg).**

We present a **child with Connexin 26** related hearing loss who experienced progressive hearing loss over **7 years of observation.**

He was given **ACEMg daily for 3 years**, during which time his **progressive hearing loss was ameliorated."**

Int J Pediatr Otorhinolaryngol 2014 https://pubmed.ncbi.nlm.nih.gov/24439969/

B-Vitamins And The Brain

Slow Brain Aging, Atrophy and Cognitive Decline:

Oxford Project to Investigate Memory and Ageing (OPTIMA) and B Vitamin Research Group
Chief Researcher: D Smith et al – Oxford University England

Study Group - 168 individuals over 70 y old with mild cognitive impairment (MCI)

Treatment: Supplementation with B- vitamins:

- folic acid - 800 mcg
- vitamin B12 - 500 mcg and
- vitamin B6 - 20 mg/d

vs Placebo

Main outcome measured - change in rate of whole brain atrophy (shrinkage) on MRI

Results:

1. On **average,** B vitamins slowed rate of brain atrophy by **30 percent.**

2. In some cases, reductions as high as **53 % were seen**

3. A **greater rate of atrophy** was associated with **lower cognitive test scores.**

Rate of Brain Atrophy After 60 yrs

- People over 60 yrs **without** MCI normally have brain shrinkage **0.5 %** a year.
- Normally **twice** as fast in people with **MCI (1%)**
- **Alzheimer's** can lose **2.5 %** brain volume each year

Why B- vitamins (researcher's comments):

1. FA, B6 & B12 – prevent rise in Homocysteine (HCY) - damages brain and blood vessels.

2. **Higher HCY** – related to accelerated brain atrophy in many studies

3. B- vitamins **– Also Increase Neurotransmitter synthesis** (Dopamine, Epinephrine, Norepinephrine, Serotonin, Melatonin)

Thus far, **only B-vitamin Supplementation** has been shown to **slow brain atrophy** in aging persons.

Presently **no drugs** or lifestyle measures have been shown to do this

B-vitamin supplementation is most effective in those with **homocysteine level above 11 umol/L (1/3 of population**) and that the addition of **omega-3 fats** was recently shown to potentiate the improvement of cognitive function in patients receiving B-vitamin supplementation

References:

The Lancet 2016: https://www.thelancet.com/pdfs/journals/laneur/PIIS1474-4422(16)30074-6.pdf

Department of Pharmacology Medical Sciences Division https://www.pharm.ox.ac.uk/research/smith-group-oxford-project-to-investigate-memory-and-ageing-optima-and-b-vitamin-research-group

Niacin (B3): Preserves Brain, Tau Protein

- Niacin (NAD) required **for ATP energy** in nerve and brain cells – oxidative phosphorylation
- Niacin also required to preserve **integrity of tau protein** in microtubular structures within nerve and brain cells. Degradation of microtubular structures leads to neurofibrillary tangles of tau protein in final stages of Alzheimer's disease

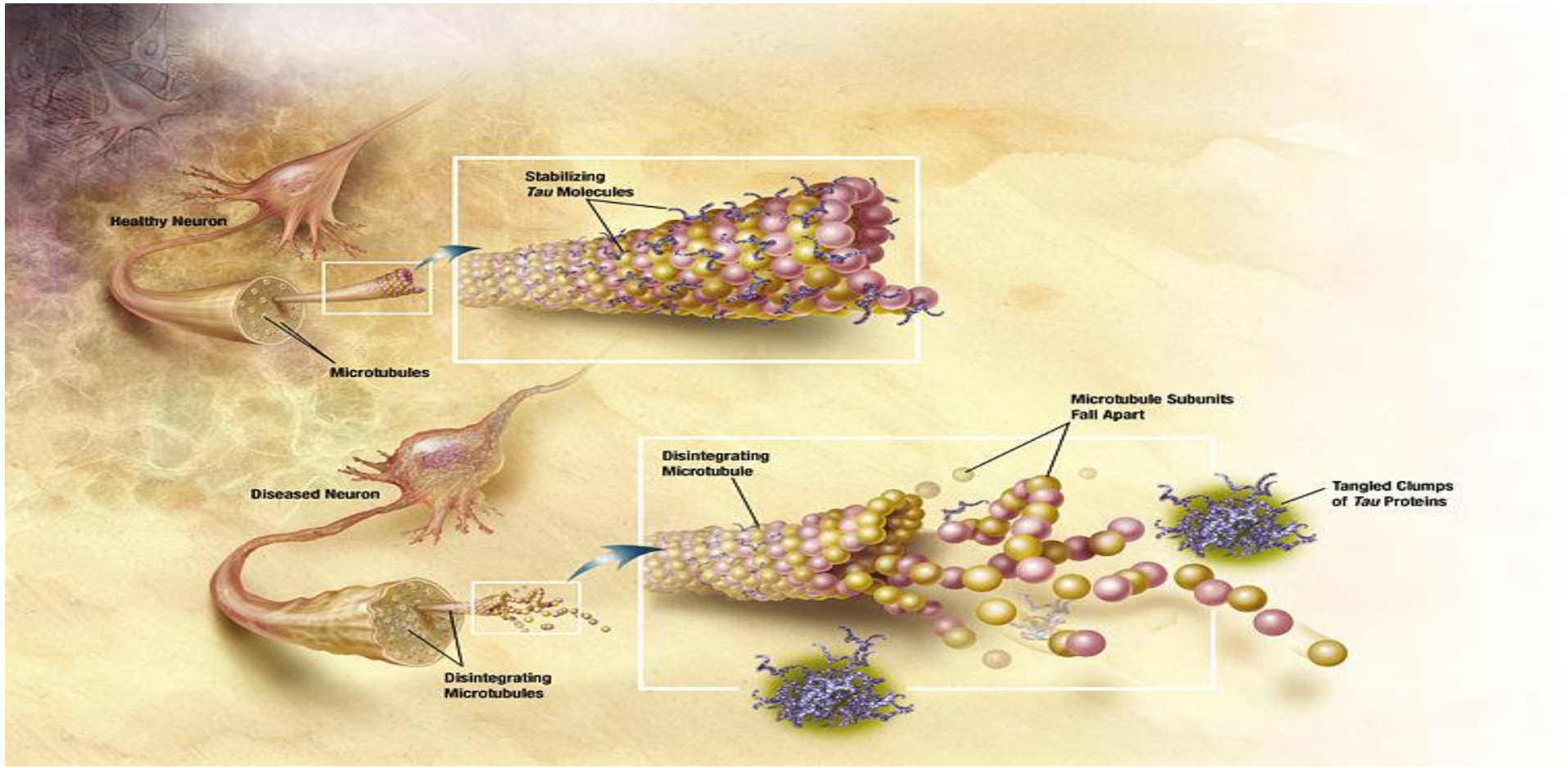
Epidemiological studies: Niacin Supplementation Reduces Alzheimer's disease:

- **Rush Institute for Health Aging in Chicago**, and colleagues **studied 3,718 65-and-older** residents of three south Chicago neighborhoods for more than five-and-a-half years. They also **performed clinical tests on 815** of these people over four years.

- **They found that those who got the least niacin were 70% more likely to develop Alzheimer's disease than those who got higher amounts (45 mg)**

Benefits of higher niacin intake began in men and women at a median intake of 17 mg per day. Those at the study's highest niacin level were getting 45 mg per day from diet and supplements.

WebMD http://www.webmd.com/food-recipes/news/20040714/niacin-in-diet-may-prevent-alzheimers



Niacin and Tau Protein Continued

Animal Studies And Niacin

- **Animal studies show niacin supplementation reduces neurofibrillary tangle development in simulated Alzheimer’s disease experiments**

- **Nicotinamide led an increase in tau proteins that strengthen microtubules**

- Nicotinamide slightly enhanced cognitive abilities in normal mice. "This suggests that not only is it good for Alzheimer's disease, but **if normal people take it, some aspects of their memory might improve**," said LaFerla, UCI neurobiology and behavior professor.

  Scientists also found that the **nicotinamide-treated animals had dramatically lower levels of the tau protein** that leads to the Alzheimer's tangle lesion.

- **Human Equivalent Dosage**: 1000 mg, three times daily (monitor liver enzymes as with nicotinic acid used to lower triglycerides and cholesterol)

- Also – Nicotinamide has fewer side effects than nicotinic acid (flushing etc.)

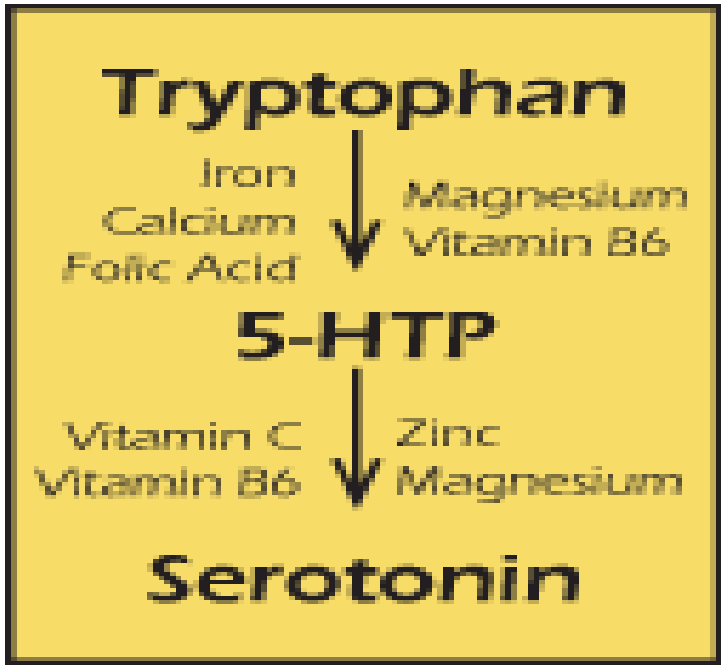
References:

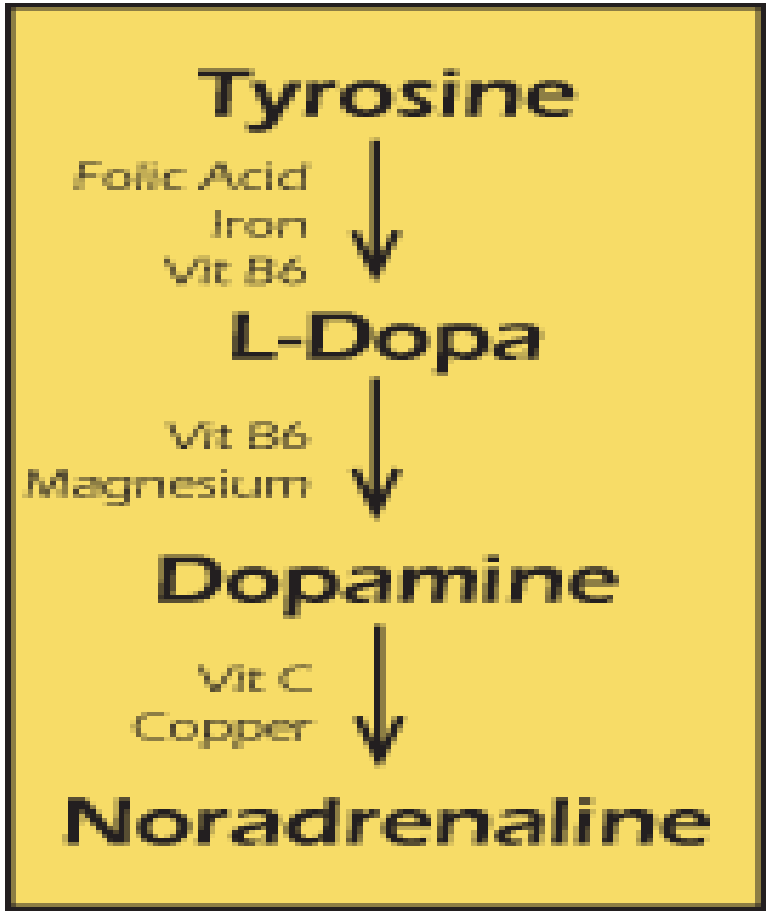
Sciencedaily 2008: https://www.sciencedaily.com/releases/2008/11/081104180926.htm

http://bvftd.blogspot.ca/2011/05/niacin-vitamin-b3-and-dementia.html (2011 update)

My Personal Perspective – supplementing with **50 mg**/d of niacin associated with decreased risk of Alzheimer's disease. Other strategies are also important.

Vits and Mins in Depression: Folic acid, Vitamin B12, B6, magnesium often deficient in mental health problems





Folic Acid Supplementation Studies

- **Folate deficiency strongly linked to depression and cognitive decline**,

as well as lack of motivation and social withdrawal which are folate-responsive symptoms.

- **Depression patients with low folate levels show poor response to anti-depressant drugs.**

- **Studies using folic acid supplementation alone, or in conjunction with psychotropic drugs (for one year) have shown good results with mood, cognitive function, and social recovery.**

- **Even in patients with normal blood folic acid levels, adding folic acid to drug treatment is recommended:**

Reference: Canadian Family Physician Journal 2011 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3173416/

Vitamin B12 and Mental Health

- Psychiatric Symptoms - Mood, behavioural changes, psychosis, memory impairment, and cognitive decline can result from low folate and/or vitamin B12.

- **Up to 1/3 of psychiatric patients, and especially psychogeriatric admissions have low serum or RBC folate, mostly without anemia or macrocytosis.**

- **About 5% have low vitamin B12, but for elderly patients – 10-20% show low vitamin B12 levels.**

- Low vitamin B12 linked primarily to cognitive decline.

Reference: http://www.direct-ms.org/sites/default/files/B12%20folic%20acid%20nervous%20system.pdf

B12 Deficiency Common In Aging: Why?

1. Decreased Stomach Acid
2. Decreased Intrinsic Factor
3. Increased use of Antacids, H2 blockers and Proton Pump Inhibitors
4. Decreased food intake

B12 storage in liver contains 1-3 year supply

Report New York Times 2011

Subject: Old Age and Vitamin B-12

New York Times Personal Health

- **It Could Be Old Age, or It Could Be Low B12**
- By JANE E. BRODY Published: November 28, 2011

(Excerpt)

- Ilsa Katz was 85 when her daughter, Vivian Atkins, first noticed that her mother was becoming increasingly confused.

- A workup at a memory clinic resulted in a diagnosis of early Alzheimer's disease, and Ms. Katz was prescribed Aricept, which Ms. Atkins said seemed to make matters worse. But the clinic also tested Ms. Katz's blood level of vitamin B12. It was well below normal, and her doctor thought that could be contributing to her symptoms.

- **Weekly B12 injections were begun**. "Soon afterward, she became less agitated, less confused and her memory was much better," said Ms. Atkins. "I felt I had my mother back, and she feels a lot better, too."
- http://www.nytimes.com/2011/11/29/health/vitamin-b12-deficiency-can-cause-symptoms-that-mimic-aging.html?ref=health

2005 Review J. Psychopharmacology

Abstract

- **Both low folate and low vitamin B12 status have been found in studies of depressive patients**, and an association between depression and low levels of the two vitamins is found in studies of the general population.

- **Low plasma or serum folate has also been found in patients with recurrent mood disorders treated by lithium and in depression due to alcoholism (low serum folic acid)**

- **Low folate levels are furthermore linked to a poor response to antidepressants, and treatment with folic acid is shown to improve response to antidepressants.**

- A recent study also suggests that **high vitamin B12 status may be associated with better treatment outcome.**

- **There is now substantial evidence of a common decrease in serum/red blood cell folate, serum vitamin B12 and an increase in plasma homocysteine in depression.**

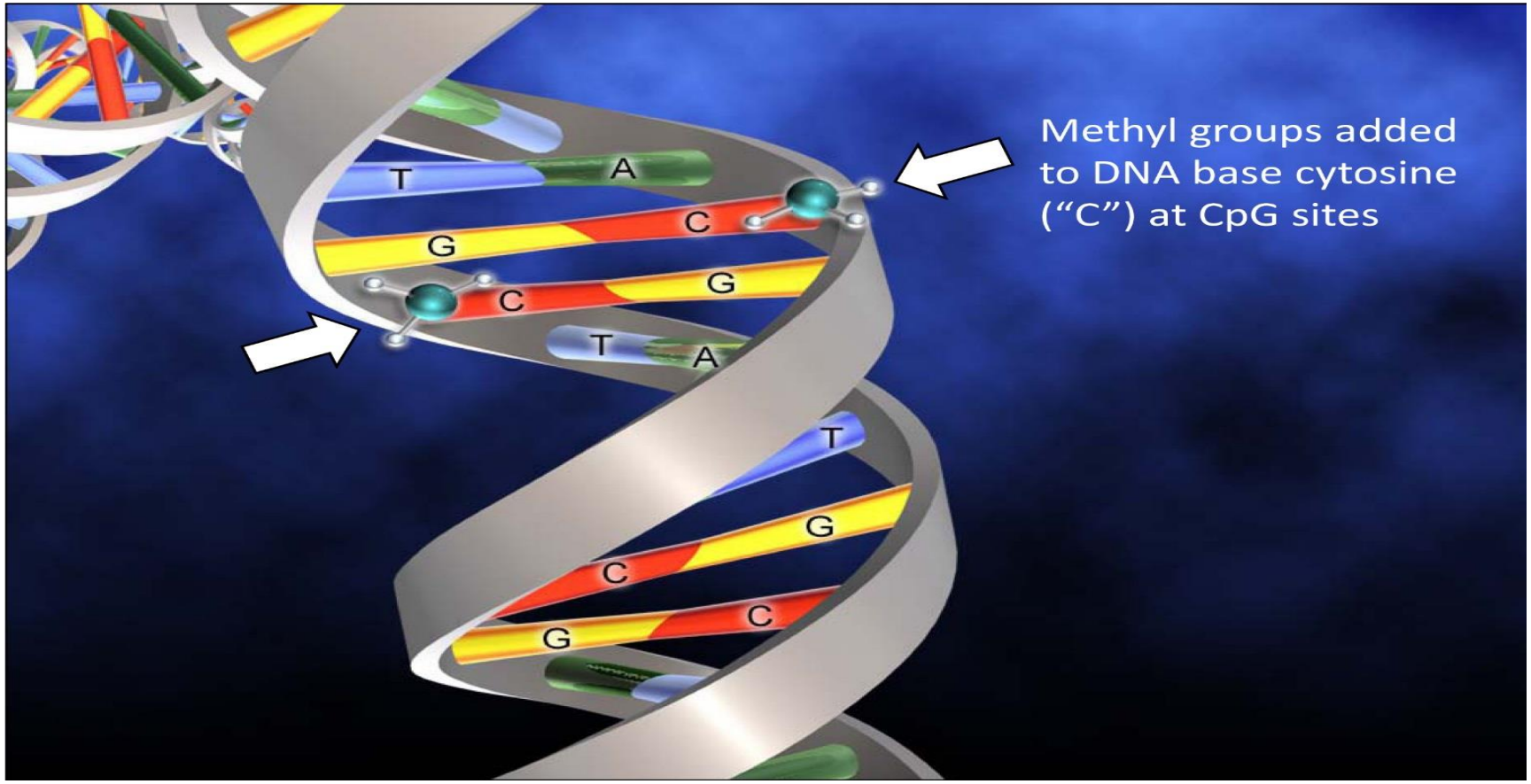
- **On the basis of current data, we suggest that oral doses of both folic acid (800 mcg daily) and vitamin B12 (1 mg daily) should be tried to improve treatment outcome in depression.**

Reference: Coopen A, Bolander-Gouaille C. Treatment of depression: time to consider folic acid an vitamin B12. J Psychopharmacol. 2005. 19(1): 59-65

But, Don’t become deficient in the first place (Folic Acid, B12)

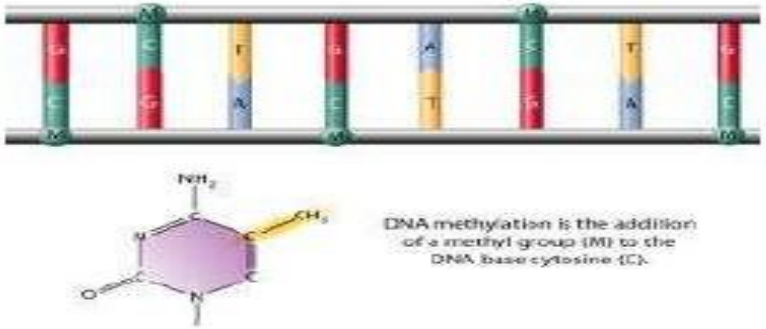
DNA Methylation In Cancer Prevention:

Requires Folic acid and B12



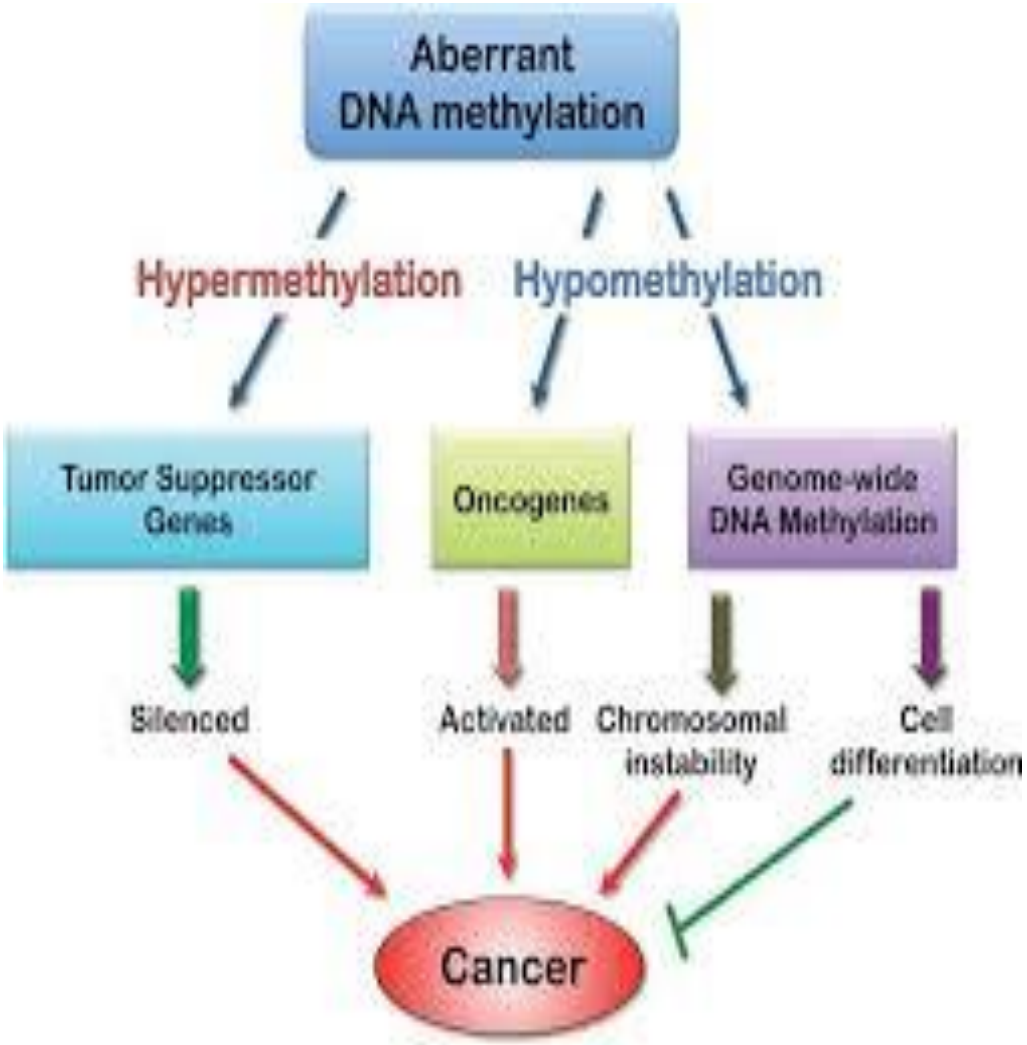
Methylation Helps Prevent Over Stimulation of Cell Division (Folic acid, Vit B12)

Introduction: DNA Methylation



- CH_3 inhibits transcription factors from attaching to DNA
- Gene(s) silenced/inactivated, esp. if promoter region is methylated
- Hypermethylation -> inactivated genes;
- Hypomethylation -> genomic instability
- Catalyzed by presence of DNA Methyltransferase (DNMT) enzymes

Hypomethylation and Cancer:
From insufficient Folic Acid, B12



Vitamin D

Ideal Blood Range above 75 or **85 nmol/L and likely below 150 nmol/L**

68% of Canadians have vitamin D level below **50 nmol/L**

https://www150.statcan.gc.ca/n1/pub/82-624-x/2013001/article/11727-eng.htm#:~:text=Just%20over%20two%2Dthirds%20of%20Canadians%20(68%25)%20had%20vitamin,14%20of%20Canadians%20were%20deficient.

Evidence strong that **1,000 IU per day** enables most people to achieve a blood level above 75nmol/L (For some individuals they require another 1,000-3,000 IU).

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1470481/

https://www.hindawi.com/journals/dm/2015/864370/ ; https://pubmed.ncbi.nlm.nih.gov/28350929/

Between October and May, cannot make vitamin D in the skin in Canada

The Maximum amount of vitamin D allowed in Multiple Vitamin in Canada = 1,000 IU

Blood Vitamin D Levels above 75 nmol/L associated with:

1. Decreased Acute Respiratory Distress Syndrome in Children
2. Faster Recovery from Respiratory Infections in Adults
3. Improved Immunity via synthesis of antimicrobial peptides – cathelicidin, defensins and TLR co-receptor CD14, required by macrophages and other immune cells

Laaksi I et al. Vitamin D supplementation for the prevention of acute respiratory tract infection: A randomized, double-blind trial among young Finnish Men. Journal of Infectious Diseases, Vol 202, Issue 5. September 2010. https://academic.oup.com/jid/article/202/5/809/1746565

Bergman P, Lindh A, Bjorkhem-Bergman, Lindh J. Vitamin D and respiratory tract infections: A systemic review and meta-analysis of randomized controlled studies. PLOS (peer-reviewed, open access journal). 2013; 8(6):e65835 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3686844

Low Blood Vitamin D levels associated with increased risk of Covid-19 deaths in Europe

Petre Cristian Ilie, Simina Stefanescu, Lee Smith. **The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality**. *Aging Clinical and Experimental Research*, 2020. https:/ link.springer.com/article/10.1007/s40520-020-01570-8

Ali Daneshkhah, Vasundhara Agrawal, Adam Eshein, Hariharan Subramanian, Hemant Kumar Roy, Vadim Backman. The Possible Role of Vitamin D in Suppressing Cytokine Storm and Associated Mortality in COVID-19 Patients. *medRxiv*, Posted April 30, 2020 https://www.medrxiv.org/content/10.1101/2020.04.08.20058578v3

Petre Cristian Ilie, Simina Stefanescu, Lee Smith. **The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality**. *Aging Clinical and Experimental Research*, 2020. https://link.springer.com/article/10.1007/s40520-020-01570-8

Vitamin D supplementation added to standard Covid-19 Rx in **Spain** – **Results**: no deaths in Vitamin D group and fewer Covid-19 hospitalized patients progressing to require ICU intervention.

Castillo ME et al. Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot study. J Biochem Mol Biol. 2020; 203:105751
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456194/

Child's IQ Impacted By Mother's Vitamin D Level

Mothers Vitamin D level in second trimester of pregnancy affects child's IQ (4-6 yrs of age)

- **13% of White U.S**. pregnant women and **80% of Black U.S** pregnant women shown to have Blood Vitamin D Level **below 50 nmol/L.**
- By 12th day after conception fetal brain expresses vitamin D receptors
- Vitamin D crosses the placenta for fetal access
- **New Recommendation – all pregnant women and those who intend to be pregnant should ensure blood Vitamin D in the ideal range**.

Melissa M Melough, Laura E Murphy, J Carolyn Graff, Karen J Derefinko, Kaja Z LeWinn, Nicole R Bush, Daniel A Enquobahrie, Christine T Loftus, Mehmet Kocak, Sheela Sathyanarayana, Frances A Tylavsky. **Maternal Plasma 25-Hydroxyvitamin D during Gestation Is Positively Associated with Neurocognitive Development in Offspring at Age 4–6 Years.** *The Journal of Nutrition*, 2020.
https://academic.oup.com/jn/advance-article/doi/10.1093/jn/nxaa309/5951845

Other Conditions Impacted by Vitamin D

Vitamin D Blood Levels above 75-85 nmol/L may also decrease risk and/or improve management of:

- Osteoporosis and Fractures
- Multiple Sclerosis
- Diabetes
- Heart Disease
- High Blood Pressure
- Alzheimer's disease/dementia
- Cancer Risk (differentiation and proliferation)- many tissues and glands have Vit D receptors
- Depression
- Parkinson's Disease
- Influenza
- Age-related Macular Degeneration

J Pharmacol Pharmacother: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3356951/

Am J Public Health: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1470481/

Calcium and Osteoporosis

Data from What We Eat In America, NHANES 2009-2010 indicated that **42% of Americans did not meet their Estimated Average Requirements** for calcium as recommended by the Institute of Medicine

https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/DBrief/13_calcium_intake_0910.pdf

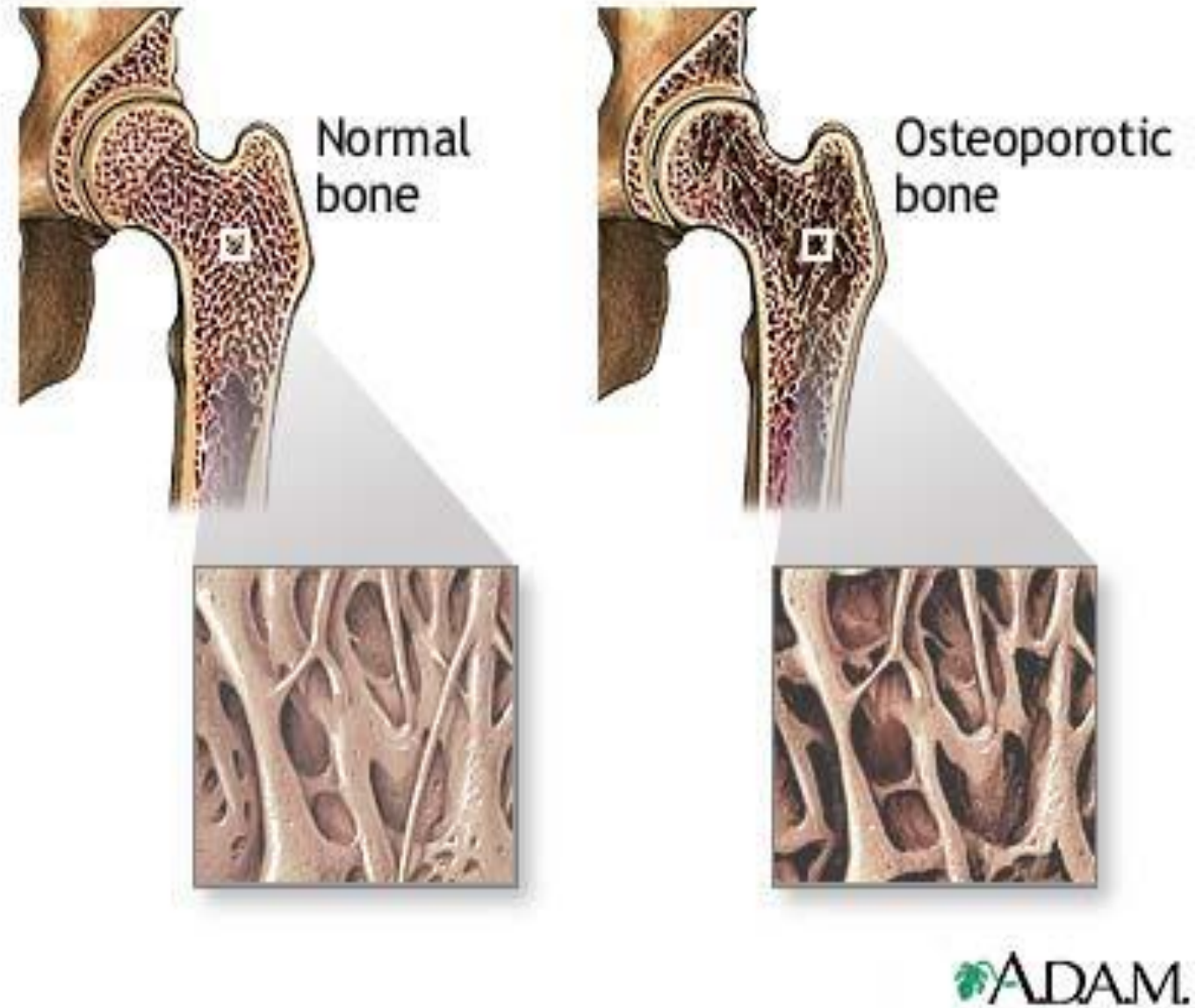
Using 1999–2000 NHANES data, Ervin et al found **median daily calcium intake** from food sources for **adults aged ≥60 y to be ≈716 mg for men and 563 mg for women** compared with the national AI (Adequate Intake) of **1200 mg. (Thus, most would benefit from at least 500 mg of elemental calcium per day from supplementation)**

In conclusion, our results show that, overall, **most US adults do not meet daily calcium AI levels** through diet alone, and that, among those taking supplements, supplemental calcium is often inadequate to overcome the deficits between dietary intake and the recommendations.

American Journal of Clinical Nutrition 200: American not meeting current calcium recommendations: (https://academic.oup.com/ajcn/article/85/5/1361/4633065)

Thoracic Compression Fractures - Common

Osteoporosis of Hip



Hip Fracture

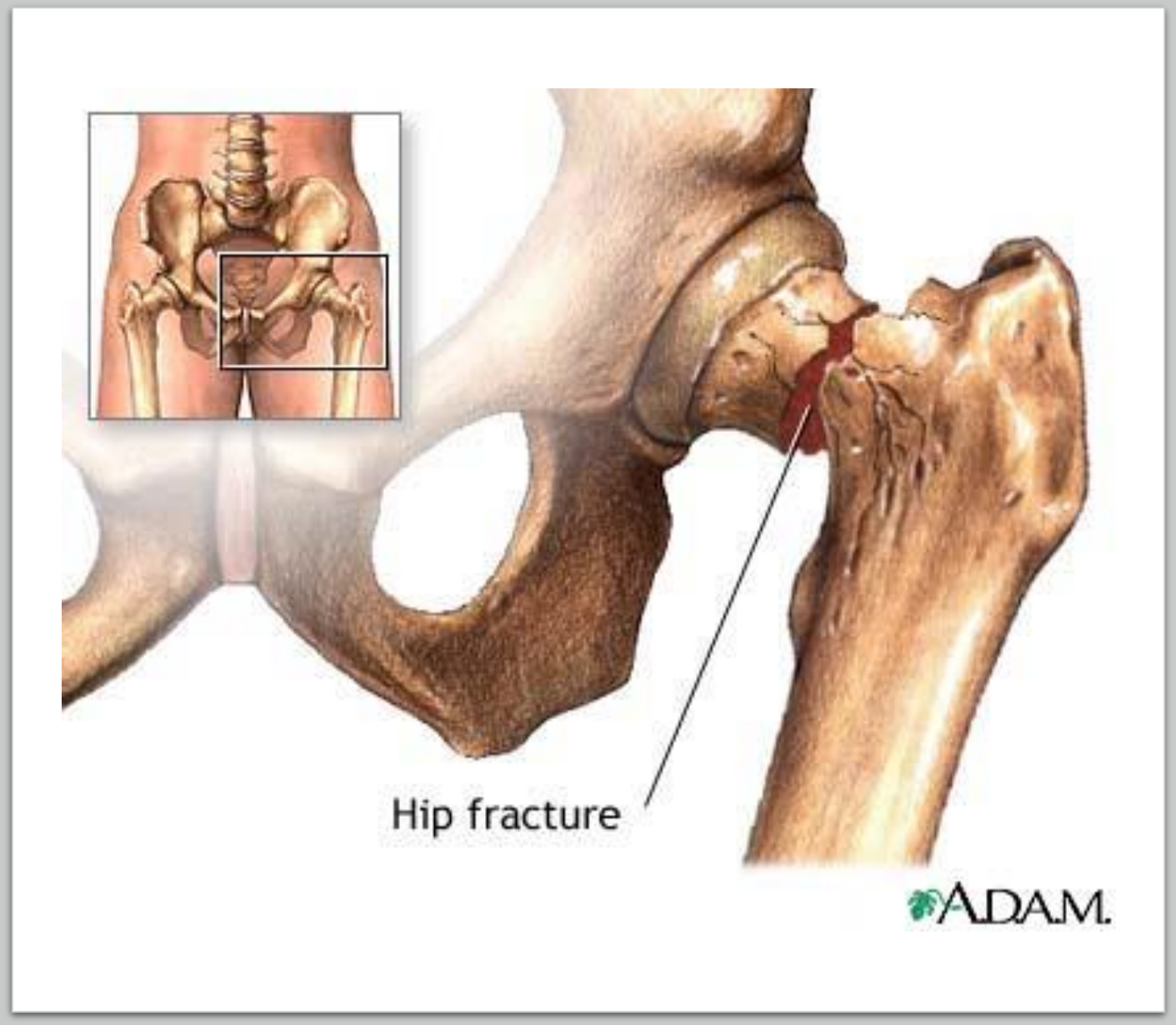
20% of women die in first year after hip fracture and 32% of men die within first year

1:4 women over have osteoporosis

1:8 men over 50 have osteoporosis

Optimal Calcium and Vitamin D are essential during entire life span.

Most people missing 500 mg calcium and 1,000 IU of vitamin D to help optimize bone density.



Calcium and Colon Cancer:

Review of studies show that for **every 300 mg calcium** ingested per day, from food and/or supplements, there is a corresponding **8-9% decrease in risk of colon cancer.**

Thus, **1200 mg per day** of calcium translates into **32-36% reduction** in colon cancer risk.

Reference:

Keum N, Aune D, Greenwood D.C., Ju W, Giovannucci E.L. Calcium intake and colorectal cancer risk: Dose-response meta-analysis of prospective observational studies. International J Cancer (2014) 135 (8): 1940-1948) https://pubmed.ncbi.nlm.nih.gov/24623471/

Colon cancer is 2nd leading cause of cancer death

Mechanism of Action:

1. Calcium **slows proliferation** rate of colon epithelial cell.

2. Calcium binds to bile acid **preventing the conversion of bile acids into secondary sterols** (deoxycholic and lithocholic acid) by gut bacteria, which otherwise increase cell division rate of colon cells, increasing genetic mistakes.

3. **Secondary Bile Acids** also induce **genotoxic effects** to colonic epithelial cells linked to colon cancer development.

References:

Milner JA, McDonald SS, Anderson DE, Greenwald P. Molecular targets for nutrients involved with cancer prevention. *Nutrition and Cancer* 2001; 41(1–2):1–16. [PubMed Abstract]

Lamprecht SA, Lipkin M. Cellular mechanisms of calcium and vitamin D in the inhibition of colorectal carcinogenesis. *Annals of the New York Academy of Sciences* 2001; 952:73–87. [PubMed Abstract]

Lutein: Macular Degeneration is leading cause of blindness in those over 55 yr. (Orange-yellow vegetables and some green one)

Dr. Johanna M. Seddon and associates **at Harvard University** found **that 6 mg per day of lutein led to a 43% lower risk for macular degeneration**

Reference: Johanna M. Seddon et al, 1994, Journal of American Medical Association 272:1413-20. https://jamanetwork.com/journals/jama/article-abstract/382145

Lycopene and Prostate Cancer:

2015 review of all available studies showed a **linear relationship between higher lycopene intake and reduced risk of prostate cancer with threshold between 9-21 mg per day** and blood levels between 2.17-85 ug/dL

Reference:

Chen P et al. Lycopene and risk of prostate cancer: A systematic review and meta-analysis. Medicine 2015;94 (33):e1260 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4616444/

Lycopene In Adjunctive Management of Prostate Cancer: Human Studies

Study 1. In one study, the effect of tomato sauce on apoptosis in **benign prostate hyperplasia (BPH) tissue and carcinomas** was examined. 26 patients who were scheduled for prostatectomy were given tomato sauce pasta entrees **(30 mg/day of lycopene)** to eat daily for 3 weeks before surgery.

- Patients scheduled for surgery who did not receive the tomato sauce pasta entrees served as control subjects.

  Results: Those who consumed the tomato sauce pasta entrees exhibited **decreased serum PSA levels and increased apoptotic cell death in BPH tissue and carcinomas**

Reference: Kim HS, Bowen P, Chen L, et al.: Effects of tomato sauce consumption on apoptotic cell death in prostate benign hyperplasia and carcinoma. Nutr Cancer 47 (1): 40-7, 2003.

Study 2. In a 2004 open-label study, patients with **hormone-refractory prostate cancer (HRPC)** received lycopene supplements daily (**10 mg/day of lycopene) for 3 months**.

- Of the study's participants**, 50% had PSA levels that remained stable, 15% showed biochemical progression, 30% showed a partial response, and one patient (5% of the total sample) exhibited a complete response after treatment**.

Reference: Ansari MS, Gupta NP: Lycopene: a novel drug therapy in hormone refractory metastatic prostate cancer. Urol Oncol 22 (5): 415-20, 2004 Sep-Oct

Study 3. Prostate Cancer Patients received lycopene supplements **(30mg/day)** or no intervention **twice daily** for **3 weeks prior to radical prostatectomy**.

- Patients who received the lycopene supplements had **smaller tumors and lower serum PSA levels** than patients who did not receive the supplements.

- These results suggest that lycopene may be beneficial in prostate cancer treatment

Reference: Kucuk O, Sarkar FH, Djuric Z, et al.: Effects of lycopene supplementation in patients with localized prostate cancer. Exp Biol Med (Maywood) 227 (10): 881-5, 2002.

Study 4. A 2006 study investigated whether lycopene supplements **(10 mg/day)** would affect PSA velocity in patients with **localized prostate cancer.**

- There was a statistically **significant decrease in PSA velocity** following lycopene treatment as well as a large, but not statistically significant, increase in PSA doubling time

Reference: Barber NJ, Zhang X, Zhu G, et al.: Lycopene inhibits DNA synthesis in primary prostate epithelial cells in vitro and its administration is associated with a reduced prostate-specific antigen velocity in a phase II clinical study. Prostate Cancer Prostatic Dis 9 (4): 407-13, 2006.

Study 5. Patients with high-grade prostate intraepithelial neoplasia (HGPIN) received **4 mg of lycopene twice a day** or no lycopene supplementation for 2 years.

Results: A **greater decrease in serum PSA levels was observed in those treated with lycopene supplements** compared with those who did not take the supplementation.

- **During follow-up, adenocarcinomas occurred more often in patients who had not received the supplements than in patients who had received lycopene.**

- These findings suggest that lycopene **may be effective in preventing HGPIN from progressing to prostate cancer**

Reference: Bunker CH, McDonald AC, Evans RW, et al.: A randomized trial of lycopene supplementation in Tobago men with high prostate cancer risk. Nutr Cancer 57 (2): 130-7, 2007

Study 6 - In a Phase II clinical trial (Vaishampayan U et al, 2007) researchers investigated the efficacy of **lycopene alone or in combination with soy isoflavones on serum PSA levels in men with prostate cancer**.

To be eligible for the study, men with prostate cancer had to have rising serum PSA following local therapy or while on hormone therapy. The study population included 71 patients who had 3 successive rising PSA levels or a minimum PSA of 10 ng/ml at 2 successive evaluations prior to starting therapy.

- Subjects were randomly assigned to receive a tomato extract capsule containing **15 mg of lycopene alone** (n = 38) **or together** with a capsule containing **40 mg of a soy isoflavone** mixture (n = 33) twice daily orally for a maximum of **6 mo.**

- One patient on the lycopene arm did not receive therapy due to his inability to ingest the study pill.

- There was no decline in serum PSA in either group. However, 35 of 37 (95%) patients in the lycopene group and 22 of 33 (67%) patients in the lycopene plus soy isoflavone group achieved stable disease, meaning that they achieved **stabilization in serum PSA level.**

- The data suggest that lycopene and soy isoflavones have important adjunctive effects in prostate cancer patients with PSA relapse disease and may delay progression of both hormone-refractory and hormone-sensitive prostate cancer.

Reference:

Vaishampayan U, Hussain M, Seren S, Sarkar F, Fontana J et al. Lycopene and Soy Isoflavones in the Treatment of Prostate Cancer. Nutri and Cancer. 2007; 59 (1): 1-7

Lycopene and Other Cancers:

Studies assessing higher intake and/or blood levels of lycopene and cancer risk also suggest **potential benefits in preventing lung, esophagus, stomach,** colorectal, pancreas**, breast and cervix cancers.**

References:

Br J Cancer 2011 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3068500/

Annu Rev Food Sci Technol 2013: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3850026/

Zinc

- 55% US adults don’t ingest RDA for zinc

- Unlike the mineral iron, body has **no way of storing zinc** to any appreciable degree, and thus, **optimal daily intake** is the required to maintain optimal tissue and circulating levels of zinc

- In North America and in many developed countries **30% of elderly individuals** are shown to have mild to moderate zinc deficiency.

- Blood tests to ensure adequate zinc nutritional status in children and adults is reflected by a zinc blood plasma level of **100 ug/dl (plus or minus 10 ug/ml).**

- **Values below 80 ug/dl** are considered in the **mild to moderate deficient range**.

- A **severe zinc deficiency** is reflected by a plasma zinc level **below 50 ug/dl.**

Recommended that adult males and non-pregnant females consume **15 mg of zinc per day**.

Studies show that adult males and females in North America average about **11 mg** of zinc intake per day from food. **Elderly individuals (over 71 yrs of age) average about 8 mg.**

The chronic sub-optimal intake can lead to signs and symptoms of mild to moderate zinc deficiency, which is not uncommon in our society.

Signs and symptoms include any combination of the following:

- **Decreased immune function** or compromised immune function (decreased natural killer cell lytic activity), decreased interleukin-2 activity of T-helper cells, decreased serum thymulin activity -required for maturation of T-lymphocytes)
- **Decreased taste acuity**
- **Decreased dark adaptation**
- **Decreased lean mass**
- **Decreased wound healing**

Zinc References:

- Gammoh NZ et al. Zinc in infection and inflammation. Nutrients 2017 (June). 9(6):624 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5490603/

- Prasad A. Zinc is an antioxidant and anti-inflammatory agent: it's role in human health. Frontiers of Nutrition (Review Article) 2014. https://www.frontiersin.org/articles/10.3389/fnut.2014.00014/full

- Briefel RR et al. Zinc intake of the U.S. population: Findings from the Third National Health and Nutrition Examination Survey, 1988-1994. The Journal of Nutrition 2000. 130(5):1367s-1373s https://academic.oup.com/jn/article/130/5/1367S/4686375

- Bird JK et al. Risk of deficiency in multiple concurrent micronutrients in children and adults in the United States. Nutrients 2017 (June). 9(7):655 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5537775/

- Micronutrient Inadequacies in the U.S. population: an overview. Oregon State University https://lpi.oregonstate.edu/mic/micronutrient-inadequacies/overview

NIH Feb 3, 2021 Zinc and Covid-19

- **"An observational study showed that COVID-19 patients had significantly lower zinc levels in comparison to healthy controls and that zinc-deficient COVID-19 patients (those with levels less than 80 µg/dl) tended to have more complications** (70.4% vs 30.0%, *p* = 0.009) and **potentially prolonged hospital stays** (7.9 vs 5.7 days, *p* = 0.048**) relative to patients who were not zinc deficient** [84]."

- "In coronaviruses specifically, *in vitro* evidence has demonstrated that the combination of zinc (Zn^{2+}) and zinc ionophores (pyrithione) **can interrupt the replication mechanisms of SARS-CoV-GFP (a fluorescently tagged SARS-CoV-1) and a variety of other RNA viruses** [85,86]. Currently, there are over twenty clinical trials registered with the intention to use zinc in a preventative or therapeutic manner for COVID-19."

Reference: Lordan R et al. Dietary Supplements and Nutraceuticals Under Investigation for Covid-19 Prevention and Treatment. National Institutes of Health Preprint Pilot. Feb 3, 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7872359/

Selenium and Immunity

- Like Zinc, **Selenium helps support immune** function in various way
- In animals, low selenium status increases risk of viral and other infections, and selenium repletion reverses the risk.
- Selenium supplementation shown to **slow progression of HIV** disease in humans
- More optimal Selenium status shown to **decrease virus MUTATION** and Replication in the body
- Selenium shown to **inhibit life-threatening cytokine** storm experimentally
- Selenium may help **prevent abnormal clots** seen is Covid-19 patients

Frontiers of Nutrition Journal Sept 2020: https://www.frontiersin.org/articles/10.3389/fnut.2020.00164/full

Selenium supplementation shown to enhance efficacy of polio virus vaccine in human studies

Mol Nutr Food Research 2013 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3723386/

Selenium shows an impressive array anti-cancer properties in human epidemiological studies and anima experiments

Int J Mol Sci. Tan HW et al. Selenium species: Current status and potentials in cancer prevention and therapy. 2019; 20(1):75
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6337524/

Mol Nutr Food Research 2013
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3723386/

Selenium Status and Covid-19

- Studies in **China, Germany and Sweden have shown that the lower a person's selenium status, the greater is the risk of mortality in Covid-19 patients**

- In **China**, the **rate of recovery from Covid-19** shown to be **3x higher in areas where selenium nutritional status is superior**

- In Germany, Very low serum Se status was present in 44.4% of their patients. 65% percent of the deceased had low Se vs 39% in those who survived. **The lowest serum Se were strongly associated with mortality.**

- **In Sweden, 71% of elderly are Se deficient when admitted to Intensive Care Unit.**

- **Studies have shown that Se supplementation has significantly reduced infections in institutionalized elderly people.**

- The **RDA** for Selenium appears to **be too low to optimize immune function (55 mcg/d)**

- The recommendation in Sweden is for citizens to supplement with **200 mcg per day** of selenium to **help optimize immune function** and **decrease viral replication and mutation.**

- **In addition, 200 micrograms of Se daily have been given in the elderly for years with significant positive results lowering viral infection rates and cardiovascular mortality**.

- Similarly, 4-year Se supplementation **(200 mcg/d)** in Swedish elderly people reduced cardiovascular mortality risk by more than 40%, even 12 years after intervention. (also included CoQ10)

Reference: Hiffler L et al. Selenium and RNA virus interactions: Potential implications for SARS-CoV-2 infection (COVID-19). Frontiers in Nutrition. September 2020: https://www.frontiersin.org/articles/10.3389/fnut.2020.00164/full

Selenium Anti-Cancer Experimental Studies

http://ar.iiarjournals.org/content/37/12/6497.full

Review of Selenium Physiological Effects:

1. Antioxidant vie Glutathione Peroxidase and other Seleno-enzymes
2. Induction of Phase II detox detoxifying carcinogens and reducing DNA adduct formation
3. Enhancement of immune function – multimodal – cytotoxicity, lymphocytes, and NK activity: **Human selenium supplementation** studies show enhanced immunity in aging with selenium supplementation: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3723386/
4. Increase activity of tumor suppressor genes, inhibiting important steps in cancer development
5. Inactivating key peptides – Protein kinase-C, in emerging cancer cells
6. Stabilizing DNA methylation
7. Inducing apoptosis of cancer cells
8. Inhibition of angiogenesis in cancer cells

Vitamin A

Vitamin A RDA: Men- 900 RAE; Women – 700 RAE

Adult men have slightly higher intakes **(649 mcg RAE)** than **adult women (580 mcg RAE).**

Vitamin A Functions:

- Vitamin A is involved in **immune function, vision, reproduction, and cellular communication**.
- Vitamin A is critical for **vision** as an essential component of **rhodopsin**, a protein that absorbs light in the retinal receptors, and because it supports the normal differentiation and functioning of the conjunctival membranes and cornea.
- Vitamin A also supports **cell growth and differentiation**, playing a critical role in the normal formation and maintenance of the heart, lungs, kidneys, and other organs.

1/6 of beta carotene intake can be converted to vitamin A if the body needs more vitamin A

Too much preformed vitamin A can be toxic. Thus, should limit Multiple Vitamin levels to 2500 IU vitamin A (plus 15,000 IU beta carotene)

Sufficient vitamin A prevents metaplasia – precancerous condition

Vitamin A Toxicity: **Liver Damage** and Increased risk of **Osteoporosis** and Fractures

Reference: https://ods.od.nih.gov/factsheets/VitaminA-HealthProfessional/

Chromium and Blood Sugar

- Evidence suggests that most people consume enough chromium to meet **recommended intake level set at 35 mcg/d for men and 25 mcg/d for women**: https://ods.od.nih.gov/factsheets/Chromium-HealthProfessional/#:~:text=Therefore%2C%20data%20on%20chromium%20intakes,day%20for%20men%20%5B32%5D

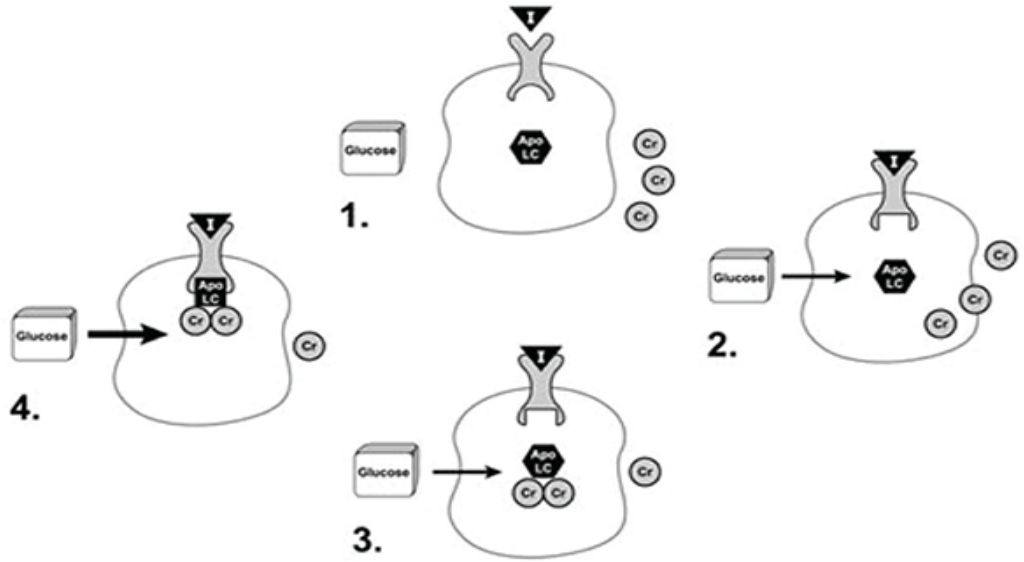
- **Yet this level of intake may not be optimal for insulin sensitivity & blood glucose regulation**

- Studies by RA Anderson have shown that supplementation with additional chromium **improves function of insulin receptors, helps to lower fasting and postprandial glucose and HbA1c, in studies that he has published over the years** **https://europepmc.org/article/med/3514054**

- **Ingesting additional 50 mcg of chromium from supplementation may be beneficial in supporting blood glucose regulation, helping to prevent type 2 diabetes and metabolic syndrome, which are increasing in incidence in our population**

Chromium Help Open Door for Blood Sugar (glucose) to Enter Cells of the Body

Figure 1. A Proposed Model for the Potential Effects of Chromium on Insulin Action



1. Insulin binds to and activates the insulin receptor.
2. Insulin receptor activation stimulates the movement of chromium into the cell.
3. Chromium binds to a peptide known as Apo-LMWCr* (Apo-LC).
4. Functional LMWCr (LC) binds to the insulin receptor and enhances its activity.

*LMWCr = low-molecular weight chromium-binding substance

Adapted from Vincent, J.B. Quest for the molecular mechanism of chromium action and its relationship to diabetes. Nutr Rev. 2000; 58: 67-72.

Magnesium

Functions and Considerations

Energy Production – ATP

Cofactor for many enzymes

Cell membrane stability, muscle contraction, cardiac function

DNA and RNA synthesis

Bone Density

Antioxidant – SOD

Insulin Function

Depleted by:

- Stress
- Alcohol
- Caffeine
  Exercise
- Refined Sugar

- Diet of many people in the United States provide less than the recommended amounts of magnesium. **RDA: 420 mg/d Men; 320 mg/d Women**

- When amount of magnesium people get from **food and dietary supplements is combined**, however, total intakes of magnesium are generally above recommended amounts. (**many people get extra magnesium from supplements – good idea)**

Reference: https://ods.od.nih.gov/factsheets/Magnesium-Consumer/

Magnesium shown to be associated with **lower risk of stroke by 2% for every 200 mg consumed** https://www.medicalnewstoday.com/articles/286839#recommended-daily-intake

Magnesium and Colon Cancer Prevention

A 2020 study published in the British Medical Journal, “Gut”, reviewed all relevant studies published in English and French in recent years examining the link between diet, lifestyle, and colon cancer.

Regarding protection against colon cancer**, magnesium intake of at least 255 mg/day was associated with a 23% lower risk compared with the lowest intake of magnesium**, **and high intake of the B-vitamin folic acid was associated with a 12-15% lower risk.**

Eating dairy products was associated with **13% to 19%** lower risk of the disease. This is probably due to the calcium content of dairy products, as seen in other studies.

Let’s Put This Altogether

Based on Research Shown in this Presentation it makes sense to supplement with the following dosages:

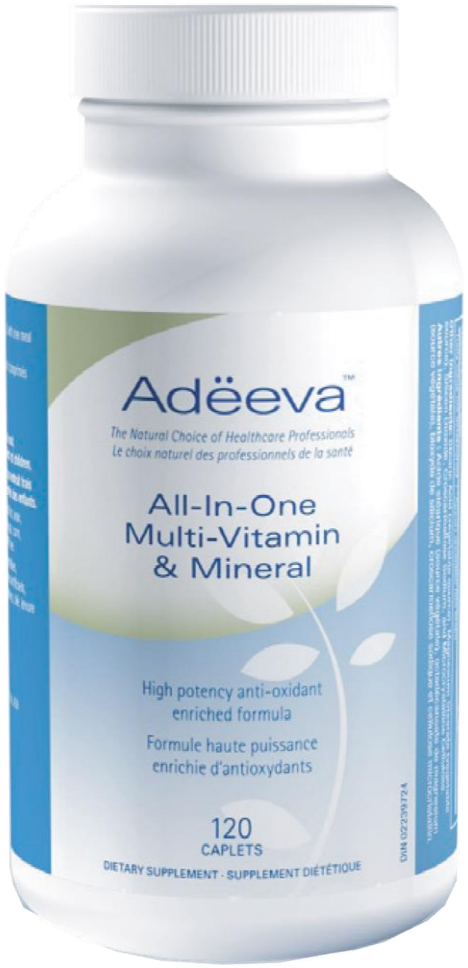
1. Vitamin C – 1,000 mg per day (500 mg, twice daily)
2. Vitamin E – 400 IU per day (as vitamin E Succinate)
3. Vitamin D – 1,000 IU
4. Calcium – 500 mg
5. B-50 complex
6. Zinc – 15 mg
7. Selenium – 200 mcg
8. Vitamin A – no more than 2500 IU
9. Chromium – 50 mcg
10. Magnesium – 200 mg
11. Lutein and Lycopene

What I Did Originally

1. Standard Multiple Vitamin and Mineral Supplement
2. Vitamin C – 500 – 1,000 mg
3. Vitamin E – 400 IU
4. B-50 Complex
5. Vitamin D – 1,000 IU
6. Calcium/Magnesium (500 mg, 200 mg)
7. Selenium – 200 mcg

Seven Different Bottles and Still Missing Adeqate Lycopene and Lutein

So, I Created This For Adeeva Nutritionals



Adeeva All-in-One Multiple Vitamin and Mineral:

Vitamin C – 1,000 mg (500 mg per dose x 2)
Vitamin E – 400 IU
Selenium – 200 mcg
Zinc – 15 mg
B-50 Complex
Vitamin D – 1,000 IU
Lycopene Powder– 6 mg
Lutein Powder - 6 mg
Bioflavonoids – 50 mg
Vitamin A – 2500 IU
Beta-Carotene – 15,000 IU
Chromium - 50 mcg
Calcium – 500 mg/ Magnesium – 200 mg
And Everything Else From A to Zinc

Dosage: 2 caplets, twice daily with food (Full Adult Dosage)

Adeeva All-in-One Multiple Vitamin and Mineral: 2 caplets, twice daily with food provides the following:

All-In-One Multi Vitamin and Mineral		
Vitamin A		2,500 I.U.
Beta Carotene		15,000 I.U.
Vitamin C		1,000 mg
Vitamin D		1000 I.U.
Vitamin E succinate		400 I.U. (natural)
Thiamin		50 mg
Riboflavin		50 mg
Niacin		50 mg
Vitamin B-6		50 mg
Folic Acid		400 mcg
Vitamin B-12		50 mcg
Biotin		300 mcg
Pantothenic Acid		50 mg

Adeeva All-in-One Multiple Vitamin and Mineral Continued

All-In-One Multi Vitamin and Mineral Continued		
Calcium		500 mg
Iron		6 mg
Magnesium		200 mg
Zinc		15 mg
Selenium		200 mcg
Copper		2 mg
Manganese		5 mg
Chromium		50 mcg
Molybdenum		50 mcg
Bioflavonoids		50 mg
Lutein		6 mg
Lycopene		6 mg

Adeeva All-in-One Multiple Vitamin and Mineral

Distinctive Features:

1. 7-8 Supplements-In-One Bottle
2. Antioxidant enriched
3. B-50 complex
4. 500 mg elemental calcium; 200 mg magnesium
5. 1000 IU Vitamin D
6. Everything from A to Zinc, plus bioflavonoids, lutein and lycopene
7. ***Vitamin E Succinate** – Anti-Cancer (each day our body makes 1-3 cancer cells, which normally undergo cell death from internal prompting or external-immune regulation)

Practical: 1 bottle instead of 8 bottles

More Economical: Less Expensive (a little over a dollar a day retail price)

If You Want to Try
Adeeva All-in-One Multiple Vitamin and Mineral

Special Offer: **15% OFF**

For Webinar Registrants who order additional Adeeva product(s), you will receive 15% OFF **on their Entire Order.**

Call Nathan: 1 888 251 1010 and Use Coupon Code Below

OR order online at www.adeeva.com and use Coupon Code at Checkout.

- **Coupon Code** for this offer is: **RTC21-05-17 (Expires May 30 2021)**

Dr. James Meschino
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