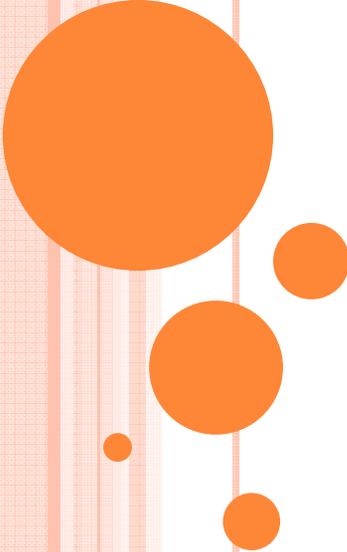
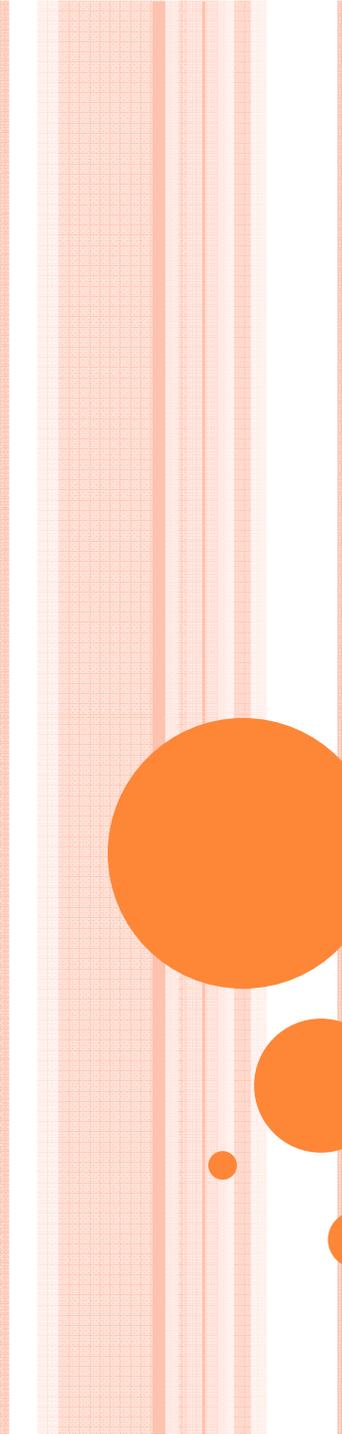




**ALAN SIMON R.PH.**  
**INTEGRATIVERX2@INSIGHTBB.COM**  
**SIMON'S PROSPECT APOTHECARY**  
**WWW.INTEGRATIVERXPHARMACY.COM**  
**(502) 228-4161**  
**9217 US Highway 42**  
**Prospect, KY 40059**



# **NUTRITION AND CANCER**

**Obstacles and Enhancements to Health**

**Alan Simon R.Ph.**





## DIET IS IMPORTANT

- **Harvard Center for Cancer Prevention**
- “It’s been estimated that the combination of poor diet and obesity cause nearly a quarter of all cancers worldwide, second only to tobacco use. Add to this the fact that most dietary factors that help lower the risk of cancer also lower the risk of heart disease, stroke, and diabetes, and the importance of a healthy diet becomes even more pronounced.”



# AN UNHEALTHY DIET AFFECTS CANCER OUTCOMES.



- August 15, 2007, *Journal of the American Medical Association*, researchers show that patients with the highest intake of a Western-pattern diet, characterized by high intakes of red meat, sugar desserts, high fat, and refined grains, have a 3-fold increase in cancer recurrences and mortality.
- Patients were enrolled in a National Cancer Institute–sponsored randomized adjuvant chemotherapy trial known as Cancer and Leukemia Group B (CALGB 89803). The trial compared therapy with weekly fluorouracil and leucovorin vs therapy with weekly irinotecan, fluorouracil, and leucovorin.
- "We identified 2 major dietary patterns, prudent and Western pattern. The prudent diet was characterized by high intake of fruits and vegetables, poultry, and fish.
- During a median follow-up of 5.3 years for the overall cohort, 324 patients had cancer recurrence. A total of 223 patients died after recurrence, and 28 died without documented recurrence. A higher intake of a Western-pattern diet after cancer diagnosis was associated with a significantly worse disease-free survival, including colon cancer recurrences or death.



# HEALTHY LIFESTYLE KEY TO CANCER PREVENTION

- The President's Cancer Panel issues a report every year that focuses on one aspect of what is happening in the United States in terms of cancer.
- This year's effort "centers on lifestyle changes, and two issues that are actually quite different," said panel member Margaret L. Kripke, executive vice president and chief academic officer at the University of Texas M. D. Anderson Cancer Center, in Houston.
- One issue is nutrition, exercise and the fight against obesity, and the other is the battle to cut tobacco use, Kripke said.
- The experts call for a move toward a "culture of wellness" in the United States. This culture would embrace healthy living as a goal and promote a healthy lifestyle as a way of achieving wellness.
- In addition, living a healthy lifestyle lowers a person's risk of cancer recurrence and improves outcomes after cancer, Kripke said.



- **Plant foods, fiber, and rectal cancer.**

- Slattery ML, Curtin KP, Edwards SL, Schaffer DM.

- Health Research Center, University of Utah, Salt Lake City, and the **Kaiser Permanente Medical Research Program**, Oakland, CA, USA. mslatter@hrc.utah.edu

- **BACKGROUND:** Associations between colon and rectal cancer and intakes of vegetables, other plant foods, and fiber have stimulated much debate. **OBJECTIVE:** We examined the association between rectal cancer and plant food and fiber intakes. **DESIGN:** Data from 952 incident cases of rectal cancer were compared with data from 1205 population-based controls living in Utah or enrolled in the Kaiser Permanente Medical Care Program in northern California **RESULTS:** Rectal cancer was inversely associated with intakes of vegetables (odds ratio: 0.72; 95% CI: 0.54, 0.98), fruit (0.73; 0.53, 0.99), and whole-grain products (0.69; 0.51, 0.94), whereas a high intake of refined-grain products was directly associated with an increased risk of rectal cancer (1.42; 1.04, 1.92). Similarly, relative to low fiber intakes, high intakes of dietary fiber reduced the risk of rectal cancer (0.54; 0.37, 0.78). The reduced risk of rectal cancer associated with vegetable (0.48; 0.29, 0.80), fruit (0.63; 0.38, 1.06), and fiber (0.40; 0.22, 0.71) intakes was strongest for persons who received the diagnosis after age 65 y. **A threshold effect at approximately 5 servings of vegetables day was needed to see a reduced risk of rectal cancer.** **CONCLUSIONS:** The results suggest that plant foods may be important in the etiology of rectal cancer in both men and women. Age at diagnosis appears to play an important role in the association.

- PMID: 14749234 [PubMed - indexed for MEDLINE]

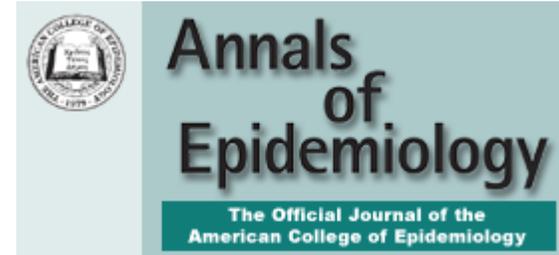


# CANCER RISK HIGHER WITH WESTERN DIET

- **Older Chinese Women Who Ate Diet Heavy on Red Meat and Sugar Had More Breast Cancer, Study Says**
- July 12, 2007 
- A new study suggests the more Western your diet is — meaning heavy on meat, starch and sugar — the higher your risk for cancer may be.
- The study followed older Asian women who had been placed on two separate diets: traditional cuisine rich in vegetables and fish and a Westernized diet heavy on red meat and sugar. Women who adopted the Western diet had higher rates of breast cancer.



# DIETARY PATTERNS AND PROSTATE CANCER RISK



- Ann Epidemiol. 2008 Feb 7
- **Dietary Patterns Identified Using Factor Analysis and Prostate Cancer Risk: A Case Control Study in Western Australia.**
- **Ambrosini GL, Fritschi L, De Klerk NH, Mackerras D, Leavy J.**
- From the School of Population Health, University of Western Australia (G.L.A., J.L.); Western Australian Institute for Medical Research (L.F.), Telethon Institute for Child Health Research, Western Australia (N.H.D.K.); and Menzies School of Health Research and Institute of Advanced Studies, Charles Darwin University, Northern Territory (D.M.), Australia.
- **PURPOSE:** Dietary patterns offer an alternative method for analyzing dietary intakes that take into account the whole diet. We investigated empirical dietary patterns and prostate cancer risk in Western Australia (WA) using a population-based case-control study. **METHODS:** Incident prostate cancer cases were identified via the WA Cancer Registry. Controls were sourced from the WA electoral roll, frequency matched on age. A food frequency questionnaire (FFQ) estimated usual dietary intake from 10 years earlier. Factor analysis identified dietary patterns in FFQ data. Effects of independent dietary patterns on prostate cancer risk were examined using unconditional logistic regression, adjusting for potential confounders. **RESULTS: A total of 546 cases and 447 controls provided data.** Three distinct dietary patterns were identified, which we labeled vegetable, Western, and health-conscious. **An increased risk for prostate cancer was observed with the Western pattern, which consisted of high intakes of red and processed meats, fried fish, hamburgers, chips, high-fat milk, and white bread.** Men in the highest quartile for Western pattern score had an odds ratio of 1.82 (95% confidence interval 1.15-2.87, trend  $p = 0.02$ ). Results were similar for aggressive cases and attenuated for non-aggressive cancers. **CONCLUSIONS: A western style diet may lead to increased risks for prostate cancer, especially aggressive prostate cancer.**
- PMID: 18261927 [PubMed - as supplied by publisher]



# JOURNAL OF THE NATIONAL CANCER INSTITUTE

- **The odds are about 50:50 that a breast cancer survivor over 60 will die as a result of something else – most likely heart disease or osteoporosis – according to a new report in the *Journal of the National Cancer Institute*. It calls for greater attention to these women's other medical problems.**
- JOURNAL OF THE NATIONAL CANCER INSTITUTE Vol. 100 Issue 4 Feb 2008 ISSN: 1460-2105
- Competing causes of death from a randomized trial of extended adjuvant endocrine therapy for breast cancer.
- **Abstract:** BACKGROUND: Older women with early-stage breast cancer experience higher rates of non-breast cancer-related death. We examined factors associated with cause-specific death in a large cohort of breast cancer patients treated with extended adjuvant endocrine therapy. METHODS: In the MA.17 trial, conducted by the National Cancer Institute of Canada Clinical Trials Group, 5170 breast cancer patients (median age = 62 years; range = 32-94 years) who were disease free after approximately 5 years of adjuvant tamoxifen treatment were randomly assigned to treatment with letrozole (2583 women) or placebo (2587 women). The median follow-up was 3.9 years (range 0-7 years). We investigated the association of 11 baseline factors with the competing risks of death from breast cancer, other malignancies, and other causes. All statistical tests were two-sided likelihood ratio criterion tests. RESULTS: During follow-up, 256 deaths were reported (102 from breast cancer, 50 from other malignancies, 100 from other causes, and four from an unknown cause). Non-breast cancer deaths accounted for 60% of the 252 known deaths (72% for those > or = 70 years and 48% for those < 70 years). Two baseline factors were differentially associated with type of death: cardiovascular disease was associated with a statistically significant increased risk of death from other causes (P.002), and osteoporosis was associated with a statistically significant increased risk of death from other malignancies (P.05). An increased risk of breast cancer-specific death was associated with lymph node involvement (P < .001). Increased risk of death from all three causes was associated with older age (P < .001). CONCLUSIONS: Non-breast cancer-related deaths were more common than breast cancer-specific deaths in this cohort of 5-year breast cancer survivors, especially among older women.}
- **Authors:** Chapman, Judith-Anne W, Meng Daniel, Shepherd Lois, Parulekar Wendy, Ingle, James N Muss, Hyman B, Palmer, Michael, Yu, Changhong, Goss, Paul E
- **Affiliation:** National Cancer Institute of Canada Clinical Trials Group, Queen's University, 10 Stuart St, Kingston, ON, Canada. jchapman@ctg.queensu.ca
- Abstract from MEDLINE®/PubMed®, a database of the U.S. National Library of Medicine



# NUTRITION



- The taking in and use of food and other nourishing material by the body.
- A 3-part process.
  - First, food or drink is consumed.
  - Second, the body breaks down the food or drink into nutrients.
  - Third, the nutrients travel through the bloodstream to different parts of the body where they are used as "fuel" and for many other purposes.
- To give the body proper nutrition, a person has to eat and drink enough of the foods that contain key nutrients (vitamins, minerals, protein, carbohydrates, fat, and water).

○ *National Cancer Institute*



**OBSTACLES AND  
ENHANCEMENTS TO HEALTH**



# COMPREHENSIVE APPROACH - REMOVE THE OBSTACLES ADD THE ENHANCEMENTS

- The field of investigation of the role of nutrition in the cancer process is very broad. **It is becoming clearer as research continues that nutrition plays a major role in cancer. It has been estimated by the American Institute for Cancer Research and the World Cancer Research Fund that 30–40 percent of all cancers can be prevented by appropriate diets, physical activity, and maintenance of appropriate body weight [1].** It is likely to be higher than this for some individual cancers.
- Most of the research on nutrition and cancer has been reductionist; that is, a particular food or a nutrient has been studied in relation to its impact on tumor formation/regression or some other end point of cancer at a particular site in the body. These studies are very helpful in seeing the details of the mechanisms of disease. However, they do not help give an overall picture of how to prevent cancer on a dietary level. Even less, they tell little of how to eat when a person already has a cancer and would like to eat a diet that is favorable to their recovery.
- 1 Food, nutrition and the prevention of cancer: a global perspective:.
- *World Cancer Research Fund / American Institute for Cancer Research 1997.*



# STANDARD AMERICAN DIET

- Average adult consumes
  - 134 lbs of refined sugar
  - 90 lbs of fats and oils
  - 365 servings of soda pop (age 12-29 was 638 cans)
  - 200 sticks of gum
  - 22 lbs of candy
  - 7 lbs of potato chips
  - 8 lbs of corn chips, popcorn, and pretzels
  - 63 dozen doughnuts
  - 60 lbs of cakes and cookies
  - 23 gallons of ice cream



# OBSTACLES

1. Lack of Fruit and Vegetables with Phytochemicals
2. Too little fiber and too much meat
3. Unhealthy Fat Intake
4. Unhealthy Sugar Intake
5. Lack of adequate healthy protein intake
6. Lack of acid alkaline food balance
7. Lack of healthy water intake
8. Lack of movement (physical activity)
9. Lack of sunshine vitamin D
10. Lack of healthy sleep



# LACK OF FRUITS AND VEGETABLES WITH PHYTOCHEMICALS

- Obstacle #1



# PHYTOCHEMICALS- FRUITS AND VEGETABLES



## ○ *National Cancer Institute*

- **Leading causes of death**, which include heart disease, high blood pressure, many cancers, diabetes and stroke, **are largely preventable through lifestyle choices such as eating more fruits and vegetables.**
- **Eating 5 to 9 servings of fruits and vegetables a day is one of the easiest things everyone can do to lower their chances for all of the diet-related diseases.**



# JOURNAL OF THE AMERICAN DIETETIC ASSOCIATION



- [1]: J Am Diet Assoc. 2000 Dec;100(12):1511-21.
- **Overview of the health benefits of fruit and vegetable consumption for the dietetics professional: selected literature.**
- Van Duyn MA, Pivonka E.
- Office of Communications, National Cancer Institute, Bethesda, Md., USA.
- **Epidemiologic evidence of a protective role for fruits and vegetables in cancer prevention is substantial.**

The strength of this scientific base guides US national policymaking in diet and health issues and facilitates community and local programs that address national dietary goals to increase fruit and vegetable consumption. Current scientific evidence also suggests a protective role for fruits and vegetables in prevention of coronary heart disease, and evidence is accumulating for a protective role in stroke. In addition, a new scientific base is emerging to support a protective role for fruits and vegetables in prevention of cataract formation, chronic obstructive pulmonary disease, diverticulosis, and possibly, hypertension. This article provides an overview of the health benefits associated with fruit and vegetable consumption for each of these conditions, including brief discussions of underlying protective mechanisms, identifies key scientific findings regarding the health benefits of fruit and vegetable consumption, and outlines applications of these findings for dietetics professionals. The evidence reviewed provides additional support for increased consumption of a wide variety of vegetables, **in particular, dark-green leafy, cruciferous, and deep-yellow-orange ones, and a wide variety of fruits, in particular, citrus and deep-yellow-orange ones.** Continued attention to increasing fruit and vegetable consumption is a practical and important way to optimize nutrition to reduce disease risk and maximize good health.
- PMID: 11138444 [PubMed - indexed for MEDLINE]



# JOURNAL OF THE AMERICAN DIETETIC ASSOCIATION

- [1]: J Am Diet Assoc. 1996 Oct;96(10):1027-39.
- **Vegetables, fruit, and cancer prevention: a review.**
- Steinmetz KA, Potter JD.
- World Cancer Research Fund, London, England.
- In this review of the scientific literature on the relationship between vegetable and fruit consumption and risk of cancer, results from 206 human epidemiologic studies and 22 animal studies are summarized. **The evidence for a protective effect of greater vegetable and fruit consumption is consistent for cancers of the stomach, esophagus, lung, oral cavity and pharynx, endometrium, pancreas, and colon.** The types of vegetables or fruit that most often appear to be protective against cancer are raw vegetables, followed by allium vegetables, carrots, green vegetables, cruciferous vegetables, and tomatoes. Substances present in vegetables and fruit that may help protect against cancer, and their mechanisms, are also briefly reviewed; these include dithiolthiones, isothiocyanates, indole-3-carbinol, allium compounds, isoflavones, protease inhibitors, saponins, phytosterols, inositol hexaphosphate, vitamin C, D-limonene, lutein, folic acid, beta carotene, lycopene, selenium, vitamin E, flavonoids, and dietary fiber. Current US vegetable and fruit intake, which averages about 3.4 servings per day, is discussed, as are possible noncancer-related effects of increased vegetable and fruit consumption, including benefits against cardiovascular disease, diabetes, stroke, obesity, diverticulosis, and cataracts. Suggestions for dietitians to use in counseling persons toward increasing vegetable and fruit intake are presented.
- PMID: 8841165 [PubMed - indexed for MEDLINE]



# NUTRITION AND CANCER JOURNAL

- Nutr Cancer. 1992;18(1):1-29.
- Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence.
- Block G, Patterson B, Subar A.
- Dept. of Social and Administrative Health Sciences, School of Public Health, University of California, Berkeley 94720.
- Approximately 200 studies that examined the relationship between fruit and vegetable intake and cancers of the lung, colon, breast, cervix, esophagus, oral cavity, stomach, bladder, pancreas, and ovary are reviewed. A statistically significant protective effect of fruit and vegetable consumption was found in 128 of 156 dietary studies in which results were expressed in terms of relative risk. **For most cancer sites, persons with low fruit and vegetable intake (at least the lower one-fourth of the population) experience about twice the risk of cancer compared with those with high intake**, even after control for potentially confounding factors. For lung cancer, significant protection was found in 24 of 25 studies after control for smoking in most instances. Fruits, in particular, were significantly protective in cancers of the esophagus, oral cavity, and larynx, for which 28 of 29 studies were significant. Strong evidence of a protective effect of fruit and vegetable consumption was seen in cancers of the pancreas and stomach (26 of 30 studies), as well as in colorectal and bladder cancers (23 of 38 studies). For cancers of the cervix, ovary, and endometrium, a significant protective effect was shown in 11 of 13 studies, and for breast cancer a protective effect was found to be strong and consistent in a meta analysis. It would appear that major public health benefits could be achieved by substantially increasing consumption of these foods.
- PMID: 1408943 [PubMed - indexed for MEDLINE]



# NATIONAL CANCER INSTITUTE



- Int J Cancer. 2008 May 15;122(10):2330-6.
- **Fruit and vegetable intake and head and neck cancer risk in a large United States prospective cohort study.**
- [Freedman ND](#), [Park Y](#), [Subar AF](#), [Hollenbeck AR](#), [Leitzmann MF](#), [Schatzkin A](#), [Abnet CC](#).
- Cancer Prevention Fellowship Program, Division of Cancer Prevention, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA.
- Squamous **head and neck cancers** include cancers of the oral cavity, pharynx and larynx are the **sixth leading cause of cancer mortality worldwide**, resulting in more than 350,000 deaths annually. Intake of fruit and vegetables may protect against head and neck cancer incidence, although few prospective studies have examined this association. We investigated this relation in 490,802 United States participants of the NIH-AARP Diet and Health cohort using Cox proportional hazard models adjusted for potential confounders. During 2,193,751 person years of follow-up from 1995/1996-2000, 787 participants were diagnosed with head and neck cancer. We found an inverse association between total fruit and vegetable intake and head and neck cancer risk (per serving/day/1,000 calories, Hazard Ratio, 95% Confidence interval: 0.94, 0.89-0.99). In models mutually adjusted for fruit and vegetable intake, the association was stronger for vegetables (fifth vs. first quintile: 0.65, 0.50-0.85) than for fruits (fifth vs. first quintile: 0.87, 0.68-1.11). When further subclassified into botanical groups, those in the highest tertile of leguminosae (dried beans, string beans and peas, 0.80, 0.67-0.96), rosaceae (apples, peach, nectarines, plums, pears and strawberries, 0.60, 0.49-0.73), solanaceae (peppers and tomatoes, 0.82, 0.69-0.98) and umbelliferae (carrots, 0.73, 0.60-0.89) had decreased risk of head and neck cancer, but no significant associations were seen for 9 other botanical groups. Results from this large prospective observational study are consistent with previous case-control studies and support the hypothesis that **total fruit and vegetable intake is associated with reduced risk of head and neck cancer.** (c) 2008 Wiley-Liss, Inc.
- PMID: 18092323 [PubMed - indexed for MEDLINE]





# **PHYTOCHEMICALS**

Another Good Reason to Eat 5-9 Servings  
of Fruits and Vegetables Every Day!

- A phytochemical is a natural bioactive compound **found in fruits and vegetables that are bright colors (yellow, green, blue, orange, red, and purple).**
- They work with nutrients and dietary fiber to protect against disease. Research suggest that phytochemicals found in fruits, vegetables, and nuts, **may help slow the aging process and reduce the risk of many diseases, including cancer,** heart disease, stroke, high blood pressure, cataracts, osteoporosis, and urinary tract infections.
- They have complementary and overlapping mechanisms of action in the body, including antioxidant effects, modulation of detoxification enzymes, stimulation of the immune system, modulation of hormone metabolism, and antibacterial and antiviral effects.
- **More than 900 different phytochemicals have been found in plant food** and more will be discovered. These protective plant compounds are an emerging area of nutrition and health, with new research reported every day.
- So remember to get your “Phytos” by eating 5-9 servings of colorful fruits and vegetables every day!



# PHYTOCHEMICALS- FRUITS AND VEGETABLES

- **Phytochemical Food Sources**
- Isothiocyanates
  - Cruciferous vegetables (cabbage, broccoli, cauliflower and kale)
- Indoles
  - Cruciferous vegetables
- Saponins
  - Beans and legumes
- Allyl sulfides
  - Onions, garlic, leeks, chives
- Isoflavones
  - Soy beans (tofu, soymilk)
- Phenolic acids
  - Tomatoes, citrus fruits, strawberries, raspberries, carrots, whole grains, nuts
- Terpenes
  - Cherries, citrus fruit peel
- Polyphenols
  - Green tea, grapes, wine



# ANTIOXIDANTS- FRUITS AND VEGETABLES

- **Antioxidants are phytochemicals** that are believed to protect the body against harmful cell damage from oxidation. **Antioxidant nutrients are in a group of vitamins and minerals and are thought to protect against cancer**, heart disease and maybe normal aging. Oxidation damages cells, and if this damage accumulates, scientists believe it can result in disease. Various antioxidants do different jobs, such as deactivate free radicals or transforming them to less toxic substances.
- **Antioxidant Food Sources**
- Selenium
  - Brazil nuts, meat, seafood, eggs, whole grains, legumes
- Vitamin E
  - Wheat germ, vegetable oil, nuts
- Vitamin C
  - Citrus fruit, melon, strawberries, pineapple, tomato, pepper, potatoes
- Carotenoids
  - Dark green leafy vegetables, and yellow, red, orange, vegetables and fruits
- Vitamin A
  - Greens, squash, carrots, pumpkins, red pepper, sweet potatoes, apricot, cantaloupe, mango, papaya, peaches



# RAW OR LIGHTLY STEAMED IS BEST

- *"Consumption of Raw Cruciferous Vegetables is Inversely Associated with Bladder Cancer Risk," Tang L, Zirpoli GR, et al, Cancer Epidemiol Biomarkers Prev, 2008; 17(4): 938-44. (Address: Department of Cancer Prevention and Control, **Roswell Park Cancer Institute**, Elm and Carlton Streets, Basic Science Building, Room 715, Buffalo, NY 14263, USA. E-mail: [Li.tang@roswellpark.org](mailto:Li.tang@roswellpark.org) ).*
- In a hospital-based, case-control study involving 275 subjects with primary bladder cancer and 825 subjects without cancer, consumption of **raw cruciferous vegetables was found to be associated with a strong and statistically significant reduced risk of bladder cancer** (adjusted odds ratio for the highest vs. the lowest consumption = 0.64). The association remained significant among smokers consuming 3 or more servings of raw cruciferous vegetables per month (adjusted OR=0.46 for current smokers; 0.60 for heavy smokers). The authors conclude, "These data suggest that cruciferous vegetables, when consumed raw, may reduce the risk of bladder cancer, an effect consistent with the role of dietary isothiocyanates as chemopreventive agents against bladder cancer." **The authors point out that cooking may significantly reduce or destroy isothiocyanates.**



# 1

Find out how many fruits and vegetables you need to eat every day.

**Women**

AGE	FRUITS	VEGETABLES
19-30	2 cups	2½ cups
31-50	1½ cups	2½ cups
51+	1½ cups	2 cups



**Men**

AGE	FRUITS	VEGETABLES
19-50	2 cups	3 cups
51+	2 cups	2½ cups



**Girls**

AGE	FRUITS	VEGETABLES
2-3	1 cup	1 cup
4-8	1 cup	1½ cups
9-13	1½ cups	2 cups
14-18	1½ cups	2½ cups



**Boys**

AGE	FRUITS	VEGETABLES
2-3	1 cup	1 cup
4-8	1½ cups	1½ cups
9-13	1½ cups	2½ cups
14-18	2 cups	3 cups



These amounts are for less active people. Visit [www.fruitsandveggiesmatter.gov](http://www.fruitsandveggiesmatter.gov) to see the amounts needed by more active people.

# 2

Learn what 1 cup and ½ a cup look like.

EACH COUNTS AS 1 CUP		EACH COUNTS AS ½ CUP	
			
1 large orange	1 large sweet potato	4 large strawberries	
			

Visit [www.fruitsandveggiesmatter.gov](http://www.fruitsandveggiesmatter.gov) for more examples.





**3** See how you can add fruits and vegetables into your day as part of a healthy diet.

BREAKFAST	Add some fruit to your cereal.	
SNACK	Grab a piece of fruit.	
LUNCH	Eat a big salad.	
SNACK	Choose raw vegetables as an afternoon snack.	
DINNER	Have two vegetables with dinner and eat fruit for dessert.	

# Cucumber Yogurt Dip

This Greek-style dip with vegetables makes a colorful party platter. Serve with baked pita chips or whole wheat pita bread.

## SNAPSHOT

SERVINGS: 6

TIME: 15 MINUTES



# RECIPES are easy to find-

<http://www.fruitsandveggiesmatter.gov/publications/index.html>

## INGREDIENTS:

---

2 cups plain low-fat yogurt

---

2 large cucumber, peeled, seeded, and grated

---

1/2 cup nonfat sour cream

---

1 Tbsp lemon juice

---

1 Tbsp fresh dill

---

1 garlic cloves, chopped

---

1 cup cherry tomatoes

---

1 cup broccoli florets

---

1 cup baby carrots

\* **Nutrition info per serving:** Calories: 100kcal; Fat 2g; Sodium 90mg; Carb 17g; Fiber 2g; Protein 7g; Vit A 70%; Vit C 35%; Calcium 20%; Iron 4%

\* Vitamin A, Vitamin C, Calcium and Iron listed as % of daily value based on 2,000 calories

## DIRECTIONS:

- 1** Peel, seed, and grate one cucumber. Slice other cucumber and set aside.
- 2** Mix yogurt, grated cucumber, sour cream, lemon juice, dill, and garlic in a serving bowl. Chill for 1 hour.
- 3** Arrange tomatoes, cucumbers, broccoli, and cucumber on a colorful platter. Serve with cucumber dip.

**HELPFUL TIP:** Cucumber dip can be made a day ahead. Keep in the refrigerator.

**VARIATION:** Add other fresh cut vegetables, such as radishes, asparagus, cauliflower, or zucchini.

# WHY SHOULD YOU CARE ABOUT PESTICIDES?

- There is growing consensus in the scientific community that small doses of pesticides and other chemicals can adversely affect people, especially during vulnerable periods of fetal development and childhood when exposures can have long lasting effects.
- **Because the toxic effects of pesticides are**
  - **worrisome**
  - **not well understood**
  - **or in some cases completely unstudied**
  - **people with compromised health may want to consider reducing their exposure to pesticides whenever possible.**





# PESTICIDES – CANCER???

- Environ Health Perspect. 2008 Apr;116(4):559-65. Links
- **Risk of childhood cancers associated with residence in agriculturally intense areas in the United States.**
- **Carozza SE, Li B, Elgethun K, Whitworth R.**
- Department of Epidemiology and Biostatistics, School of Rural Public Health, Texas A&M Health Science Center, College Station, Texas, USA.
- **BACKGROUND:** The potential for widespread exposure to agricultural pesticides through drift during application raises concerns about possible health effects to exposed children living in areas of high agricultural activity. **OBJECTIVES:** We evaluated whether residence in a county with greater agricultural activity was associated with risk of developing cancer in children < 15 years of age. **METHODS:** Incidence data for U.S. children 0-14 years of age diagnosed with cancer between 1995 and 2001 were provided by member registries of the North American Association of Central Cancer Registries. We determined percent cropland for each county using agricultural census data, and used the overall study distribution to classify agriculturally intense counties. We estimated odds ratios and 95% confidence intervals for all ages and 5-year age groups for total cancers and selected cancer sites using logistic regression. **RESULTS:** Our study results showed statistically significant increased risk estimates for many types of childhood cancers associated with residence at diagnosis in counties having a moderate to high level of agricultural activity, with a remarkably consistent dose-response effect seen for counties having  $\geq 60\%$  of the total county acreage devoted to farming. Risk for different cancers varied by type of crop. **CONCLUSIONS:** Although interpretation is limited by the ecologic design, in this study we were able to evaluate rarer childhood cancers across a diverse agricultural topography. **The findings of this exploratory study support a continued interest in the possible impact of long-term, low-level pesticide exposure in communities located in agriculturally intense areas.**
- PMID: 18414643 [PubMed - in process]



# PESTICIDES- REPRODUCTIVE HORMONES

- J Occup Environ Med. 1998 Dec;40(12):1038-47. Links
- **Reproductive hormone profile among pesticide factory workers.**
- [Padungtod C](#), [Lasley BL](#), [Christiani DC](#), [Ryan LM](#), [Xu X](#).
- Occupational Health Program, Harvard School of Public Health, Boston, MA 02115, USA.
- Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone levels, as well as urinary levels of FSH, LH, and E1C, a metabolite of testosterone, were measured to investigate the adverse reproductive effects of organophosphate pesticides among Chinese factory workers who were occupationally exposed to ethylparathion and methamidophos. Thirty-four exposed workers were randomly chosen and recruited from a large pesticide factory, and 44 unexposed workers were selected from a nearby textile factory. A quantitative pesticide exposure assessment was performed among a subset of the exposed and unexposed workers. Information on potential confounders was collected in an interview. A single blood sample was collected at the end of a work shift, when each subject also donated a semen sample. Three first-voided urine samples were collected from each worker on 3 consecutive days. Urinary p-nitrophenol level at 1 hour after the work shift correlated with serum ( $r = 0.71$ ,  $P < 0.01$ ) and urinary ( $r = 0.51$ ,  $P = 0.04$ ) FSH levels. Stratifying by the subjects' exposure status, we found a significant negative correlation among the exposed group between urinary FSH level and sperm count ( $r = -0.61$ ,  $P < 0.01$ ) and between urinary FSH level and sperm concentration ( $r = -0.53$ ,  $P = 0.03$ ). Pesticide exposure alone was significantly associated with serum LH level (beta [coefficient of exposure effect] = 0.79; 95% confidence interval [CI] = 0.42, 1.16) but not with serum FSH or testosterone or with any urinary hormone levels. With adjustment for age, rotating shift work, current cigarette smoking, and current alcohol consumption, exposure significantly increased the serum LH level by 1.1 mIU/mL (95% CI = 0.34, 1.82). Meanwhile, the serum FSH level was slightly elevated (beta [coefficient of exposure effect] = 1.38; 95% CI = -0.09, 2.85) and the serum testosterone level was decreased (beta = -55.13; 95% CI = -147.24, 37) with increased pesticide exposure. Age and rotating shift work appeared to act as confounders. **We conclude that organophosphate pesticides have a small effect on male reproductive hormones, suggestive of a secondary hormonal disturbance after testicular damage.**
- PMID: 9871879 [PubMed - indexed for MEDLINE]



# BETTER PREPPING FRUITS AND VEGETABLES REDUCE RISK???

- J Expo Anal Environ Epidemiol. 2000 Nov-Dec;10(6 Pt 2):710-22.
- **Factors influencing total dietary exposures of young children.**
- [Akland GG, Pellizzari ED, Hu Y, Roberds M, Rohrer CA, Leckie JO, Berry MR.](#)
- Research Triangle Institute, Research Triangle Park, North Carolina 27709-2194, USA. akland@rti.org
- A deterministic model was developed to identify the critical input parameters needed to assess dietary intakes of young children. The model was used as a framework for understanding the important factors in data collection and data analysis. Factors incorporated into the model included transfer efficiencies of pesticide from surfaces to food, transfer efficiencies of pesticide from surfaces to hands to food, and more accurate microactivity data related to contact frequency for the three variables of interest--hands, surfaces, and food. Results from range-finding measurements of transfer efficiencies using an aqueous pesticide solution of a mixture of malathion, diazinon, and chlorpyrifos sprayed on the surfaces indicate that a higher pesticide transfer occurred from hard surfaces to food (hardwood, plastic), with low transfer from soft surfaces (carpet, cloth). Six children, all less than 4 years old, were videotaped to obtain realistic contact frequency and times for the interaction of hands, surfaces, and foods during eating meals and snacks while in their homes or day care centers. The time range of eating events varied from about 2 to 55 min, with an average of about 20 min. The average number of contact frequencies between food and hands was 19 times for each eating event, with a range of 10-40. Contacts between the surface and hand were about the same as the food and hands. Contacts between foods and surfaces ranged from 0 to 32, but only five or less of the contacts per eating event were associated with surfaces other than eating utensil. The children's microactivity data collected during the eating events, together with the laboratory results from the transfer studies, were provided as input into a Monte Carlo simulation of the dietary ingestion model. **Simulation results indicate that children's handling of the food could contribute 20-80% of the total dietary intake of pesticides. Dietary exposure due to residues in the food before handling accounted for 16% and 47%, respectively, of the total mean intake from simulations for a child's consumption of an apple or banana.** These results indicated that transfer efficiencies for foods on various surfaces typically found in homes as well as children's hand contacts with the food and surfaces are important as determinants of dietary exposure.
- PMID: 11138663 [PubMed - indexed for MEDLINE]



# OR EATING ORGANIC???

- Environ Health Perspect. 2008 Apr;116(4):537-42.
- **Dietary intake and its contribution to longitudinal organophosphorus pesticide exposure in urban/suburban children.**
- **Lu C, Barr DB, Pearson MA, Waller LA.**
- Department of Environmental and Occupational Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA.
- **BACKGROUND:** The widespread use of organophosphorus (OP) pesticides has led to frequent exposure in adults and children. Because such exposure may cause adverse health effects, particularly in children, the sources and patterns of exposure need to be studied further. **OBJECTIVES:** We assessed young urban/suburban children's longitudinal exposure to OP pesticides in the Children's Pesticide Exposure Study (CPES) conducted in the greater Seattle, Washington, area, and used a novel study design that allowed us to determine the contribution of dietary intake to the overall OP pesticide exposure. **METHODS:** Twenty-three children 3-11 years of age who consumed only conventional diets were recruited for this 1-year study conducted in 2003-2004. Children switched to organic diets for 5 consecutive days in the summer and fall sampling seasons. We measured specific urinary metabolites for malathion, chlorpyrifos, and other OP pesticides in urine samples collected twice daily for a period of 7, 12, or 15 consecutive days during each of the four seasons. **RESULTS:** By substituting organic fresh fruits and vegetables for corresponding conventional food items, the median urinary metabolite concentrations were reduced to nondetected or close to non-detected levels for malathion and chlorpyrifos at the end of the 5-day organic diet intervention period in both summer and fall seasons. We also observed a seasonal effect on the OP urinary metabolite concentrations, and this seasonality corresponds to the consumption of fresh produce throughout the year. **CONCLUSIONS:** **The findings from this study demonstrate that dietary intake of OP pesticides represents the major source of exposure in young children.**
- PMID: 18414640 [PubMed - in process]





## WILL WASHING AND PEELING HELP?

- While washing and rinsing fresh produce may reduce levels of some pesticides, it does not eliminate them.
  - Peeling also reduces exposures, but valuable nutrients often go down the drain with the peel.
- The best option is to eat a varied diet, wash all produce, and choose organic when possible to reduce exposure to potentially harmful chemicals.
- Inexpensive method to wash and remove waxes:
  - Spray vinegar to remove waxes.
  - Spray hydrogen peroxide to kill bacteria.



[WWW.EWG.ORG](http://www.ewg.org)

## ENVIRONMENTAL WORKING GROUP

- A produce ranking was developed by analysts at the not-for-profit Environmental Working Group (EWG)
  - **based on the results of nearly 43,000 tests for pesticides on produce collected by the U.S. Department of Agriculture and the U.S. Food and Drug Administration between 2000 and 2005.**
  - A detailed description of the criteria used in developing the rankings is available as well as a full list of fresh fruits and vegetables that have been tested.
- EWG is a not-for-profit environmental research organization dedicated to improving public health and protecting the environment by reducing pollution in air, water and food. For more information please visit [www.ewg.org](http://www.ewg.org).

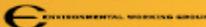


Environmental Working Group  
**SHOPPER'S GUIDE TO PESTICIDES in PRODUCE**

**DIRTY DOZEN** Buy These Organic  
**CLEANEST 12** Lowest in Pesticides

<b>WORST</b>	Peaches	Onions	<b>BEST</b>
	Apples	Avocado	
	Sweet Bell Peppers	Sweet Corn (Frozen)	
	Celery	Pineapples	
	Nectarines	Mango	
	Strawberries	Sweet Peas (Frozen)	
	Cherries	Asparagus	
	Lettuce	Kiwi	
	Grapes (Imported)	Bananas	
	Pears	Cabbage	
	Spinach	Broccoli	
	Potatoes	Eggplant	

Don't see your favorites? Get the full results at [www.foodnews.org](http://www.foodnews.org) & support EWG research with an online gift.



## GET YOUR OWN GUIDE

Download a copy or get more information:

<http://www.foodnews.org>

### Why Should You Care About Pesticides?

There is growing consensus in the scientific community that small doses of pesticides and other chemicals can adversely affect people, especially during vulnerable periods of fetal development and childhood when exposures can have long lasting effects. Because the toxic effects of pesticides are worrisome, not well understood, or in some cases completely unstudied, shoppers are wise to minimize exposure to pesticides whenever possible.

### What's the Difference?

An EWG simulation of thousands of consumers eating high and low pesticide diets shows that people can lower their pesticide exposure by almost 90 percent by avoiding the top twelve most contaminated fruits and vegetables and eating the least contaminated instead. Eating the 12 most contaminated fruits and vegetables will expose a person to about 14 pesticides per day, on average. Eating the 12 least contaminated will expose a person to less than 2 pesticides per day. Less dramatic comparisons will produce less dramatic reductions, but without doubt using the Guide provides people with a way to make choices that lower pesticide exposure in the diet.

### Will Washing and Peeling Help?

Nearly all of the data used to create these lists already considers how people typically wash and prepare produce (for example, apples are washed before testing, bananas are peeled). While washing and rinsing fresh produce may reduce levels of some pesticides, it does not eliminate them. Peeling also reduces exposures, but valuable nutrients often go down the drain with the peel. The best option is to eat a varied diet, wash all produce, and choose organic when possible to reduce exposure to potentially harmful chemicals.

### How Was This Guide Developed?

The produce ranking was developed by analysts at the not-for-profit Environmental Working Group (EWG) based on the results of nearly 51,000 tests for pesticides on produce collected by the U.S. Department of Agriculture and the U.S. Food and Drug Administration between 2000 and 2005. A detailed description of the criteria used in developing the rankings as well as a full list of fresh fruits and vegetables that have been tested is available at [www.foodnews.org](http://www.foodnews.org).



## The Full List: 43 Fruits & Veggies

RANK	FRUIT OR VEGGIE	SCORE
1 (worst)	Peaches	100 (highest pesticide load)
2	Apples	96
3	Sweet Bell Peppers	86
4	Celery	85
5	Nectarines	84
6	Strawberries	83
7	Cherries	75
8	Lettuce	69
9	Grapes - Imported	68
10	Pears	65
11	Spinach	60
12	Potatoes	58
13	Carrots	57
14	Green Beans	55
15	Hot Peppers	53
16	Cucumbers	52
17	Raspberries	47
18	Plums	46
19	Oranges	46
20	Grapes-Domestic	46
21	Cauliflower	39
22	Tangerine	38
23	Mushrooms	37
24	Cantaloupe	34
25	Lemon	31
26	Honeydew Melon	31
27	Grapefruit	31
28	Winter Squash	31
29	Tomatoes	30
30	Sweet Potatoes	30
31	Watermelon	25
32	Blueberries	24
33	Papaya	21
34	Eggplant	19
35	Broccoli	18
36	Cabbage	17
37	Bananas	16
38	Kiwi	14
39	Asparagus	11
40	Sweet Peas-Frozen	11
41	Mango	9
42	Pineapples	7
43	Sweet Corn-Frozen	2
44	Avocado	1
45 (best)	Onions	1 (lowest pesticide load)





## EWG SHOPPERS GUIDE RESULTS

- An EWG simulation of thousands of consumers eating high and low pesticide diets shows that
  - people can lower their pesticide exposure by almost 90 percent by avoiding the top twelve most contaminated fruits and vegetables and eating the least contaminated instead.
  - Eating the 12 most contaminated fruits and vegetables will expose a person to about 14 pesticides per day, on average. Eating the 12 least contaminated will expose a person to less than 2 pesticides per day.
  - Less dramatic comparisons will produce less dramatic reductions, but without doubt using the Guide provides people with a way to make choices that lower pesticide exposure in the diet.



# ORGANIC MEAT?

- Organic Meat - means the animals were not fed food with pesticides.
- Pesticides and chemicals store more readily in animal fat.
- This is why it is a good idea to only eat healthy portions of leaner meats.
  - Sirloin, filet, or very lean cuts of red meat
  - Lean whole (not preformed) turkey
  - Lean cuts of chicken (white is leaner than dark)
- And not eat heavy fat meats such as bacon, sausage, hot dogs, or high fat luncheon meats.



# CURED MEATS VS. UNCURED MEAT

- **Sodium Nitrate /Nitrite- Used to cure meat- ham, lunchmeats, hot dogs, bacon.**
- Nitrate itself is not carcinogenic, but instead acts as a "procarcinogen", meaning that it reacts with other chemicals to form carcinogenic compounds via a multiple step process. First, nitrate is converted into nitrite after consumption. Second, the nitrite reacts with natural or synthetic organic compounds (known as secondary amines or amides) in food or water to form new combinations, called N-Nitroso compounds (either nitrosamines or nitrosamides), many of which are carcinogens.
- In animal or human studies, this class of compounds has been associated with 15 different types of cancers, including tumors in the bladder, stomach, brain, esophagus, bone and skin, kidney, liver, lung, oral and nasal cavities, pancreas, peripheral nervous system, thyroid, trachea, acute myelocytic leukemia, and T and B cell lymphoma -- a wider range of tumors than any other group of carcinogens (Mirvish 1991). More than one hundred of these N-Nitroso compounds have been tested for carcinogenicity in animals, and 75-80% of them have been found to be carcinogens (NAS 1977).
- **There is strong evidence that many of these compounds are carcinogenic in humans.** In 1978, the International Agency for Research on Cancer reviewed 11 N-Nitroso compounds for which adequate data was available, and concluded that all 11 "should be regarded for practical purposes as if [they] were carcinogenic in man" (IARC 1978). Citing several human epidemiological studies, the National Academy of Sciences noted that "there is no reason to suppose that man is not susceptible." (NAS 1977). In humans, the organs thought to be most at risk from cancers caused by nitrosamine formation are the stomach, esophagus, nasopharyngeal cancer, and cancer of the bladder.



# NATURAL MEAT IS NOT ORGANIC MEAT

- Meat labeled **natural** does not mean **organic** unless it is labeled organic as well.
- Natural denotes animal was raised without antibiotics or hormones.
  - Hormones are given to increase growth rate of animal.
  - Many of these hormones are in question as long term safety in humans if ingested.
  - Many question the effect of antibiotics on humans immune system if consuming in everyday foods.
- Hormones can not be given to chickens or pigs thus labeling natural only means antibiotics are not given.
- Hormones are given to cows thus hormone free or natural does have importance on the label of beef or dairy.



# TOO LITTLE FIBER AND TOO MUCH MEAT

- Obstacle #2



# DETOXIFICATION IS THE KEY

- The link between our detoxification system's effectiveness and our susceptibility to environmental toxins, such as carcinogens, is exemplified in a study of chemical plant workers in Turin, Italy.
  - Chemical plant workers were known to have a high risk of bladder cancer due to exposure to the chemical.
  - **The difference- Only those with the highest levels of liver detoxification activity did not get cancer.**
  - A good detoxification (Sanitation) system is KEY.
  - G.Talska et al., "*Genetically based n-acetyltransferase metabolic polymorphism and low-level environmental exposure to carcinogens.*" Nature 369 (1994): 154-156



# SANITATION SYSTEM

- Good Sanitation system
  - Less meat more fiber
  - Adequate fluid intake
- Dietary Fiber
  - Brushes to cleanse intestinal wall
  - Sponges to absorb toxins
- Meat
  - Slowest transit time through bowel

Where's  
the  
Garbage?



## ONLY FIBER FROM WHOLE GRAINS

- Researchers at the National Institutes of Health (NIH)
  - analyzed survey results from a large prospective cohort study called the NIH-AARP Study, which involves more than 291,000 men and 197,000 women aged 50 to 71.
- The scientists analyzed the participant's intake of fiber from many different food sources
  - but only fiber from whole grains was associated with lower risk of colorectal cancer.
  - the fiber one gets from whole grains is different than the fiber one gets from “starchy” foods like white bread and processed cereal



# THE “WHOLE” STORY



- All grains start out as kernels.
  - The bran (outermost layer of the kernel) - most of the fiber is found.
  - The germ (kernel's center) most of the vitamins, minerals, & fatty acids reside.
  - In between lies the endosperm, which contains a few vitamins and minerals and most of the starch.
- **Because the refining process removes the bran and germ, the main component of white bread and other products made from refined grains or white flour is starch.**
  - The reason whole grain products *are* darker and chewier than refined grain products is because all three layers of the kernel are ground together to make whole grain flour. **This provides the kernel's full complement of protein, antioxidants, fatty acids and a host of phytochemicals.**
- **The fiber content of whole grains can be as much as four times that of refined grains.**
- Recently, a Cornell University researcher discovered that whole grains are packed with more antioxidants than was previously expected. These potent health-promoting substances bind directly to the two layers (the germ and the bran) that are discarded in the refining process.



# EAT A VARIETY OF BOTH FIBERS – NOT JUST PSYLLIUM (PILLS OR DRINKS)

## Soluble Fiber

- Promote healthy weight, cholesterol, gall bladder function, and stabilize blood sugar.
- Found in apples, carrots, oats, barley and legumes (lentils, beans, and peas)

## Insoluble Fiber

- Speed up bowel elimination processes, improve bowel function and health.
- Found in stringy and cruciferous vegetables, potatoes, fruits with connective tissues or seeds, wheat bran, brown rice and flax seeds



# RESULTS OF HEALTHIER FIBER INTAKE

- Decrease inflammatory bowel disease flare-ups
- Normalize serum cholesterol levels
- Stabilize blood sugar levels
- Promote weight loss by creating a feeling of fullness
- Speed up elimination and regulate bowel habits
- Decreases the risk of breast, colon, esophagus, mouth, ovarian, pharynx, rectum, stomach and prostate cancers.
- Reduce and/or absorb toxins



# THE AMERICAN DIETETIC ASSOCIATION



- recommends eating 25–35 g of fiber daily
- A person can meet this fiber requirement by
  - **consuming 2-3 servings of fruits and 3-5 servings of vegetables every day**
  - **Using whole grains, rice, and beans**
- To increase fiber intake, a person should eat more of the following high-fiber foods:
  - whole grains, beans, fruits (preferably with skins on), roots and leafy vegetables, broccoli or carrots.
- As an added bonus, he or she will also receive other health benefits provided by the vitamins, minerals, antioxidants and cancer-fighting phytochemicals in these foods.



# HOW TO ADD FIBER TO YOUR DIET

## ○ Start slowly!

- Gradually move from low fiber to high fiber food items. If you progress too quickly, your digestive tract will let you know by causing uncomfortable gas, bloating and cramping.

## ○ Drink fluids!

- You must drink more fluids with fiber rich foods, otherwise you could end up with terrible constipation. Remember, adequate water is necessary to help bulk up the stool for easy passage through the colon.

## ○ Go for the grains!

- Eat brown rice instead of white rice; whole grain flour instead of white. Choose crackers, cereals and breads that contain whole grains like wheat, rye, buckwheat, oats, quinoa, millet or amaranth. Remember that whole grains are more perishable than refined grains because of the oil in the germ. They are best stored in a cool, dry place.

## ○ Crunch that produce!

- Choose fruits and vegetables with edible skins and seeds. Raw, whole foods will contain the most fiber, but you still can derive fiber from frozen or canned produce (but lose vitamins). Juice usually contains very little fiber.

## ○ Lunch on some legumes!

- Dried beans and peas may cause some intestinal gas if you aren't used to eating them. Lentils, split peas and lima beans are most easily digested. Work up to navy, pinto, kidney or black beans and peas.



# DAILY FIBER WORKSHEET HANDOUT

Food group	servings (#)	value	approximate fiber amount (grams)
<b>Whole Grains (serving size)</b> 1 slice whole-wheat bread; 1 ounce whole-grain cereal; 1/2 cup cooked bulgur, brown rice, or other whole-grain; 1/2 bran or whole-grain muffin.	_____	x 2.0 =	_____
<b>Refined grains (serving size)</b> 1 slice white bread; 1/2 cup cooked, white or spinach pasta, white rice or other processed grains; 1/2 bagel, bun or muffin.	_____	x 0.5 =	_____
<b>Breakfast Cereals</b> Check the package for serving size and amount of fiber	_____	x (grams indicated on label)=	_____
<b>Vegetables</b> Serving size: 1/2 cup cooked or chopped raw, or 1 cup raw leafy vegetables.	_____	x 2.0 =	_____
<b>Fruits</b> Serving size: 1 medium size fruit, 1/2 cup canned or chopped raw, 1/2 cup berries, 1/4 cup dried fruit.	_____	x 2.5 =	_____
<b>Beans, lentils, split peas</b> Serving size: 1/2 cup cooked	_____	x 7.0 =	_____
<b>Nuts, seeds</b> Serving size: 1/4 cup seeds or nuts; 2 tbsp. peanut butter.	_____	x 2.5 =	_____



# UNHEALTHY FAT INTAKE

- Obstacle #3



# OMEGA-3 FATTY ACIDS TO AUGMENT CANCER THERAPY

- © 2002 [The American Society for Nutritional Sciences](#) J. Nutr. 132:3508S-3512S, November 2002

**Supplement: International Research Conference on Food, Nutrition & Cancer**

- **Omega-3 Fatty Acids to Augment Cancer Therapy<sup>1</sup>**
- **W. Elaine Hardman<sup>2</sup>**
- *Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA 70808*
- <sup>2</sup>To whom correspondence should be addressed. E-mail: [hardmawe@pbrc.edu](mailto:hardmawe@pbrc.edu) .
- The results of animal studies have demonstrated that the consumption of omega-3 fatty acids can slow the growth of cancer xenografts, increase the efficacy of chemotherapy and reduce the side effects of the chemotherapy or of the cancer. Molecular mechanisms postulated to contribute to the multiple benefits of omega-3 fatty acids include 1) suppressing the expression of cyclooxygenase-2 in tumors, thus decreasing proliferation of cancer cells and reducing angiogenesis in the tumor; 2) decreasing the expression of *AP-1* and *ras*, two oncogenes implicated in tumor promotion; 3) inducing differentiation of cancer cells; 4) suppressing nuclear factor-B activation and *bcl-2* expression, thus allowing apoptosis of cancer cells; and 5) reducing cancer-induced cachexia. It seems reasonable to assume that after appropriate cancer therapy, consumption of omega-3 fatty acids might slow or stop the growth of metastatic cancer cells, increase longevity of cancer patients and improve their quality of life.



# PROMOTING HEALTHY CELL MEMBRANES

## OMEGA 3 VS OMEGA 6

- To perform optimal function the cell membrane must maintain its integrity and fluidity.
  - Cells without a healthy membrane
    - lose their ability to hold water and vital nutrients.
    - lose their ability to communicate with other cells.
  - Researchers believe that loss of cell to cell communication is one of the physiological events that leads to growth of cancerous tumors.



# PROMOTING HEALTHY CELL MEMBRANES

## OMEGA 3 VS OMEGA 6

- Because cell membranes are made up of fat, the integrity and fluidity of our cell membranes are determined in large part by the type of fat we eat.
  - Remember that saturated fats are solid at room temperature, while omega 3 fats are liquid at room temperature. Researchers believe that diets containing large amounts of saturated or hydrogenated fats produce cell membranes that are hard and lack fluidity.
  - On the other hand, diets rich in omega 3 fats produce cell membranes with a high degree of fluidity.



# PROMOTING HEALTHY CELL MEMBRANES

## OMEGA 3 VS OMEGA 6

- In addition, recent *in vitro* (test tube) evidence suggests when omega 3 fatty acids are incorporated into cell membranes they may help to protect against cancer, notably of the breast.
  - They are suggested to promote breast cancer cell apoptosis via several mechanisms including: inhibiting a pro-inflammatory enzyme called cyclooxygenase 2 (COX 2), which promotes breast cancer; activating a type of receptor in cell membranes called peroxisome proliferator-activated receptor (PPAR)- $\alpha$ , which can shut down proliferative activity in a variety of cells including breast cells; and, increasing the expression of BRCA1 and BRCA2, tumor suppressor genes that, when functioning normally, help repair damage to DNA, thus helping to prevent cancer development.



# AMERICAN HEART ASSOCIATION NATIONAL CANCER INSTITUTE

- Both AHA and NCI state eat a diet low in fat.
- By eating only healthy servings of meat and increasing your fruits and vegetables you will naturally lower your fat intake.
- Nutrition labels include fat grams.
  - 12 grams of fat = 1 TBSP butter
  - 96 grams is a stick of butter
  - Burger and medium fry is 50 grams of fat
  - Tuna sandwich w/mayo 55 grams of fat



# OMEGA 6 TO 3 RATIO SHOULD BE 1:1 AMERICANS EAT 20:1

## Omega 3

- **Plant Food Sources**
  - Flax seed 2 tbs **3.56g**
  - Walnuts ¼ cup **2.27g**
  - Soybeans cooked 1 cup **1.03g**
  - Oat germ **1.4g**
  - Spinach, raw **0.9g**
  - Wheat germ **0.7g**
  - Kale, raw **0.2g**
  - Broccoli, raw **0.1g**
- **Fish Sources**
  - Salmon, Pacific 4 oz **2.09g**
  - Shrimp 4 oz **.37g**

## Omega 6

- - Safflower oil
- Sunflower oil
- Corn oil
- Sesame oil
- Hemp oil
- Pumpkin oil
- Soybean oil
- Walnut oil
- Wheat germ oil



# OMEGA 6 TO 3 RATIO SHOULD BE 1:1 AMERICANS EAT 20:1

## Omega 3

- Reduce inflammation
- Maintain healthy cell membranes
- Lower lipids (LDL TG)
- Prevent excessive blood clotting
- Relax and dilate arteries
- Reduce the inflammatory response in the arteries
- Reduce the risk of obesity & improve body's ability to respond to insulin
- Help prevent cancer cell growth

## Omega 6

- Increases inflammatory markers
- Elevate LDL cholesterol
- Encourages blood clotting
- Constricts blood flow
- Increases bronchial constrictions (asthma)
- Produce prostaglandins 2 (PG2) (inflammation)
- May promote cancer cell growth



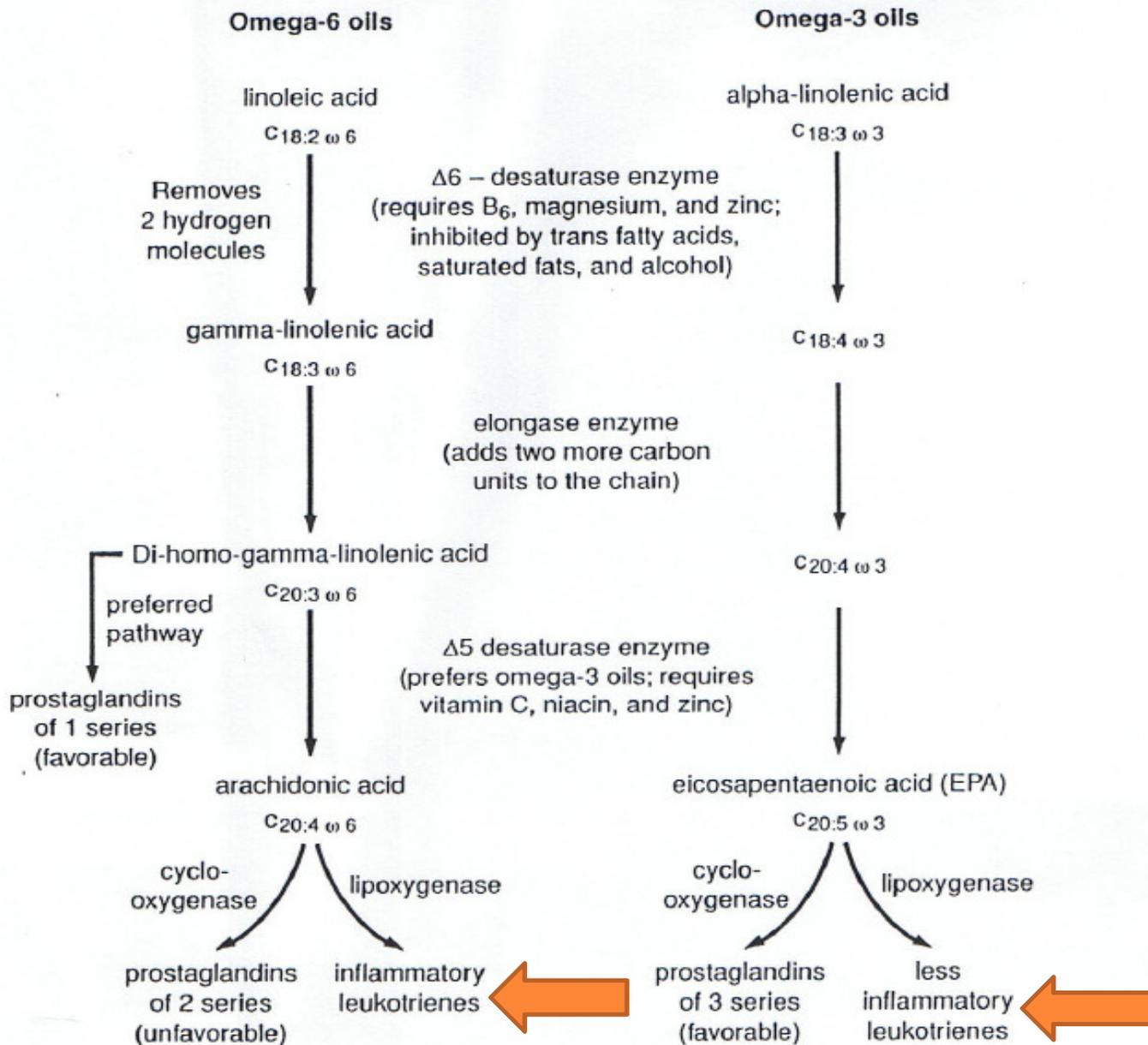


FIGURE 3.1 Prostaglandin metabolism

## OTHER CONDITIONS OR SYMPTOMS INDICATE A NEED FOR MORE HIGH-OMEGA-3 FOODS?

- Depression
- Cardiovascular Disease
- Type 2 Diabetes
- Fatigue

- Dry, itchy skin
- Brittle hair/nails
- Inability to concentrate
- Joint pain





## TRANS FATS

- Basically, *trans* fat is made when manufacturers add hydrogen to vegetable oil—
  - a process called hydrogenation. Hydrogenation increases the shelf life and flavor stability of foods containing these fats.
- *Trans* fat can be found in
  - vegetable shortenings, some margarines, crackers, cookies, snack foods, and other foods made with or fried in partially hydrogenated oils.
- *Trans* fat,
  - like saturated fat and dietary cholesterol, raises the LDL cholesterol that increases your risk for CHD.



# HARVARD SCHOOL OF PUBLIC HEALTH

- The combined results of metabolic and epidemiological studies strongly support an adverse effect of trans fats on Coronary Heart Disease.
- Adverse effect is even stronger than that of saturated fats (animal fat/meat)
- “By our most conservative estimate, replacement of partially hydrogenated fat in the US diet with natural unhydrogenated vegetable oils would prevent approximately 30,000 premature coronary deaths per year, and epidemiologic evidence suggests this number is closer to 100,000 premature deaths annually.”



# TRANS FATS INHIBIT THE BODY'S USE OF OMEGA 3 FATTY ACIDS

## ○ Trans Fat Grams Per Serving In Popular Foods:

- Albertson's brand fruit and grain cereal bars: 1g
- Locos Nachos 1.5 g
- Digiorno microwave pizza: 1.5 g
- Edwards Chocolate Silk Pie: 4 g
- Owens Border Breakfast Tacos: 1g
- Fleischmann's Margarine: 2g
- Ready Crust: 2g
- Betty Crocker cake mix: .5g
- Bisquick: 1.5g
- Betty Crocker's Pour & Frost: 2.5g
- Chips Ahoy: .5 g
- Bear Creek Cheddar Broccoli soup mix: 2g



Look for NO  
TRANS FATS  
on label!!  
NOT ZERO



# TRANS FATS AND PROSTATE CANCER

## HARVARD SCHOOL OF PUBLIC HEALTH

- **A prospective study of blood *trans* fatty acid levels and risk of prostate cancer**
- **Jorge Chavarro, Meir Stampfer, Hannia Campos, Tobias Kurth, Walter Willett and Jing Ma**
- Purpose: Results from two previous studies suggest a positive association between markers of *trans* fatty acid (TFA) intake and prostate cancer. We therefore prospectively evaluated the association between blood TFA levels and risk of prostate cancer. Methods: We conducted a nested case-control study among 14,916 U.S. physicians who provided a blood sample in 1982. Blood samples were frozen at baseline and kept at  $-82^{\circ}\text{C}$  until assayed. Incident prostate cancer cases accrued through 1995 were matched to controls by age, smoking status at baseline and length of follow-up. TFA levels as percentage of total fatty acids were determined for 479 cases and their 491 matched controls using gas chromatography. Cases and controls were divided into quintiles according to the distribution of TFA levels among the controls. Conditional logistic regression models were used to estimate the relative risk (RR) and 95% confidence interval (95% CI) of prostate cancer in a given quintile of TFA level in relation to the lowest quintile. Results: Levels of 16:1, 18:1 and total TFAs were not associated with prostate cancer risk. There was a weak positive association between levels of 18:2 TFAs, which result from the hydrogenation of linoleic acid, and prostate cancer risk. The RRs (95% CI) for men in successively higher quintiles of TFA levels were 0.87 (0.57–1.33), 1.24 (0.83–1.87), 1.69 (1.12–2.55) and 1.24 (0.81–1.88), compared to men in the lowest quintile ( $P_{\text{trend}} = 0.09$ ). The association was similar for the three 18:2 *trans* isomers examined: n-6 *trans trans*(tt), *cis trans*(ct) and *trans cis*(tc). When results were divided according to tumor stage at diagnosis, levels of 18:1, 18:2 and total TFAs were positively related to the risk of developing organ confined, but not advanced, tumors. The RRs (95% CI;  $P_{\text{trend}}$ ) of localized prostate cancer comparing the highest and lowest quintile of TFAs were 2.11 (1.22–3.64; 0.05) for total, 1.85 (1.08–3.16; 0.15) for 18:1, and 1.84 (1.05–3.22; 0.003) for 18:2 TFAs. Similar results were obtained for non-aggressive tumors (organ confined and Gleason 7). The RRs (95% CI;  $P_{\text{trend}}$ ) of non-aggressive prostate cancer comparing extreme quintiles of total, 18:1 and 18:2 TFA levels were 2.47 (1.32–4.63; 0.01), 2.10 (1.13–3.91; 0.06) and 2.29 (1.22–4.30; <0.001), respectively. None of the TFAs explored were associated with advanced (stage C or D) or aggressive tumors (stage C, D, or Gleason > 7). Further adjustment for potential confounders did not substantially change these results. Conclusions: Our prospective data suggests that blood levels of *trans* fatty acids, in particular *trans* fats resulting from the hydrogenation of vegetable oils, are associated with an increased prostate cancer risk. This association appears to be specific to organ confined and non-aggressive tumors.



# HARVARD SCHOOL OF PUBLIC HEALTH, BRIGHAM AND WOMEN'S HOSPITAL

- **Dietary intake of trans fatty acids and systemic inflammation in women.**

Mozaffarian D, Pischon T, Hankinson SE, Rifai N, Joshiपुरa K, Willett WC, Rim EB.

Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA. darymd@hotmail.com

**BACKGROUND: trans Fatty acid (TFA) intake predicts risks of coronary artery disease and diabetes.** Systemic inflammation may be involved in the pathogenesis of such conditions; however, relations between TFA intake and systemic inflammation are not well established. **OBJECTIVE:** We investigated the relations between TFA intake and inflammatory markers. **DESIGN:** In 823 generally healthy women in the Nurses' Health Study I and II, concentrations of soluble tumor necrosis factor alpha receptors 1 and 2 (sTNF-R1, sTNF-R2), interleukin 6 (IL-6), and C-reactive protein (CRP) were measured. Usual dietary intakes assessed from 2 semiquantitative food-frequency questionnaires were averaged for each subject. **RESULTS:** In age-adjusted analyses, TFA intake was positively associated with sTNF-R1 and sTNF-R2 (P for trend < 0.001 for each): sTNF-R1 and sTNF-R2 concentrations were 10% (+108 pg/mL; 95% CI: 50, 167 pg/mL) and 12% (+258 pg/mL; 138, 377 pg/mL) higher, respectively, in the highest intake quintile than in the lowest. These associations were not appreciably altered by adjustment for body mass index, smoking, physical activity, aspirin and nonsteroidal antiinflammatory drug use, alcohol consumption, and intakes of saturated fat, protein, n-6 and n-3 fatty acids, fiber, and total energy. Adjustment for serum lipid concentrations partly attenuated these associations, which suggests that they may be partly mediated by effects of TFAs on serum lipids. TFA intake was not associated with IL-6 or CRP concentrations overall but was positively associated with IL-6 and CRP in women with higher body mass index (P for interaction = 0.03 for each).

**CONCLUSIONS: TFA intake is positively associated with markers of systemic inflammation in women.** Further investigation of the influences of TFAs on inflammation and of implications for coronary disease, diabetes, and other conditions is warranted.



# TRANS FATS INCREASE LEPTIN (“THE FAT HORMONE”)

- HPB (Oxford). 2007;9(2):92-7.
- **Hepato-pancreato-biliary fat: the good, the bad and the ugly.**
- Henry A. Pitt, Professor of Surgery City
- Henry A. Pitt, Indiana University, 535 Barnhill Drive, RT 130D, Indianapolis IN 46202, USA, Phone: +1 317 274 2304, Fax: +1 317 274 4554, Email: [hapitt@iupui.edu](mailto:hapitt@iupui.edu) .
- Obesity has become epidemic in the United States, in Europe, and in many urban areas in the developing world. The globalization of certain 'fast foods' and 'soft drinks' may, in part, be contributing to this epidemic. **Diets high in saturated fatty acids and trans fats as well as drinks that have high fructose corn syrup levels may be particularly harmful.** Recent research suggests that fat is a dynamic endocrine organ and that visceral fat is associated with the metabolic syndrome. Central obesity leads to organ steatosis and altered serum adipokines including reduced adiponectin and markedly elevated leptin. This abnormal adipokine milieu results in increased tissue infiltration of monocytes and macrophages which produce proinflammatory cytokines that alter organ function. **Over many years, the combination of steatosis and local inflammation leads to fibrosis and eventually to cancer.** Nonalcoholic fatty liver disease (NAFLD) is a precursor for nonalcoholic steatohepatitis (NASH). NAFLD and NASH (1) lead to cirrhosis and hepatocellular carcinoma, (2) increase the risk of liver resection, and (3) compromise the outcome of liver transplantation. Similarly, in the pancreas nonalcoholic fatty pancreas disease (NAFPD) may lead to nonalcoholic steatopancreatitis (NASP). NAFPD and NASP may (1) promote the development of chronic pancreatitis and pancreatic cancer, (2) exacerbate the severity of acute pancreatitis, and (3) increase the risk of pancreatic surgery. In the gallbladder nonalcoholic fatty gallbladder disease (NAFGBD, cholecystosteatorosis) may lead to steatocholecystitis. Cholecystosteatorosis may be an explanation for (1) the increased incidence of chronic acalculous cholecystitis and (2) the increased number of cholecystectomies.
- PMID: 18333122 [PubMed - in process]
- **Good human data have shown that patients with breast, endometrial, prostate, and colon cancer have reduced adiponectin and elevated serum leptin levels. Moreover, adiponectin decreases cell growth and angiogenesis whereas leptin promotes these pathogenetic factors. In addition, leptin has been shown to reduce immune function.**



# MAJOR FOOD SOURCES OF TRANS FAT FOR AMERICAN ADULTS

- 40% cakes, cookies, crackers, pies, bread, etc.
- 21% animal products
- 17% margarine
- 8% fried potatoes
- 5% potato chips, corn chips, popcorn
- 4% household shortening
- 3% salad dressing
- 1% breakfast cereal
- 1% candy
  
- Data based on FDA's economic analysis for the final trans fatty acid labeling rule, "Trans Fatty Acids in Nutrition Labeling, Nutrient Content Claims, and Health Claims" (July 11, 2003)



# FOCUS ON HEALTHFUL FATS

DAVID KATZ, M.D., M.P.H., DIRECTOR OF THE YALE  
PREVENTION RESEARCH CENTER

- **High-fat diets appear to impair the immune system**
  - by decreasing the function of T-lymphocytes.
- **Reducing fat, on the other hand, can boost immune function**
  - by enhancing T-lymphocyte function.
  - However, the type of fat you consume is equally important as the amount.
  - Trans fats (found in margarines and many commercial baked goods) can contribute to chronic low-grade inflammation in the body. "The immune system can become tied up dealing with inflammation -- and the damage to cells and tissues that results -- rather than defending the body," Katz says.
- **What to do:**
  - **Limit your total fat intake** to 30 percent of daily calories, with five to 10 percent from saturated fats. For the remaining 20 to 25 percent, look for sources of unsaturated fats, such as canola oil, olive oil, nuts, avocados, and seeds.
  - **And increase your intake of omega-3 fatty acids** (from fatty fish like salmon and sardines), which help fight inflammation and free your immune system to defend against antigens.



# UNHEALTHY SUGAR INTAKE

- Obstacle #4



# UNHEALTHY SUGAR INTAKE

- 100 grams of sugar can reduce immune function for 5-6 hours by 50%<sup>1</sup>
- Sugar intake increases obesity risk. Obesity increases cancer risk.
- Sugar acidifies the body linked to degeneration of tissues.
- Sugar is void of healthy nutrients and replaces healthy food choices.
- Sugar depletes zinc disrupting healthy taste and smell, making other foods taste bland.
- Sugar slows down intestinal transit times leading to constipation and/or poor bowel health.



# UNHEALTHY SUGAR INTAKE

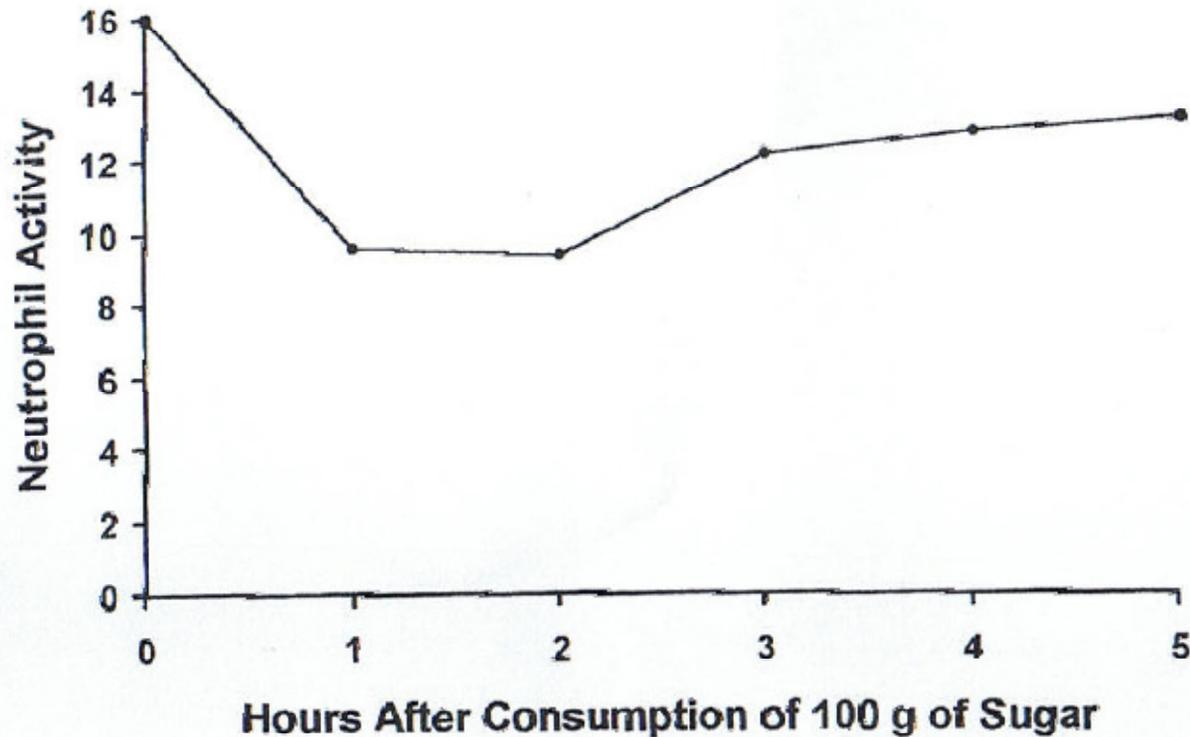


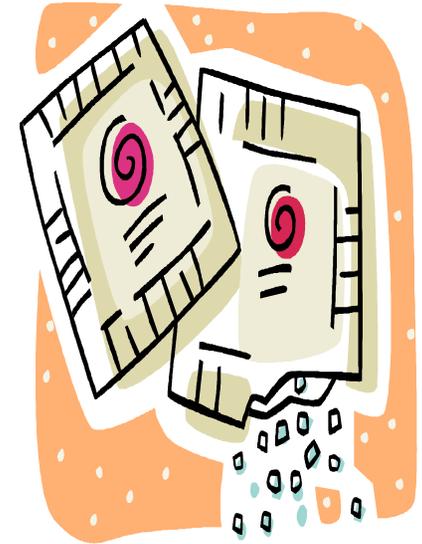
FIGURE 1 The Effects of Sugar on White Cell Phagocytic Activity

1. A. Sanchez, J. Reeves, H. Lau, et al "Role of Sugars in Human Neutrophilic Phagocytosis" *Am J Clin Nutr* 26 (1973):1180-4



# UNHEALTHY SUGAR INTAKE

- 1 packet = 4 grams sugar
- 12 ounce soft drink or juice
  - can contain up to 16 packets of sugar.
- Learn to look for sugar grams on food labels.



CALORIES, FAT & CARBOHYDRATES IN

# SODAS, SOFT DRINKS: COCA-COLA, CLASSIC

[COCA-COLA](#)

Serving Size: 1 x can (12 fl.oz)

Nutrition Facts		
Calories 143 (Kilojoules 599)		
		% DV**
Total Fat	0 g	0%
Sat. Fat	0 g	0%
Trans Fat	0 g	
Cholesterol	0 mg	0%
Sodium	49 mg	2%
Total Carbs.	39.9 g	13%
Dietary Fiber	0 g	0%
Sugars	39.9 g	
Protein	0 g	
Potassium	0 mg	

Note: A dash indicates no data is available.

Look up foods anywhere.  
[Buy our best-selling \\$8 book](#)



Fat 0 cal (0%)  
Carbs. 160 cal (100%)  
Protein 0 cal (0%)

$$39.9 \div 4 = 10 \text{ packets}$$

[Mark favorite](#) | [Add to diary](#) |

## SEARCH FOR MORE FOODS

Search:



The world's largest diabetes research center, diabetes clinic, and provider of diabetes education.

- [Joslin Diabetes Center](#)
- [Joslin Clinical guidelines](#)
- [Locations](#)
- [Contact Joslin](#)

## EXERCISE REQUIRED

To burn the calories in this food you could do any of the following:

- 39 mins of walking
- 16 mins of jogging
- 12 mins of swimming
- 22 mins of cycling

# Based off a 35 year old female that's 5.74ft tall and weighs 144lbs.

[JOIN NOW](#) to get a more accurate calculation based on your measurements



LARGE OJ = 57 GRAMS

MILK SHAKE = 158 GRAMS (40 PACKETS)

Select Category:  
Beverages

Select Menu Item:

1% Partly Skimmed Chocolate Milk - 200 ml

ADD

Menu Items	Serving Size	Calories	Fat (g)	Fat % Daily Value	Saturated Fat (g)	Trans Fat (g)	Saturated Fat - Trans Fat % DV	Cholesterol (mg)	Sodium (mg)	Sodium % DV	Carbohydrates (g)	Carbohydrates % DV	Fibre (g)	Fibre % DV	Sugars (g)	Protein (g)	Vitamin A % DV	Vitamin C % DV	Calcium % DV	
<input type="checkbox"/> <a href="#">Orange Juice - Large***</a>	570ml	280	0	0	0	0	0	5	0	64	21	0	0	57	0	0	340	0	0	
<input type="checkbox"/> <a href="#">Triple Thick Milkshake® - Chocolate, Large</a>	698g	1160	29	45	18	0.5	93	115	860	36	204	68	2	8	158	24	30	6	70	25
<input type="checkbox"/> <a href="#">Barg's® Root Beer - Medium***</a>	495ml	230	0	0	0	0	0	45	2	59	20	0	0	59	0	0	0	0	0	
<input type="checkbox"/> <a href="#">Nestea® Iced Tea - Medium***</a>	495ml	160	0	0	0	0	0	15	1	40	13	0	0	40	0	0	0	0	0	
<input type="checkbox"/> <a href="#">Nescafé Frothy - French Vanilla (Small)</a>	296ml	200	6	9	6	0	30	2	180	8	33	11	0	0	23	3	0	0	10	0
<input type="checkbox"/> <a href="#">Carnation Hot Chocolate (Small)</a>	296ml	190	4	6	3	0	15	0	290	12	39	13	1	4	37	1	0	0	0	6
<input type="checkbox"/> <a href="#">1% Partly Skimmed Milk - 200 ml</a>	200ml	90	2	3	1	0	5	10	95	4	10	3	0	0	10	7	8	0	25	0
<b>Total</b>		<b>2300</b>	<b>41</b>	<b>63</b>	<b>28</b>	<b>0.5</b>	<b>143</b>	<b>125</b>	<b>1500</b>	<b>63</b>	<b>449</b>	<b>150</b>	<b>4</b>	<b>16</b>	<b>384</b>	<b>35</b>	<b>35</b>	<b>350</b>	<b>110</b>	<b>35</b>

\*\*\* Additional minerals (sodium, calcium and iron) may be contributed by local water supply.



# WHERE TO START

- Eliminate high sugar added foods, cola, and juices. No Corn Syrup and high fructose corn syrup.
  - The country eats more sweetener made from corn than from sugarcane or beets, gulping it down in drinks as well as in frozen food and baked goods. Even ketchup is laced with it.
- Eat whole fruits or make smoothie (fruit and ice) drinks out of whole fruits.
  - Limit your consumption of fruit to 2-3 servings so as not to replace other healthy foods such as vegetables and protein foods.
- I suggest do not substitute Artificial sweeteners.



# ASPARTAME - WHY TAKE THE RISK?

- **First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats.**
- **Soffritti M, Belpoggi F, Degli Esposti D, Lambertini L, Tibaldi E, Rigano A.**
- Cesare Maltoni Cancer Research Center, European Ramazzini Foundation of Oncology and Environmental Sciences, Bologna, Italy. [crcfr@ramazzini.it](mailto:crcfr@ramazzini.it)
- The Cesare Maltoni Cancer Research Center of the European Ramazzini Foundation has conducted a long-term bioassay on aspartame (APM), a widely used artificial sweetener. APM was administered with feed to 8-week-old Sprague-Dawley rats (100-150/sex/group), at concentrations of 100,000, 50,000, 10,000, 2,000, 400, 80, or 0 ppm. The treatment lasted until natural death, at which time all deceased animals underwent complete necropsy. Histopathologic evaluation of all pathologic lesions and of all organs and tissues collected was routinely performed on each animal of all experimental groups. The results of the study show for the first time that APM, in our experimental conditions, causes a) an increased incidence of malignant-tumor-bearing animals with a positive significant trend in males ( $p < \text{or} = 0.05$ ) and in females ( $p < \text{or} = 0.01$ ), in particular those females treated at 50,000 ppm ( $p < \text{or} = 0.01$ ); b) an increase in lymphomas and leukemias with a positive significant trend in both males ( $p < \text{or} = 0.05$ ) and females ( $p < \text{or} = 0.01$ ), in particular in females treated at doses of 100,000 ( $p < \text{or} = 0.01$ ), 50,000 ( $p < \text{or} = 0.01$ ), 10,000 ( $p < \text{or} = 0.05$ ), 2,000 ( $p < \text{or} = 0.05$ ), or 400 ppm ( $p < \text{or} = 0.01$ ); c) a statistically significant increased incidence, with a positive significant trend ( $p < \text{or} = 0.01$ ), of transitional cell carcinomas of the renal pelvis and ureter and their precursors (dysplasias) in females treated at 100,000 ( $p < \text{or} = 0.01$ ), 50,000 ( $p < \text{or} = 0.01$ ), 10,000 ( $p < \text{or} = 0.01$ ), 2,000 ( $p < \text{or} = 0.05$ ), or 400 ppm ( $p < \text{or} = 0.05$ ); and d) an increased incidence of malignant schwannomas of peripheral nerves with a positive trend ( $p < \text{or} = 0.05$ ) in males. **The results of this mega-experiment indicate that Aspartame is a multipotential carcinogenic agent, even at a daily doses of 20 mg/kg body weight, much less than the current acceptable daily intake. On the basis of these results, a reevaluation of the present guidelines on the use and consumption of Aspartame is urgent and cannot be delayed.**
- PMID: 16507461 [PubMed - indexed for MEDLINE]



# SUCRALOSE - WHY TAKE THE RISK?

- **Sucralose: assessment of teratogenic potential in the rat and the rabbit.**
- Kille JW, Tesh JM, McAnulty PA, Ross FW, Willoughby CR, Bailey GP, Wilby OK, Tesh SA. *Food Chem Toxicol.* 2000;38 Suppl 2:S43-52. "
- The teratogenic potential [*the potential to cause malformations of an embryo or fetus*] of sucralose was examined . . .There was no evidence of teratogenicity for either species. The only observed response to treatment in rats was a slight increase in water intake. **Some adult rabbits receiving 700mg/kg/day exhibited marked gastrointestinal disturbance. . . considered to be responsible for two maternal deaths and four abortions. . .** .maternal consumption of high levels of sucralose during the period of organogenesis **has no effect on normal fetal development in the rat or rabbit.** "
- **NOTE:** This study was done by McNeil Specialty Products Company, the makers of Sucralose/Splenda.
- One would think that 2 deaths and 4 failed pregnancies in a group of 18 rabbits could be considered an adverse effect.



# SWEETENERS- HEALTHY?

- **Honey, maple syrup, etc.** are still sugars
  - **Agave Nectar (cactus juice)** taste like honey but has 1/10<sup>th</sup> the insulin factor.
- **Fruit Juices**
  - are concentrated sugar or if not concentrated lose fiber and vitamins in processing.
- **Eat the fruit or add fruit to dishes to add sweet flavoring**
  - **but keep fruit intake at healthy intake per your age and body weight as shown in previous charts.**
- **Sugar alcohols (maltitol, sorbitol, etc)**
  - often found in diabetic foods can increase soft stool, gas, or diarrhea.
- **Xylitol**
  - can also cause some gas.
- **Stevia extract**
  - is bitter unless high % of steviolosides. Check the label. Does not cause intestinal issues.



# LACK OF ADEQUATE HEALTHY PROTEIN SOURCES

- Obstacle #5



# PROTEIN- IMMUNE SYSTEM

- Simin Nikbin Meydani, Ph.D., associate director of the Jean Mayer Research Center on Aging at Tufts University in Boston, Massachusetts
  - **The amino acids that are found in protein form the building blocks of all the body's cells – including the cells that power your immune system.** If you don't consume enough protein, you'll manufacture fewer white blood cells.
- **What to do:**
  - **Consume 0.8 to 1 gram** of protein per kilogram(2.2 lbs) of your body weight.
    - ***That means if you weigh 130 pounds, which equals about 59kg, consume at least 47 grams of protein per day.***
  - But remember that quality counts: **To avoid saturated fat, choose 3 to 4 ounce portions of lean protein such as fish, seafood, poultry (without the skin), eggs, lentils, beans, and for some soy products.**



# PROTEIN – IT DOES A BODY GOOD!

- The body uses protein to
  - promote growth
  - repair tissue
  - maintain the lining of the gastrointestinal tract
  - for healthy Skin
  - For healthy white blood cells and the immune system.
- People with cancer who do not get enough protein may be slow to recover from illness and especially vulnerable to infection. After surgery, chemotherapy, or radiation treatments, extra protein is necessary to heal tissues and to help prevent infection.



# THE DIET IS AN IMPORTANT PART OF CANCER TREATMENT



- Eating the right kinds of foods before, during, and after treatment can help the patient feel better and stay stronger. To ensure proper nutrition, a person has to eat and drink enough of the foods that contain key nutrients (vitamins, minerals, protein, carbohydrates, fat, and water).
- For many patients, however, some side effects of cancer and cancer treatments make it difficult to eat well.
  - Symptoms that interfere with eating include anorexia, nausea, vomiting, diarrhea, constipation, mouth sores, trouble with swallowing, and pain. Appetite, taste, smell, and the ability to eat enough food or absorb the nutrients from food may be affected. Malnutrition (lack of key nutrients) can result, causing the patient to be weak, tired, and unable to resist infections or withstand cancer therapies.
  - **Eating too little protein and calories is the most common nutrition problem facing many cancer patients. Protein and calories are important for healing, fighting infection, and providing energy.**



# CANCER CAN CHANGE THE WAY THE BODY USES FOOD- CACHEXIA



- Tumors may produce chemicals that change the way the body uses certain nutrients. The body's use of protein, carbohydrates, and fat may be affected, especially by tumors of the stomach or intestines. A patient may appear to be eating enough, but the body may not be able to absorb all the nutrients from the food. **Diets higher in protein and calories can help correct and prevent the onset of cachexia.** Drugs may also be helpful. It is important to monitor nutrition early, as cachexia is difficult to completely reverse.
- **Drugs may help relieve cancer symptoms and side effects that cause weight loss.**
- Early treatment of cancer symptoms and side effects that affect eating and cause weight loss is important. **Both nutrition therapy and drugs can help the patient maintain a healthy weight.** The types of drugs commonly used to relieve these symptoms and side effects include the following:
  - Medicines to prevent nausea and vomiting.
  - Medicines to prevent diarrhea.
  - Pancreatic enzymes.
  - Laxatives (to promote bowel movements).
  - Medicines for mouth problems (to clean the mouth, stimulate saliva, prevent infections, relieve pain, and heal sores).
  - Pain medications.



# LACK OF PH BALANCE IN FOOD INTAKE

- Obstacle #6



# PH- ACID ALKALINE BALANCE

- Nobel Prize winner Dr. Otto Warburg believes he discovered that cancer cells only thrive in a low-oxygen state
  - When body cells and tissue are ACIDIC (below pH of 6.5 - 7.0), they lose their ability to exchange oxygen
  - Alkaline tissue holds 20 times more oxygen than does acidic tissue
  - Do they require blood flow for oxygen or actually glucose?
  - Does the cell membrane become more selective to resist oxygen and accept glucose?
  - The question remains but we know that a more alkaline diet aligns with a healthy diet.



# PH- ACID ALKALINE BALANCE

- **Dr Warburg believed nearly all those with cancer have high acidity. There are two main reasons for a high acidic body environment.**

## **The first and most significant is prolonged stress.**

- This causes a depletion of adrenaline in the body's cells. It is the job of adrenaline to remove / utilize glucose (sugar) from the body's cells for energy for the body. Depleted adrenaline results in a build up of glucose (sugar) in the body's cells, and restricts oxygen to cells, causing a break in the krebs cycle of the cell and cell mutation. Pathogenic (harmful) microbes (virus, bacteria, fungus) inhabit cancer cells and feed on this glucose causing fermentation. The body becomes acidic (low pH) due to the waste by-products of these pathogenic microbes fermentating glucose in cancer cells and also fermentation of stress hormones.

- **The second is poor nutrition / diet.**

- Every food has a pH value from very acidic to very alkaline. Raw fruits and vegetables are very alkaline, while poor foods, beer, soda, coffee, etc are very acidic. This is why those who eat certain types of foods are more or less at risk of certain types of cancers.



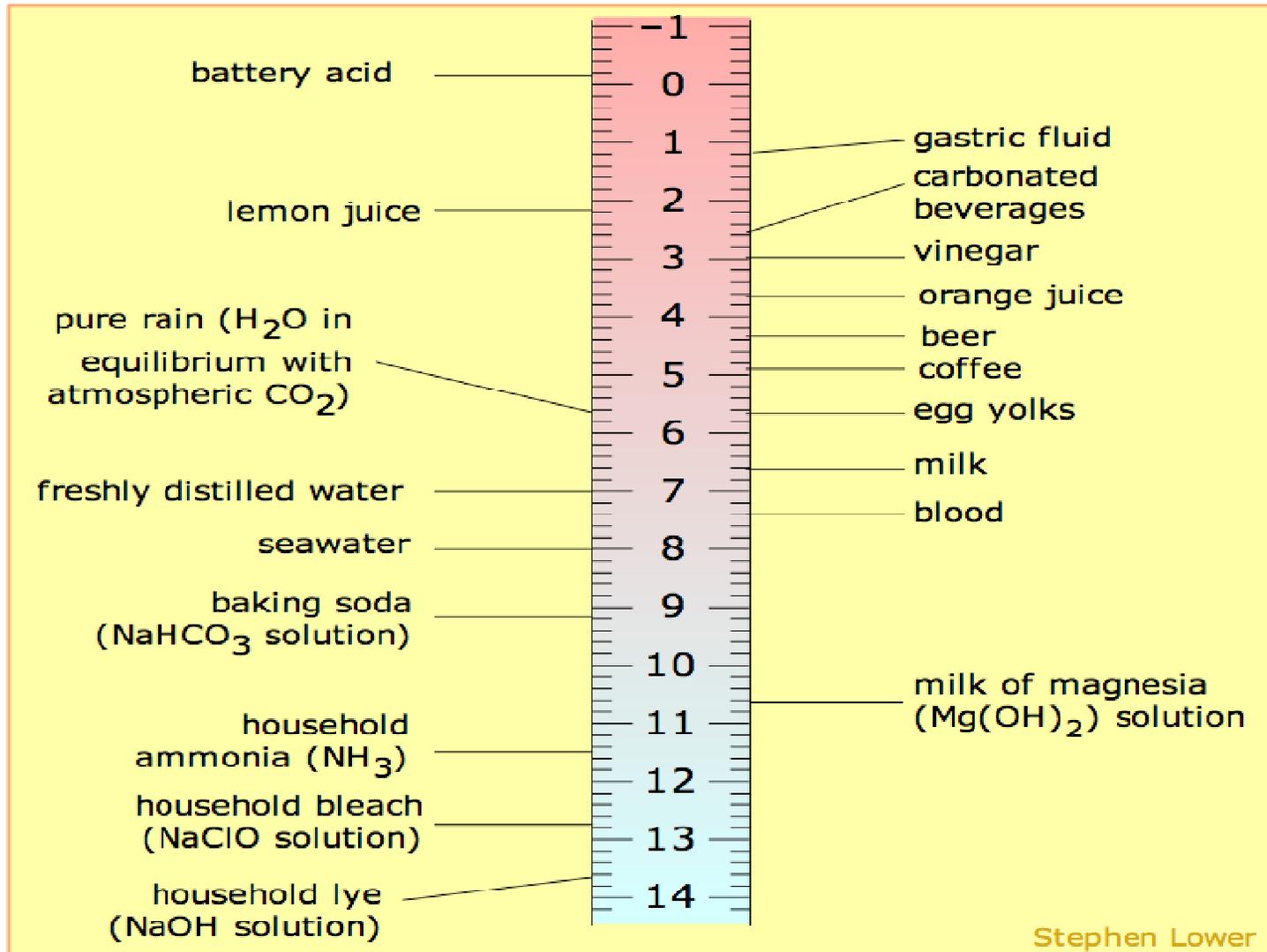
# FOOD CHART

- The human body's metabolic, enzymatic, immunologic, and repair mechanisms function the best in an alkaline environment.
  - The internal environment of our bodies is maintained at a pH of just about 7.0.
  - Maintenance of this state is a dynamic, not static process.
  - Our lungs, kidneys, intestines, and skin are keys to maintaining this healthy pH.
- Most vegetables and fruits contain higher proportions of alkaline forming elements than any other foods.
- Good oxygen intake, water, and minerals also support an alkaline pH.
- For this reason it is important to eat foods that are highly alkaline.
  - Foods are divided into those that are acidic producing and those that are alkaline producing.



# PH SCALE

## SEE HANDOUT



1-6 is  
ACIDIC

7 is  
NEUTRAL

8-14 is  
ALKALINE

Many Fruits  
and  
Vegetables  
are alkaline.



# EFFECT OF DIET ON ACID ALKALINE BALANCE- AMERICAN JOURNAL OF KIDNEY DISEASE

- Am J Kidney Dis. 2002 Aug;40(2):265-74.
- **Effect of low-carbohydrate high-protein diets on acid-base balance, stone-forming propensity, and calcium metabolism.**
- **Reddy ST, Wang CY, Sakhaee K, Brinkley L, Pak CY.**
- Department of Internal Medicine, Section of General Internal Medicine, The University of Chicago, IL 60637, USA. sreddy@medicine.bsd.uchicago.edu
- **BACKGROUND:** Low-carbohydrate high-protein (LCHP) diets are used commonly for weight reduction. This study explores the relationship between such diets and acid-base balance, kidney-stone risk, and calcium and bone metabolism. **METHODS:** Ten healthy subjects participated in a metabolic study. Subjects initially consumed their usual non-weight-reducing diet, then a severely carbohydrate-restricted induction diet for 2 weeks, followed by a moderately carbohydrate-restricted maintenance diet for 4 weeks. **Results:** Urine pH decreased from 6.09 (Usual) to 5.56 (Induction;  $P < 0.01$ ) to 5.67 (Maintenance;  $P < 0.05$ ). Net acid excretion increased by 56 mEq/d (Induction;  $P < 0.001$ ) and 51 mEq/d (Maintenance;  $P < 0.001$ ) from a baseline of 61 mEq/d. Urinary citrate levels decreased from 763 mg/d (3.98 mmol/d) to 449 mg/d (2.34 mmol/d;  $P < 0.01$ ) to 581 mg/d (3.03 mmol/d;  $P < 0.05$ ). Urinary saturation of undissociated uric acid increased more than twofold. Urinary calcium levels increased from 160 mg/d (3.99 mmol/d) to 258 mg/d (6.44 mmol/d;  $P < 0.001$ ) to 248 mg/d (6.19 mmol/d;  $P < 0.01$ ). This increase in urinary calcium levels was not compensated by a commensurate increase in fractional intestinal calcium absorption. Therefore, estimated calcium balance decreased by 130 mg/d (3.24 mmol/d;  $P < 0.001$ ) and 90 mg/d (2.25 mmol/d;  $P < 0.05$ ). Urinary deoxypyridinoline and N-telopeptide levels trended upward, whereas serum osteocalcin concentrations decreased significantly ( $P < 0.01$ ). **CONCLUSION:** **Consumption of a High Protein Low Carbohydrate diet for 6 weeks delivers a marked acid load to the kidney, increases the risk for stone formation, decreases estimated calcium balance, and may increase the risk for bone loss.**
- PMID: 12148098 [PubMed - indexed for MEDLINE]



# LACK OF HEALTHY WATER INTAKE

- Obstacle #7



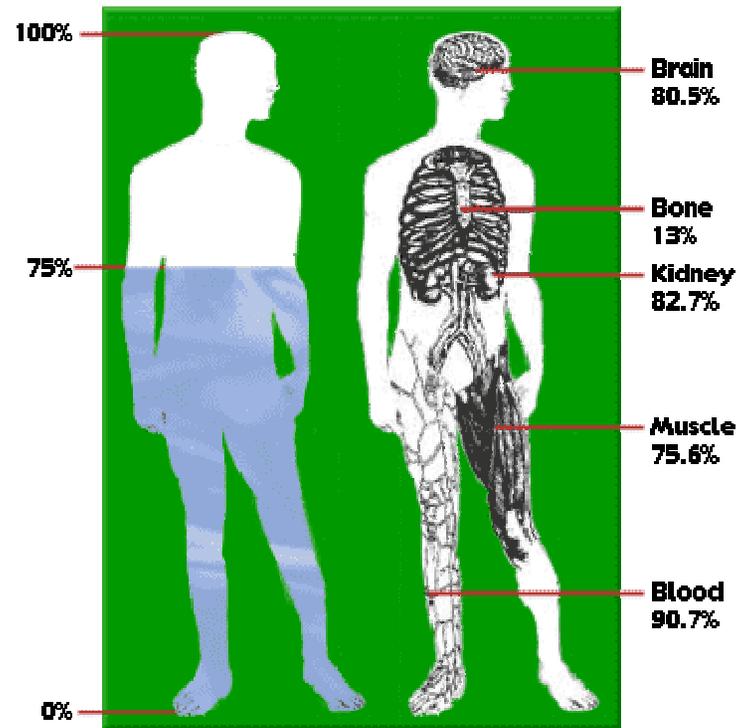
# WATER - THE MOST BASIC CHEMICAL CONSTITUENT OF ALL LIVING ORGANISMS

- **The omni-presence of water throughout the body gives it powerful local and systemic influence over everything that happens within human being to sustain life.**
  - At birth, the body of a full-term baby is 78% water. As we age, that percentage declines to 72% of fat-free body weight for normal young adults and 50% among the elderly.
- **In an average adult weighing 150 pounds the 72% water content amounts to 45 quarts, 30 of which are located within cells (intracellular) and 15 quarts are located outside the cells (extracellular).**
  - Of the 15 quarts of extracellular water, 3 quarts comprise the plasma of the blood.
- With so much water in the human body, we could actually think of it as bags of water walking around on two legs. Optimal hydration is absolutely essential to good health and vitality.
- **The average daily water loss is 2.5 L though natural body processes (e.g., urination, feces, expired breath, sweat).**



# WATER PERCENTAGE IN VARIOUS BODY PARTS:

- Teeth 10%
- Lungs 80%
- Bones 13%
- Brain 80.5%
- Cartilage 55%
- Bile 86%
- Red blood cells 68.7%
- Plasma 90%
- Liver 71.5%
- Blood 90.7%
- Muscle 75%
- Lymph 94%
- Spleen 75.5%
- Saliva 95.5%



# SIGNS AND SYMPTOMS OF DEHYDRATION:

- Fatigue and weakness
- Headaches
- Rough dry skin
- Dry mucus membranes in the nose, mouth, and throat
- Nosebleeds
- Dark, concentrated, strong-smelling urine
- Irritability
- Constipation
- Nausea
- Intestinal and muscle cramps
- Weak, irregular pulse
- Low blood pressure
- Shallow, rapid breathing



# WATER – HOW MUCH

- For healthier detoxification and hydration it is suggested to increase water intake to 2 quarts a day. (Unless you are dealing with kidney issues.)
- Eating healthier food such as fruits and vegetables that also include natural fluids is supportive.
- Consuming caffeine beverages is suspect of reducing fluids, and many suggest not to count caffeine beverages.
  - If you consume 1 cup of caffeine you should also consume an additional cup of water for that day.



# WATER – HOW TO- BEWARE OF MARKETING ADVICE ON FILTERS

## ○ **On the go**

- If you don't take it with you; you probably won't drink it.
- Drink out of glass or stainless steel. Plastic can leach into the water from water bottles and is suspect of being a toxin.

## ○ **Reduce additional exposure to toxins by choosing to reduce chlorine and other chemicals by purification systems:**

- Carbon Filters such as those that fit on your faucet or in a pitcher only REDUCE not ELIMINATE impurities. (also Carbon can store up bacteria. Only certain types of countertop filters have anti bacteria growth.)
- Reverse osmosis loses much water in making filtered water. Steam distillation is lengthy time consuming process. Do your research before purchasing these expensive systems.
- If purchasing bottled water be sure many processes are done. Label will include steam distillation, ozonation, reverse osmosis and/or ultraviolet light. Large cloudy plastic jugs are best as non leaching plastic into the water.
- 10-stage counter top filters best cost value, lowest cost of filter replacement (1 x a year) and are anti bacterial.



# LACK OF MOVEMENT- PHYSICAL ACTIVITY

- Obstacle #8



# PHYSICAL ACTIVITY

- Helps detox the body through sweating
- Moves Lymph fluid
  - The Lymph system is part of your immune defense.
  - Lymph system does not have a system to move it, such as the heart moves blood through the blood vessels. Movement or physical activity is what makes the lymph system move.



# WALKING IMPROVES BREAST CANCER SURVIVAL

- Researchers from Brigham and Women's Hospital and Harvard University drew on the Nurses' Health Study
  - looking at 2296 women with stages I, II, and III breast cancer, diagnosed between 1984 and 1996. Risk of death from breast cancer was reduced 19% in those who walked or did similar exercise 1-3 hours per week, by 54% for walking 3-5 hours per week (30 minutes a day would do it), 42% for those walking 5-7 hours per week (60 minutes a day) and 29% for those putting in over 7 hours of exercise per week.
- **"We were able to show that even a moderate amount of physical activity improved the odds of surviving breast cancer,"** said lead investigator Michelle D. Holmes, M.D., Dr.P.H.
- "It is especially heartening for women recovering from breast cancer to know that the benefit is as readily accessible as walking for 30 minutes on most days of the week."



# EXERCISE REDUCES MARKERS OF CANCER RISK

- Researchers from the Fred Hutchinson Cancer Research Center in Seattle
  - **studied 114 postmenopausal, overweight, sedentary women. They found that moderate exercise reduced markers of cancer risk.** Researchers put the women on a moderate exercise program of 45 minutes a day, five days a week, for a year. They tested them for two blood factors that show inflammation in the body - C-reactive protein (CRP) and serum amyloid A, which have been associated with cancer risk and survival. These factors are often elevated in overweight people.
- "Among obese women, those with a body mass index of 30 or higher," Cornelia M. Ulrich, PhD reported, "concentrations of CRP declined steadily over the course of the year from a baseline of 0.40 milligrams per deciliter to 0.32 milligrams. **This effect of exercise on inflammatory markers may help to explain in part the associations observed between increased physical activity and reduced risk for cancer and other chronic disease.**"



# WALKING REDUCES ENDOMETRIAL CANCER RISKS

- **Walking for 60 minutes a day, or doing housework for 4 hours a day, reduced the risk of endometrial cancer by 30% according to researchers from the Vanderbilt University Medical Center in Nashville.** This is great news for walkers, showing the effects of moderate physical activity.
  - Interestingly, risks weren't reduced if you biked.
  - **"In recent years, we have accumulated strong evidence that an active lifestyle can reduce the risk of colon and breast cancer. Now we are finding that physical activity may also reduce risk of endometrial cancer"** said Charles E. Matthews, Ph.D., of Vanderbilt, the lead author of this report.
- "We were particularly pleased to see the beneficial effect on endometrial cancer risk of more accessible and lower intensity forms of activity like walking for transportation and doing household chores, as well as intentional exercise," he added. "Our results support the idea that the risk of cancer can be reduced by maintaining an active lifestyle."



# LACK OF SUNSHINE VITAMIN D

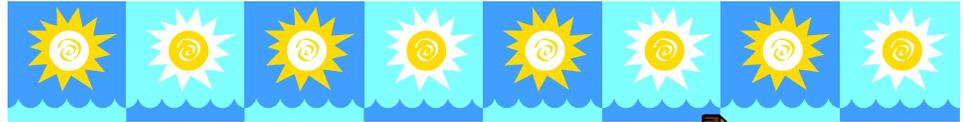
- Obstacle #9



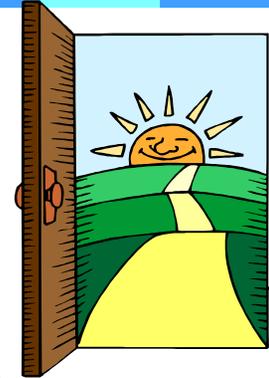
# SUNSHINE VITAMIN CANCER PREVENTION?

- Curr Med Res Opin. 2008 Jan;24(1):139-49.
- **Molecular basis of the potential of vitamin D to prevent cancer.**
- **Ingraham BA, Bragdon B, Nohe A.**
- University of Maine, Orono, ME 04469-5737, USA. bingraham@umche.maine.edu
- OBJECTIVE: To review current research findings in cell biology, epidemiology, preclinical, and clinical trials on the protective effects of vitamin D against the development of cancers of the breast, colon, prostate, lung, and ovary. Current recommendations for optimal vitamin D status, the movement towards revision of standards, and reflections on healthy exposure to sunlight are also reviewed. Search methodology: A literature search was conducted in April and updated in September 2007. **The Medline and Web of Knowledge databases were searched for primary and review articles published between 1970 and 2007,** using the search terms 'vitamin D', 'calcitriol', 'cancer', 'chemoprevention', 'nuclear receptor', 'vitamin D receptor', 'apoptosis', 'cell cycle', 'epidemiology', and 'cell adhesion molecule'. Articles that focused on epidemiological, preclinical, and clinical evidence for vitamin D's effects were selected and additional articles were obtained from reference lists of the retrieved articles. FINDINGS: **An increasing body of research supports the hypothesis that the active form of vitamin D has significant, protective effects against the development of cancer. Epidemiological studies show an inverse association between sun exposure, serum levels of 25(OH)D, and intakes of vitamin D and risk of developing and/or surviving cancer.** The protective effects of vitamin D result from its role as a nuclear transcription factor that regulates cell growth, differentiation, apoptosis and a wide range of cellular mechanisms central to the development of cancer. A significant number of individuals have serum vitamin D levels lower than what appears to protect against cancer, and the research community is currently revising the guidelines for optimal health. This will lead to improved public health policies and to reduced risk of cancer. CONCLUSIONS: Research strongly supports the view that efforts to improve vitamin D status would have significant protective effects against the development of cancer. The clinical research community is currently revising recommendations for optimal serum levels and for sensible levels of sun exposure, to levels greater than previously thought. Currently, most experts in the field believe that intakes of between 1000 and 4000 IU will lead to a more healthy level of serum 25(OH)D, at approximately 75 nmol/L that will offer significant protection effects against cancers of the breast, colon, prostate, ovary, lungs, and pancreas. The first randomized trial has shown significant protection against breast cancer, and other clinical trials will follow and ultimately lead to improved public health policies and significantly fewer cancers.





## WALKING AND SUNSHINE COMBINED



- Both physical activity and another important factor (Sunshine Vitamin) can be obtained by daily walking outside.
  - Getting Sunshine Vitamin does not mean getting sun-burned.
  - Antioxidants have shown to protect the skin.
- Use sunscreen with pro-longed exposure.
- Get professional advice about exposure!



# LACK OF HEALTHY SLEEP

- Obstacle #10



# LIGHT AT NIGHT- NIGHT SHIFT WORKERS

- Several studies, beginning in the 90's, found that nurses who had worked night shift for many years had approximately double the incidence of breast cancer as nurses who had not worked night shift.
- Human beings, kept in darkness, make melatonin about 10 hours a night according to a Harvard study. Most Americans only make melatonin for 6 or 7 hours a night. Exposure to light reduces melatonin production.



# SLEEP HYGIENE- MANY FACTORS AFFECT

- To promote rest and treat sleep disorders the following may be considered:
- **Create an environment that decreases sleep interruptions by:**
  - **Lowering noise.**
  - **Dimming or turning off lights.**
  - **Adjusting room temperature.**
  - Keeping bedding, chairs, and pillows clean, dry, and wrinkle-free.
  - Using bedcovers for warmth.
  - Placing pillows in a supportive position.
  - Encouraging the patient to dress in loose, soft clothing.
- **Encourage regular bowel and bladder habits to minimize sleep interruptions, such as**
  - No drinking before bedtime.
  - Emptying the bowel and bladder before going to bed.
  - Increasing consumption of fluids and fiber during the day.
  - Taking medication for incontinence before bedtime.
- Rest in patients with cancer may also be promoted by:
- **Eating a high- protein snack 2 hours before bedtime.**
- **Avoiding heavy, spicy, or sugary foods 4 to 6 hours before bedtime.**
- **Avoiding drinking alcohol or smoking 4 to 6 hours before bedtime.**
- **Avoiding drinks with caffeine.**
- **Exercising (which should be completed at least 2 hours before bedtime).**
- **Keeping regular sleeping hours.**



# SLEEP HYGIENE



- The most common reasons for sleep disruption
  - LIGHT-
    - shuts down sleep chemical – melatonin
    - Eyelids even when closed can allow some light in
    - From outside (streetlights) or inside (hall lights, nightlights)
  - NOISE
    - Any noise louder than the noise you hear upon going to sleep will alert the brain
    - White noise or ear plugs often used if un-avoidable
  - URINATION
    - Do not consume beverages within 1-2 hours before bedtime and void several times before retiring to bed
  - CAFFEINE
  - ROOM TEMPERATURE
    - hot room and/or cold feet



# POOR SLEEP ALTERS HORMONES THAT INFLUENCE CANCER CELLS

- SOURCES: Sephton, S. *Brain, Behavior and Immunity*, October 2003; vol 17: pp 321-328. David Spiegel, MD, the Jack, Lulu and Sam Wilson Professor in the School of Medicine; associate chairman, department of psychiatry and behavioral sciences, Stanford University Medical Center, Stanford, Calif. Len Lichtenfeld, MD, deputy chief medical officer, the American Cancer Society, Atlanta. WebMD Medical News: "Does Stress Cause Breast Cancer?"
- By [Sid Kirchheimer](#) WebMD Medical News
- Oct. 1, 2003 -- **A new study shows that how well you sleep may determine how well your body fights cancer -- and may help explain how mental well-being plays into cancer recovery and progression.**
- After analyzing previous studies, Stanford University psychiatrist David Spiegel, MD, and colleague Sandra Sephton, MD, say that sleep problems alter the balance of at least two hormones that influence cancer cells.
- One is cortisol, which helps to regulate immune system activity –
  - including the release of certain "natural killer" cells that help the body battle cancer. Cortisol levels typically peak at dawn, after hours of sleep, and decline throughout the day.
  - Spiegel tells WebMD that night shift workers, who have higher rates of breast cancer than women who sleep normal hours, are more likely to have a "shifted cortisol rhythm," in which their cortisol levels peak in the afternoon. At least two studies show those women typically die earlier from breast cancer.
  - We also found that people who wake up repeatedly during the night are also more likely to have abnormal cortisol patterns.
  - Cortisol is the so-called "stress" hormone triggered, along with others, during times of anxiety and may play a role in the development and worsening of cancer and other conditions.
- The other hormone affected by sleep is melatonin.
  - Produced by the brain during sleep, melatonin may have antioxidant properties that help prevent damage to cells that can lead to cancer.
  - In addition, melatonin lowers estrogen production from the ovaries. Thus, a lack of sleep leads to too little melatonin. This series of events may expose women to high levels of estrogen and may increase the risk of breast cancer.
  - Spiegel says that women shift workers who are up all night produce less melatonin.
- **"There's a definite hormonal pattern that is affected by sleep that in itself, can predict a more rapid progression of cancer,"**



# LACK OF SLEEP AFFECTS WEIGHT-

- **studies show weight begins to increase beginning with those who average less than 7 hours of sleep a night.** Since 2000, 13 large population studies have linked less sleep with higher weight. Those who are most severely obese are one of the few exceptions. This is most likely because sleep apnea (breathing difficulty during sleep) and other sleep disorders caused by obesity may leave people so tired that they sleep more hours. Adults over 50 years old may be another exception. It is not clear whether older adults need less sleep, or if the effects of inadequate sleep are hidden among other health issues in this group.

Several studies show that lack of sleep seems to change the levels of two appetite-related hormones.

- A hormone called ghrelin that stimulates appetite may increase
  - The hormone leptin that tells our body we have had enough food may decrease Together these changes would lead us to feel we need to eat more, even when we may have consumed all the calories we need. Some research suggests that other hormones, including those affecting blood sugar, may also be affected by lack of sleep.
- National Sleep Foundation Report
    - at least 2/3 of adults say sleepiness interferes with their concentration and ability to handle stress. That means that we may be more likely to eat in an effort to increase energy or cope with stress. When we are not well rested, we may not exercise at all or exercise at a lower intensity.



## SUPPLEMENTAL SUPPORT

- Use or Misuse of Supplementation



# ONCOLOGY

FEBRUARY 2007 • VOLUME 21 NUMBER 2

- Upward Trend in Liver Cancer Deaths Despite Decline in Deaths From Other Cancers
- ..... in order to drive down rates of liver cancer, we urge Americans to focus immediately on liver wellness. Only when we stop the growth of liver disease in America can we slow down the increase in liver cancer.



# IMMUNE SYSTEM - LIVER

- **Milk Thistle**
- **Background and Health Claims**

The milk thistle plant, also known as marian thistle, is native to Europe. The ripe fruits, often called seeds, are the medicinal portion of the plant.
- **Milk thistle is being studied for its liver protecting effects and anticancer activity.** Flavolignans (especially silymarin) are the compounds in milk thistle that provide protection against a variety of toxins that may damage the liver, including poisonous mushrooms, ethanol (found in alcoholic beverages) and carbon tetrachloride (a solvent used in pharmaceutical preparation).
- Silymarin and other flavolignans seem to protect undamaged liver cells by acting on the cell membranes to prevent the entry of toxins. Milk thistle also stimulates protein synthesis, which accelerates cell regeneration within the liver. It is believed to have antioxidant properties.
- In two studies using mice, topical application of milk thistle after exposure to ultraviolet B sun rays reduced the effects of a carcinogen known to promote skin cancer. A third study found that another component of milk thistle (flavonoid silibinin), given before chemotherapy with the drug cisplatin, significantly decreased toxic effects in the kidneys of rats without inhibiting the therapy's antitumor activity.
- **Precautions**

At this time, no adverse effects have been associated with milk thistle use. However, occasional mild laxative effects and allergic reactions have been observed. Milk thistle is not recommended for patients with liver damage known as decompensated cirrhosis.
- **Milk thistle may be useful for patients receiving chemotherapy agents that are especially toxic to the kidney or liver;** however, controlled human studies are needed to determine the effects of milk thistle's long-term use.
- Milk thistle tea is considered an ineffective form.
- **Dose**

The reported adult dose of milk thistle is 12-15 g of seeds daily, or an equivalent formulation of 200-400 mg silymarin, calculated as silybin.



# LIVER SUPPORT

- Cancer Res. 2008 Mar 15;68(6):2043-50. Links
- **Silibinin inhibits colorectal cancer growth by inhibiting tumor cell proliferation and angiogenesis.**
- **Singh RP, Gu M, Agarwal R.**
- Department of Pharmaceutical Sciences, School of Pharmacy, University of Colorado Denver, CO 80262, USA.
- Herein, for the first time, we investigated in vivo efficacy and associated molecular biomarkers and mechanisms of a chemopreventive agent, silibinin, against human colorectal carcinoma (CRC) HT29 xenograft growth. Nude mice were implanted with HT29 cells and fed with vehicle (carboxymethyl cellulose or phosphatidylcholine) or 200 mg/kg/d dose of silibinin or 100 and 200 mg/kg/d doses of silybin-phytosome (5 days per week) for 32 days. **Silibinin inhibited tumor growth that accounted for 48% (P = 0.002) decrease in tumor volume and 42% (P = 0.012) decrease in tumor weight at the end of the experiment without any adverse health effect.** A stronger antitumor efficacy was observed with silybin-phytosome preparation. Silibinin decreased proliferation index by 40% (P < 0.001), increased apoptotic index by approximately 2-fold (P = 0.001), and reduced microvessel density by 36% (P = 0.001) in tumors. Antiproliferative and proapoptotic effects of silibinin were associated with down-regulation of extracellular signal-regulated kinase 1/2 (ERK1/2) and Akt phosphorylation as well as cyclin D1 expression. Antiangiogenic effect of silibinin was coupled with a strong decrease in inducible nitric oxide synthase (NOS) and NOS3, cyclooxygenase-1 (COX-1) and COX-2, and hypoxia-inducing factor-1 alpha (HIF-1 alpha) and vascular endothelial growth factor (VEGF). These findings suggest in vivo antitumor efficacy of silibinin against CRC involving its antiproliferative, proapoptotic, and antiangiogenic activities. The inhibition of ERK1/2 and Akt signaling may account for antiproliferative and proapoptotic effects, whereas down-regulation of NOS, COX, HIF-1 alpha, and VEGF expression could lead to antiangiogenic effect of silibinin against CRC. Overall, potential use of silibinin against human CRC could be suggested.
- PMID: 18339887 [PubMed - indexed for MEDLINE]



# SILIBININ- HUMAN PROSTATE CARCINOMA

- Int J Cancer. 2003 Sep 20;106(5):699-705. Links
- **Silibinin sensitizes human prostate carcinoma DU145 cells to cisplatin- and carboplatin-induced growth inhibition and apoptotic death.**
- [Dhanalakshmi S](#), [Agarwal P](#), [Glode LM](#), [Agarwal R](#).
- Department of Pharmaceutical Sciences, School of Pharmacy, University of Colorado Health Sciences Center, Denver, CO 80262, USA.
- **In several recent studies, we have shown that silibinin inhibits the growth of human prostate cancer cells (PCA) both in vitro and in vivo.** Here, we investigated the effect of silibinin in combination with cisplatin and carboplatin on human PCA DU145 cell growth and apoptosis. Cisplatin alone at 2 microg/ml dose produced 48% cell growth inhibition, whereas a combination with 50-100 microM silibinin resulted in 63-80% ( $p < 0.05-0.001$ ) growth inhibition. Similarly, compared to 68% growth inhibition at 20 microg/ml carboplatin, addition of 50-100 microM doses of silibinin caused 80-90% inhibition ( $p < 0.005-0.001$ ). In the studies assessing the effect of these combinations on cell cycle progression, a combination of cisplatin or carboplatin with silibinin resulted in a stronger G2-M arrest, compared to these agents alone showing a moderate G2-M and G1 arrests in case of cisplatin and silibinin, and a complete S phase arrest with carboplatin, respectively. A stronger G2-M arrest by these combinations was accompanied by a substantial decrease in the levels of cdc2, cyclin B1 and cdc25C. Silibinin/platinum compound combinations were also effective in inducing apoptosis where cisplatin and carboplatin when combined with silibinin enhanced apoptosis from 8 to 15% and from 20 to 40%, respectively. Apoptosis induction was further confirmed by PARP and caspases 3, 9 and 7 whose cleaved levels were also enhanced by combination treatment. In addition, there was a significant increase in cytochrome c release in the cytosol following treatment of DU145 cells with these combinations. **Together, these results show a substantial increase in the efficacy of platinum compounds on human PCA cells, when combined with silibinin,** which provide a rationale for further investigations with these combinations. Copyright 2003 Wiley-Liss, Inc.
- PMID: 12866029 [PubMed - indexed for MEDLINE]



# SILYMARIN/ SILIBIN FROM MILK THISTLE

- The most beneficial component in milk thistle is silymarin, a mixture of flavonoids with a long history of liver support.\*<sup>2-4</sup>
  - Supports the health of Kupffer cells, specialized liver cells responsible for removing bacteria, old blood cells, and other foreign matter from the liver's blood supply.\*<sup>1-4</sup>
  - Scavenges free radicals (superoxide anion radical and nitric oxide) produced by activated Kupffer cells, supports healthy leukotriene levels, and supports glutathione production that is used in detoxification.\*<sup>2-5</sup>
  - Silymarin also supports the health of hepatocytes, highly versatile liver cells with unique physiologic functions.\*<sup>1-4</sup>
  - Studies of silymarin have demonstrated that it supports the health of the hepatocyte outer membrane, which is crucial to the liver's detoxification processes.\*<sup>6</sup>
  - Silymarin also supports the healthy regenerative ability of the liver through support of protein synthesis in the hepatocytes.\*<sup>7</sup>
- The use of silymarin in several clinical studies has established silymarin's safety in particular and milk thistle's safety as a whole.\*<sup>8-13</sup>
- **Concomitant use of Silymarin and other compounds in milk thistle with chemotherapeutic agents has been examined.\*<sup>14</sup>** Researchers have also studied milk thistle's safety and support of liver health in a variety of health situations.\*<sup>15-22</sup>



# SILYMARIN/ SILIBIN FROM MILK THISTLE

## REFERENCES

1. Porth CM. The liver and hepatobiliary system. In: *Pathophysiology: Concepts of Altered Health States*. 5th ed. Philadelphia, Pa: Lippincott; 1998:745-753.
2. Milk thistle. In: Fleming T., ed. *PDR® for Herbal Medicines*. Montvale, NJ: Medical Economics Company; 2000: 516-520.
3. Milk thistle fruit. In: Blumenthal M, Goldberg A, Brinckmann J., ed. *Herbal Medicine. Expanded Commission E Monographs*. Austin, Tex: American Botanical Council; Integrative Medicine Communications; 2000: 257-263.
4. Robbers JE, Tyler VE. Milk thistle. In: *Tyler's Herbs of Choice*. Binghamton, NY: The Haworth Herbal Press; 1999: 76-79.
5. Dehmlow C, Erhard J, de Groot H. Inhibition of Kupffer cell functions as an explanation for the hepatoprotective properties of silibinin. *Hepatology*. 1996;23:749-54.
6. Gonzalez-Correa JA, de la Cruz JP, Gordillo J, Urena I, Redondo L, Sanchez de la Cuesta F. Effects of silymarin MZ-80 on hepatic oxidative stress in rats with biliary obstruction. *Pharmacology*. 2002;64:18-27.
7. Dvorak Z, Kosina P, Walterova D, Simanek V, Bachleda P, Ulrichova J. Primary cultures of human hepatocytes as a tool in cytotoxicity studies: cell protection against model toxins by flavonolignans obtained from *Silybum marianum*. *Toxicol Lett*. 2003;137:201-12.
8. Wellington K, Jarvis B. Silymarin: a review of its clinical properties in the management of hepatic disorders. *BioDrugs*. 2001;15:465-489.
9. Savio D, Harrasser PC, Basso G. Softgel capsule technology as an enhancer device for the absorption of natural principles in humans. A bioavailability cross-over randomised study on silybin. *Arzneimittelforschung*. 1998;48:1104-1106.
10. Buzzelli G, Moscarella S, Giusti A, et al. A pilot study on the liver protective effect of silybin-phosphatidylcholine complex (IdB 1016) in chronic active hepatitis. *Int J Clin Pharmacol Ther Toxicol*. 1993;31:456-460.
11. Buzzelli G, Moscarella S, Giusti A, Duchini A, Marena C, Lampertico M. A pilot study on the liver protective effect of silybin-phosphatidylcholine complex (IdB1016) in chronic active hepatitis. *Int J Clin Pharmacol Ther Toxicol*. 1993;31:456-460.



# SILYMARIN/ SILIBIN FROM MILK THISTLE

## REFERENCES

12. Pares A, Planas R, Torres M, et al. Effects of silymarin in alcoholic patients with cirrhosis of the liver: results of a controlled, double-blind, randomized and multicenter trial. *J Hepatol.* 1998;28:615–621.
13. Ferenci P, Dragosics B, Dittrich H, et al. Randomized controlled trial of silymarin treatment in patients with cirrhosis of the liver. *J Hepatol.* 1989;9:105–113.
14. Bokemeyer C, Fels LM, Dunn T, et al. Silibinin protects against cisplatin-induced nephrotoxicity without compromising cisplatin or ifosfamide anti-tumour activity. *Br J Cancer.* 1996;74:2036-2041.
15. Masini A, Ceccarelli D, Giovannini F, Montosi G, Garuti C, Pietrangelo A. Iron-induced oxidant stress leads to irreversible mitochondrial dysfunctions and fibrosis in the liver of chronic iron-dosed gerbils. The effect of silybin. *J Bioenerg Biomembr.* 2000;32:175-82.
16. Shear NH, Malkiewicz IM, Klein D, Koren G, Randor S, Neuman MG Acetaminophen-induced toxicity to human epidermoid cell line A431 and hepatoblastoma cell line Hep G2, in vitro, is diminished by silymarin. *Skin Pharmacol.* 1995;8:279-291.
17. Muriel P, Garciapina T, Perez-Alvarez V, et al. Silymarin protects against paracetamol-induced lipid peroxidation and liver damage. *J Appl Toxicol.* 1992;12:439–442.
18. Vogel G, Tuchweber B, Trost W, Mengs U. Protection by silibinin against Amanita phalloides intoxication in beagles. *Toxicol Appl Pharmacol.* 1984;73:355-362.
19. Carducci R, Armellino MF, Volpe C, Basile G, Caso N, Apicella A, Basile V. Silibinin and acute poisoning with Amanita phalloides. *Minerva Anesthesiol.* 1996;62:187-193.
20. Sierralta A, Jeria ME, Figueroa G, et al. Mushroom poisoning in the IX region. Role of Amanita gemmata. *Rev Med Chil.* 1994;122:795-802.
21. Rambousek V, Janda J, Sikut M. Severe Amanita phalloides poisoning in a 7-year-old girl *Cesk Pediatr.* 1993;48:332-333.
22. Szilard S, Szentogyorgyi D, Demeter I. Protective effect of Legalon in workers exposed to organic solvents. *Acta Med Hung.* 1988;45:249–256.



# MILK THISTLE SUPPLEMENTATION

- Milk Thistle is only beneficial if:
  - standardized for its active components to be effective (silymarin/silibin)
  - in a phytosome form to saturate liver cells
  - Guaranteed quality and quantity pill to pill
  - **MUST WORK WITH YOUR INDIVIDUAL TREATMENT PROGRAM**



# PROBIOTICS

- In 1905, Dr Elie Metchnikoff, a Russian scientist working at the famous Institut Pasteur in Paris, was the first to write about the health benefits of probiotics.
  - Dr Metchnikoff, who later won a Nobel Prize for his research on the immune system, wrote that Bulgarian peasants who consumed large amounts of yogurt lived long healthy lives. Examination of the yogurt by Dr Metchnikoff led to his discovery of a unique lactic acid producing bacteria that helped digestion and improved the immune system.\*<sup>1</sup>
- **Investigations during the past several decades have demonstrated numerous health supportive properties of probiotics on human health.\*<sup>1-4</sup>**
- Numerous strains of probiotic microflora reside on the walls of the small intestine ( $10^6$ - $10^8$ /gram of small intestinal contents); even more are present in the colon ( $10^{11}$ - $10^{12}$ /gram of colon contents). Intestinal microflora promotes healthy bacterial and yeast balance and stimulates certain immune system components.\*<sup>4</sup>
- There are over 400 different species in the human gastrointestinal tract.

1. Goossens D, Jonkers D, Stobberingh E, van den Bogaard A, Russel M, Stockbrugger R. Probiotics in gastroenterology: indications and future perspectives. *Scand J Gastroenterol Suppl.* 2003;(239):15-23.
2. Isolauri E. Probiotics in human disease. *Am J Clin Nutr.* 2001;73:1142S-1146S.
3. The United States Probiotics Organization. What are probiotics? Accessed on August 1, 2007. Available at: <http://www.usprobiotics.org/index.htm>
4. Porth CM. Gastrointestinal tract function. In: *Pathophysiology: Concepts of Altered Health States.* 7th ed. Philadelphia, Pa: Lippincott; 2004:617-622.



# PROBIOTICS AND IMMUNE SUPPORT

- *Lactobacillus acidophilus* and *Bifidobacterium longum* have been shown to possess immuno-protective and immuno-modulatory properties.
- These benefits include modulation of:
  - cytokine and various interleukin production
  - autoimmunity
  - natural killer cell cytotoxicity
  - lymphocyte proliferation
  - antibody production.\*<sup>1</sup>
- In an open, randomized, controlled trial, *Lactobacillus acidophilus* and *Bifidobacterium bifidum* were supportive of colon health in older adults.\*
  - **B cell (important antibody producing immune cells) levels increased as compared with the untreated group.\*<sup>2</sup>**
  - The probiotics were very well tolerated, with no significant side effects or variations in clinical chemistry or hematologic parameters.<sup>2</sup>

1. Famularo C, Moretti S, Marcellini, De Simone C. Stimulation of immunity by probiotics. In: Fuller, R ed. *Probiotics 2 Applications and Practical Aspects*. London, England: Chapman & Hall; 1997:133-161.
2. Gibson GR, Saavedra JM, Macfarlane S, Macfarlane GT. Probiotics and intestinal infections. In: Fuller, R ed. *Probiotics 2 Applications and Practical Aspects*. London, England: Chapman & Hall; 1997:10-39.



# PROBIOTICS AND RADIATION INDUCED DIARRHEA PREVENTION

- World J Gastroenterol. 2007 Feb 14;13(6):912-5. Links
- **Use of probiotics for prevention of radiation-induced diarrhea.**
- [Delia P](#), [Sansotta G](#), [Donato V](#), [Frosina P](#), [Messina G](#), [De Renzis C](#), [Famularo G](#).
- Institute of Radiology, Oncologic Radiotherapy Unit, Azienda Ospedaliera Universitaria, Messina, Italy.
- AIM: To investigate the efficacy of a high-potency probiotic preparation on prevention of radiation-induced diarrhea in cancer patients. METHODS: This was a double-blind, placebo-controlled trial. Four hundred and ninety patients who underwent adjuvant postoperative radiation therapy after surgery for sigmoid, rectal, or cervical cancer were assigned to either the high-potency probiotic preparation VSL#3 (one sachet t.i.d.) or placebo starting from the first day of radiation therapy. Efficacy endpoints were incidence and severity of radiation-induced diarrhea, daily number of bowel movements, and the time from the start of the study to the use of loperamide as rescue medication. RESULTS: More placebo patients had radiation-induced diarrhea than VSL#3 patients (124 of 239 patients, 51.8%, and 77 of 243 patients, 31.6%;  $P<0.001$ ) and more patients given placebo suffered grade 3 or 4 diarrhea compared with VSL#3 recipients (55.4% and 1.4%,  $P<0.001$ ). Daily bowel movements were 14.7 +/- 6 and 5.1 +/- 3 among placebo and VSL#3 recipients ( $P<0.05$ ), and the mean time to the use of loperamide was 86 +/- 6 h for placebo patients and 122 +/- 8 h for VSL#3 patients ( $P<0.001$ ). CONCLUSION: **Probiotic lactic acid-producing bacteria are an easy, safe, and feasible approach to protect cancer patients against the risk of radiation-induced diarrhea.**
- PMID: 17352022 [PubMed - indexed for MEDLINE]



# PROBIOTICS AND BREAST CANCER

- Breast Cancer Res. 2005;7(4):R477-86. Epub 2005 Apr 26. Links
- **Effects of milk fermented by *Lactobacillus helveticus* R389 on a murine breast cancer model.**
- **de Moreno de LeBlanc A, Matar C, LeBlanc N, Perdigón G.**
- Département de Chimie-Biochimie, Université de Moncton, NB, Canada. demoreno@cerela.org.ar
- **INTRODUCTION:** Antitumour activity is one of the health-promoting effects attributed to the lactic acid bacteria and their products of fermentation. Previous studies in mice demonstrated that bioactive compounds released in milk fermented by *Lactobacillus helveticus* R389 contribute to its immunoenhancing and antitumour properties. The aim of the present work was to study the effects of the consumption of milk fermented by *L. helveticus* R389 or its proteolytic-deficient variant, *L. helveticus* L89, on a murine hormone-dependent breast cancer model. **METHODS:** Mice were fed with milk fermented by *L. helveticus* R389 or *L. helveticus* L89, during 2 or 7 days. The tumour control group received no special feeding. At the end of the feeding period, the mice were challenged by a subcutaneous injection of tumour cells in the mammary gland. Four days post-injection, the mice received fermented milk on a cyclical basis. The rate of tumour development and the cytokines in serum, mammary gland tissue and tumour-isolated cells were monitored. Bcl-2-positive cells in mammary glands and cellular apoptosis in tumour tissue were also studied. **RESULTS:** Seven days of cyclical administration of milk fermented by either bacterial strain delayed or stopped the tumour development. Cytokines demonstrated that *L. helveticus* R389 modulated the immune response challenged by the tumour. IL-10 and IL-4 were increased in all the samples from this group. In comparison with the tumour control, all test groups showed a decrease of IL-6, a cytokine involved in oestrogen synthesis. Seven days of cyclical feeding with milk fermented by *L. helveticus* R389 produced an increase in the number of apoptotic cells, compared with all other groups. **CONCLUSION: This study demonstrated that 7 days of cyclical administration of milk fermented by both strains of *L. helveticus* diminishes tumour growth, stimulating an antitumour immune response.** Compounds released during milk fermentation with *L. helveticus* R389 would be implicated in its immunoregulatory capacity on the immune response in mammary glands and tumour, which were correlated with the cytokines found at the systemic level. The milk fermented by *L. helveticus* R389 was able to modulate the relationship between immune and endocrine systems (by IL-6 diminution), which is very important in oestrogen-dependent tumour and induced cellular apoptosis.
- PMID: 15987453 [PubMed - indexed for MEDLINE]



# BLADDER CANCER RECURRENCE

- Curr Opin Urol. 2003 Sep;13(5):379-83.
- **Bladder cancer recurrence: Part II. What do I tell my patients about lifestyle changes and dietary supplements?**
- **Moyad MA.**
- University of Michigan Medical Center, Department of Urology, Ann Arbor, Michigan 48109-0330, USA. moyad@umich.edu
- **PURPOSE OF REVIEW:** The purpose of this review is to provide the clinician with an adequate summary of current potential recommendations for reducing the risk of bladder cancer recurrence so that this topic can be discussed with patients that are dealing with this specific situation. **RECENT FINDINGS:** Several potential novel methods to reduce the risk of recurrence should be discussed with patients. Non-selective and selective cyclo-oxygenase 2 inhibitors have preliminary data from from laboratory and epidemiologic investigations. **Several preliminary trials have found that a combination dietary supplement of vitamins and minerals or a probiotic agent (Lactobacillus casei) may impact recurrence rates.** Smoking cessation may be one of the best routes for reducing recurrence and reducing the risk of overall early morbidity and mortality. Garlic or fluid intake need more clinical data. **SUMMARY:** Clinical recommendations for reducing the risk of bladder cancer recurrence need more attention. Preliminary data seem to support a potential role of numerous lifestyle and dietary supplement regimens. In the future, more reviews on the potential impact of reducing recurrence should be separated from reviews on prevention because these can be confusing when treated as a single subject.
- PMID: 12917513 [PubMed - indexed for MEDLINE]



# PROBIOTICS TARGET REDUCTION OF CARCINOGENS

- **Probiotics could target causes of liver cancer by excretion of carcinogens**
- The biggest risk factor for the disease is said to be chronic hepatitis B virus infection, but consumption of foods contaminated with aflatoxins are also established causes of liver cancer.
  - The double-blind, placebo-controlled trial with two parallel groups randomly assigned the volunteers to either the intervention group - two probiotic capsules per day or placebo (cellulose).
- **The reduction in excretion levels of the aflatoxin metabolite indicates that the concentration within the body of carcinogens was decreasing.**
- *The results of the present probiotic intervention are encouraging for additionally studies on an approach of probiotic use that can beneficially influence the toxicokinetics of unavoidable exposures to aflatoxins and other natural and environmental carcinogens," concluded the researchers.*
- *The American Journal of Clinical Nutrition* (Vol. 83, pp. 1199-1203).



# INTESTINAL IMMUNE SUPPORT- PROBIOTICS

- J Clin Gastroenterol. 2006 Mar;40(3):270-4. Links
- **Probiotics and chronic disease.**
- **Broekaert IJ, Walker WA.**
- Mucosal Immunology Laboratory, **Massachusetts General Hospital for Children, Harvard Medical School**, Boston, MA 02129, USA.
- **In today's climate, changed lifestyles and the increased use of antibiotics are significant factors that affect the preservation of a healthy intestinal microflora.** The concept of probiotics is to restore and maintain a microflora advantageous to the human body. Probiotics are found in a number of fermented dairy products, infant formula, and dietary supplements. Basic research on probiotics has suggested several modes of action beneficial for the human body and clinical research has proven its preventive and curative features in different intestinal and extraintestinal diseases. Chronic diseases cause considerable disablement in patients and represent a substantial economic burden on healthcare resources. Research has demonstrated a crucial role of nutrition in the prevention of chronic disease. **Thus, positive, strain-specific effects of probiotics have been shown in diarrheal diseases, inflammatory bowel diseases, irritable bowel syndrome, and Helicobacter pylori-induced gastritis, in atopic diseases and in the prevention of cancer.** As the majority of probiotics naturally inhabit the human intestinal microflora, their use has been regarded as very safe. However, in view of the range of potential benefits on health that might be achieved by the use of some probiotic bacteria, major and thorough evaluation is still necessary. In conclusion, probiotics act as an adjuvant in the prevention and treatment of a wide variety of chronic diseases.
- PMID: 16633135 [PubMed - indexed for MEDLINE]



# INTESTINAL IMMUNE SUPPORT- PROBIOTICS- TUFTS UNIVERSITY

- Expert Rev Anti Infect Ther. 2006 Apr;4(2):261-75. Links
- **Probiotics: their role in the treatment and prevention of disease.**
- **Doron S, Gorbach SL.**
- Division of Geographic Medicine and Infectious Diseases, **Tufts-New England Medical Center**, Boston, MA 02111, USA. sdoron@tufts-nemc.org
- A probiotic is a "live microbial food ingredients that, when ingested in sufficient quantities, exerts health benefits on the consumer". **Probiotics exert their benefits through several mechanisms; they prevent colonization, cellular adhesion and invasion by pathogenic organisms, they have direct antimicrobial activity and they modulate the host immune response.** The strongest evidence for the clinical effectiveness of probiotics has been in their use for the prevention of symptoms of lactose intolerance, treatment of acute diarrhea, attenuation of antibiotic-associated gastrointestinal side effects and the prevention and treatment of allergy manifestations. More research needs to be carried out to clarify conflicting findings on the use of probiotics for prevention of travelers' diarrhea, infections in children in daycare and dental caries, and elimination of nasal colonization with potentially pathogenic bacteria. Promising ongoing research is being conducted on the use of probiotics for the treatment of *Clostridium difficile* colitis, treatment of *Helicobacter pylori* infection, treatment of inflammatory bowel disease and prevention of relapse, treatment of irritable bowel syndrome, treatment of intestinal inflammation in cystic fibrosis patients, and prevention of necrotizing enterocolitis in premature infants. Finally, areas of future research include the use of probiotics for the treatment of rheumatoid arthritis, prevention of cancer and the treatment of graft-versus-host disease in bone marrow transplant recipients.
- PMID: 16597207 [PubMed - indexed for MEDLINE]



# CLINICAL INDICATIONS FOR PROBIOTICS

## TUFTS UNIVERSITY

- Clin Infect Dis. 2008 Feb 1;46 Suppl 2:S96-100; discussion S144-51. Links
- **Clinical indications for probiotics: an overview.**
- Goldin BR, [Gorbach SL](#)
- Tufts University School of Medicine, Boston, Massachusetts 02111, USA. [barry.goldin@tufts.edu](mailto:barry.goldin@tufts.edu)
- Probiotic bacteria are used to treat or prevent a broad range of human diseases, conditions, and syndromes. In addition, there are areas of medical use that have been proposed for future probiotic applications. Randomized double-blind studies have provided evidence of probiotic effectiveness for the treatment and prevention of acute diarrhea and antibiotic-induced diarrhea, as well as for the prevention of cow milk-induced food allergy in infants and young children. Research studies have also provided evidence of effectiveness for the prevention of traveler's diarrhea, relapsing *Clostridium difficile*-induced colitis, and urinary tract infections. There are also studies indicating that probiotics may be useful for prevention of respiratory infections in children, dental caries, irritable bowel syndrome, and inflammatory bowel disease. **Areas of future interest for the application of probiotics include colon and bladder cancers, diabetes, and rheumatoid arthritis.**
- PMID: 18181732 [PubMed - in process]



# PROBIOTICS LEUKEMIA-

## BAYLOR COLLEGE OF MEDICINE

- Cell Microbiol. 2008 Mar 26 [Epub ahead of print] Links
- **Probiotic Lactobacillus reuteri promotes TNF-induced apoptosis in human myeloid leukemia-derived cells by modulation of NF-kappaB and MAPK signalling.**
- **Iyer C, Kosters A, Sethi G, Kunnumakkara AB, Aggarwal BB, Versalovic J.**
- Department of Pathology, Baylor College of Medicine, Houston, TX 77030, USA.
- The molecular mechanisms of pro-apoptotic effects of human-derived Lactobacillus reuteri ATCC PTA 6475 were investigated in this study. L. reuteri secretes factors that potentiate apoptosis in myeloid leukemia-derived cells induced by tumour necrosis factor (TNF), as indicated by intracellular esterase activity, terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end-labelling assays and poly (ADP-ribose) polymerase cleavage. L. reuteri downregulated nuclear factor-kappaB (NF-kappaB)-dependent gene products that mediate cell proliferation (Cox-2, cyclin D1) and cell survival (Bcl-2, Bcl-xL). L. reuteri suppressed TNF-induced NF-kappaB activation, including NF-kappaB-dependent reporter gene expression in a dose- and time-dependent manner. L. reuteri stabilized degradation of IkappaBalpha and inhibited nuclear translocation of p65 (RelA). Although phosphorylation of IkappaBalpha was not affected, subsequent poly-ubiquitination necessary for regulated IkappaBalpha degradation was abrogated by L. reuteri. In addition, L. reuteri promoted apoptosis by enhancing mitogen-activated protein kinase (MAPK) activities including c-Jun N-terminal kinase and p38 MAPK. In contrast, L. reuteri suppressed extracellular signal-regulated kinases 1/2 in TNF-activated myeloid cells. L. reuteri may regulate cell proliferation by promoting apoptosis of activated immune cells via inhibition of IkappaBalpha ubiquitination and enhancing pro-apoptotic MAPK signalling. **An improved understanding of L. reuteri-mediated effects on apoptotic signalling pathways may facilitate development of future probiotics-based regimens for prevention of colorectal cancer and inflammatory bowel disease.**
- PMID: 18331465 [PubMed - as supplied by publisher]



# PROBIOTIC SUPPLEMENTATION

- Probiotics are beneficial if:
  - They are protected from oxygen (oxygen kills probiotics)
  - They are protected from stomach acid with more than enteric coating.
    - Enteric coating doesn't prevent stomach acid from getting into the probiotic pill. 90% is lost from non-protected forms.
  - Guaranteed quality and quantity pill to pill
  - **MUST WORK WITH YOUR INDIVIDUAL TREATMENT PROGRAM**



# IP6

- **IP-6 Background and Health Claims**
- IP-6, also known as inositol hexophosphate or phytic acid, is a sugar molecule with six phosphate groups attached. **Naturally present in whole grains and high fiber foods, IP-6 recently has gained popularity as a cancer fighter.** Experts feel that it also may play a role in the prevention and treatment of heart disease, kidney stones and liver disease.
- It may decrease the proliferation of cancer cells, act as an antioxidant, enhance the immune system by boosting the activity of natural killer cells (which destroy abnormal cells), or influence cells' ability to dedicate themselves to a particular function.
- Much of the scientific research completed with IP-6 has been done by Abulkalam Shamsuddin, a scientist at the University of Maryland School of Medicine. Several of Dr. Shamsuddin's animal and human cancer cell line studies have shown promising results with colon, prostate, liver and breast cancer. Epidemiological studies show that people who eat lots of foods that contain IP-6 have lower incidences of cancer of the breast, colon and prostate. Foods that are significant sources of IP-6 include soybeans, rice, sesame, beans, legumes, corn and cereals.
- **Precautions**  
IP-6 reduces platelet activity; therefore, people with low blood cell counts, or who are taking aspirin or other blood thinning medications, may want to avoid using IP-6. Because of its **antioxidant** properties, IP-6 may not be appropriate for patients receiving radiation or chemotherapy. Supplemental forms of IP-6 may also bind with calcium, magnesium, copper, iron and zinc and should therefore not be taken with food.
- **Dose**  
Although Dr. Shamsuddin indicates that further research must be completed before making more specific dosage recommendations, he gives the following guidelines: 1-2 g of IP-6 daily for cancer prevention, 4 g daily for people with an increased cancer risk, and up to 8 g daily for those with cancer. Patients who are considering an IP-6 supplement should consult with their physician or dietician.
- 



# IP6 AND BARRETT'S CARCINOMA

- Oncol Rep. 2008 Feb;19(2):563-6.
- **Corn-derived carbohydrate inositol hexaphosphate inhibits Barrett's adenocarcinoma growth by pro-apoptotic mechanisms.**
- **McFadden DW, Riggs DR, Jackson BJ, Cunningham C.**
- Department of Surgery, **Robert C. Byrd Health Science Center**, West Virginia University, Morgantown, WV 26506, USA. david.mcfadden@vtmednet.org
- Inositol hexaphosphate (IP6) is a naturally occurring polyphosphorylated carbohydrate that is found in food sources high in fiber content. IP6 has been reported to have significant inhibitory effects against a variety of primary tumors. We hypothesized that IP6 would inhibit the cell growth rate of Barrett's adenocarcinoma in vitro. Two Barrett's-associated adenocarcinoma cell lines, SEG-1 and BIC-1, were treated with IP6 at 0.5, 1.0 and 5.0 mM concentrations. Cell viability was measured by MTT assay. Apoptosis and necrosis were evaluated by the Annexin V FITC assay. Reductions ( $P < 0.001$ ) in cellular proliferation were observed in both cell lines. IP6 decreased late apoptosis and necrosis in BIC cells, whereas in SEG-1 cells, early apoptosis, late apoptosis and necrosis were all increased by IP6. IP6 decreases cellular growth by pro-apoptotic mechanisms. **Our findings suggest that IP6 has the potential to become an effective adjunct for Barrett's adenocarcinoma.** Further studies are needed to evaluate safety and clinical utility of this agent in patients with Barrett's adenocarcinoma.
- PMID: 18202808 [PubMed - indexed for MEDLINE]



# IP6 – PANCREATIC CANCER



- [Volume 126, Issue 2](#), Pages 199-203 (15 June 2005)
- **Inositol Hexaphosphate (IP6): A Novel Treatment for Pancreatic Cancer**<sup>1</sup>
- Presented in poster form at the 38th Association for Academic Surgery Annual Meeting, Houston, TX, November 2004.
- [Ponnandai Somasundar](#), M.D. <sup>□†</sup>, [Dale R. Riggs](#), M.S. <sup>†</sup>, [Barbara J. Jackson](#), B.S. <sup>†</sup>, [Cynthia Cunningham](#), Ph.D. <sup>‡</sup>, [Linda Vona-Davis](#), Ph.D. <sup>†</sup>, [David W. McFadden](#), M.D. (F.A.C.S.) <sup>†</sup>
- **Background**
- Inositol hexaphosphate (IP6) is a naturally occurring polyphosphorylated carbohydrate found in food sources high in fiber content. IP6 has been reported to have significant inhibitory effects against a variety of primary tumors including breast and colon. The effects of IP6 have not been evaluated in pancreatic cancer. We hypothesized that IP6 would significantly inhibit cell growth and increase the apoptotic rate of pancreatic cancer *in vitro*.
- **Materials and methods**
- Two pancreatic cancer cell lines (MIAPACA and PANC1) were cultured using standard techniques and treated with IP6 at doses of 0.5, 1.0, and 5.0 mm. Cell viability was measured by MTT at 24 and 72 h. Apoptosis was evaluated by Annexin V-FITC and results calculated using FACS analysis. Statistical analysis was performed by ANOVA.
- **Results**
- Significant reductions ( $P < 0.01$ ) in cellular proliferation were observed with all IP6 concentrations tested in both cell lines and at both time points. Reductions in cell proliferation ranged from 37.1 to 91.5%. IP6 increased early and late apoptotic activity ( $P < 0.01$ ).
- **Conclusions**
- **Treatment of pancreatic cancer with the common dietary polyphosphorylated carbohydrate IP6 significantly decreased cellular growth and increased apoptosis.** Our findings suggest that IP6 has the potential to become an effective adjunct for pancreatic cancer treatment. Further *in vivo* and human studies are needed to evaluate safety and clinical utility of this agent in patients with pancreatic cancer.



# IP6- MELANOMA



- J Surg Res. 2006 Jun 1;133(1):3-6. Epub 2006 Mar 23. Links
- **Inositol hexaphosphate (IP6) inhibits cellular proliferation in melanoma.**
- **Rizvi I, Riggs DR, Jackson BJ, Ng A, Cunningham C, McFadden DW.**
- Department of Surgery, Robert C. Byrd Health Science Center, West Virginia University, Morgantown, West Virginia 26506, USA.
- **BACKGROUND:** Inositol Hexaphosphate (IP6) is a naturally occurring polyphosphorylated carbohydrate found in food sources high in fiber content. We have previously reported IP6 to have significant inhibitory effects against pancreatic cancer in vitro. We hypothesized that the IP6 would significantly inhibit cell growth of cutaneous melanoma in vitro. **MATERIALS AND METHODS:** The melanoma line HTB68 was cultured using standard techniques and treated with IP6 at doses ranging from 0.2 to 1.0 mM/well. Cell viability was measured by MTT at 72 h. VEGF production was measured in the cell supernatants by ELISA. Apoptosis was evaluated by Annexin V-FITC and results calculated using FACS analysis. Statistical analysis was performed by ANOVA. **RESULTS:** Significant reductions ( $P < 0.001$ ) in cellular proliferation were observed with IP6. Overall, IP6 exhibited a mean inhibition of cell growth of 52.1 +/- 11.5% (range, 1.6-83.0%) at 72 h of incubation. VEGF production was significantly reduced ( $P < 0.001$ ) by the addition of IP6 (7.5 pg/ml) compared to control (40.9 pg/ml). IP6 significantly increased ( $P = 0.029$ ) late apoptosis from 5.3 to 7.0% gated events. No changes in necrosis or early apoptosis were observed. **CONCLUSIONS:** Adjuvant treatment of melanoma continues to challenge clinicians and patients. **Our findings that IP6 significantly decreased cellular growth, VEGF production and increased late apoptosis in melanoma suggest its potential therapeutic value. Further in vivo studies are planned to evaluate safety and clinical utility of this agent.**
- PMID: 16563438 [PubMed - indexed for MEDLINE]





# IP6 – PROSTATE CANCER

- Clin Cancer Res. 2004 Jan 1;10(1 Pt 1):244-50. Links
- **In vivo suppression of hormone-refractory prostate cancer growth by inositol hexaphosphate: induction of insulin-like growth factor binding protein-3 and inhibition of vascular endothelial growth factor.**
- **Singh RP, Sharma G, Mallikarjuna GU, Dhanalakshmi S, Agarwal C, Agarwal R.**
- Department of Pharmaceutical Sciences, University of Colorado Cancer Center, University of Colorado Health Sciences Center, Denver, Colorado, USA.
- **PURPOSE:** Diet composition is an important etiologic factor in prostate cancer (PCA) growth and has significant impact on clinical PCA appearance. Because inositol hexaphosphate (IP6) is a dietary phytochemical present in cereals, soy, legumes, and fiber-rich foods, we evaluated efficacy of IP6 against PCA growth and associated molecular events. **EXPERIMENTAL DESIGN:** DU145 cells were injected into nude mice, and animals were fed normal drinking water or 1 or 2% IP6 in drinking water for 12 weeks. Body weight, diet, water consumption, and tumor sizes were monitored. Tumors were immunohistochemically analyzed for proliferating cell nuclear antigen, terminal deoxynucleotidyl transferase-mediated nick end labeling, and CD31. Tumor-secreted insulin-like growth factor binding protein (IGFBP)-3 and vascular endothelial growth factor (VEGF) were quantified in plasma by ELISA. **RESULTS:** IP6 feeding resulted in suppression of hormone-refractory human prostate tumor growth without any adverse effect on body weight gain, diet, and water consumption during entire study. At the end of study, tumor growth inhibition by 1 and 2% IP6 feeding was 47 and 66% ( $P = 0.049-0.012$ ) in terms of tumor volume/mouse and 40 and 66% ( $P = 0.08-0.003$ ) in terms of tumor weight/mouse, respectively. Tumor xenografts from IP6-fed mice showed significantly ( $P < 0.001$ ) decreased proliferating cell nuclear antigen-positive cells but increased apoptotic cells. Tumor-secreted IGFBP-3 levels were also increased up to 1.7-fold in IP6-fed groups. Additionally, IP6 strongly decreased tumor microvessel density and inhibited tumor-secreted VEGF levels. **CONCLUSIONS:** **IP6 suppresses hormone-refractory PCA growth accompanied by inhibition of tumor cell proliferation and angiogenesis and increased apoptosis.** IP6-caused increase in IGFBP-3 and decrease in VEGF might have a role in PCA growth control.
- PMID: 14734476 [PubMed - indexed for MEDLINE]



# IP6 SUPPLEMENTATION

- Inositol and Inositol hexaphosphate must be in the correct weight and ratio to create the key active component IP3
- Guaranteed quality and quantity pill to pill
- **MUST WORK WITH YOUR INDIVIDUAL TREATMENT PROGRAM**



# GLUTATHIONE

- Br J Pharmacol. 2008 Apr;153(7):1364-72. Epub 2008 Feb 18. Links
- **N-Acetylcysteine prevents ifosfamide-induced nephrotoxicity in rats.**
- **Chen N, Aleksa K, Woodland C, Rieder M, Koren G.**
- 1Department of Physiology and Pharmacology, University of Western Ontario, London, Ontario, Canada.
- Background and purpose: Ifosfamide nephrotoxicity is a serious adverse effect for children undergoing cancer chemotherapy. Our recent in vitro studies have shown that the antioxidant N-acetylcysteine (NAC), which is used extensively as an antidote for paracetamol (acetaminophen) poisoning in children, protects renal tubular cells from ifosfamide-induced toxicity at a clinically relevant concentration. To further validate this observation, an animal model of ifosfamide-induced nephrotoxicity was used to determine the protective effect of NAC. Experimental approach: Male Wistar albino rats were injected intraperitoneally with saline, ifosfamide (50 or 80 mg kg<sup>-1</sup>) daily for 5 days, NAC (1.2 g kg<sup>-1</sup>) daily for 6 days) or ifosfamide+NAC (for 6 days). Twenty-four hours after the last injection, rats were killed and serum and urine were collected for biochemical analysis. Kidney tissues were obtained for analysis of glutathione, glutathione S-transferase and lipid peroxide levels as well as histology analysis. Key results: NAC markedly reduces the severity of renal dysfunction induced by ifosfamide with a significant decrease in elevations of serum creatinine (57.8±2.3 vs 45.25±2.1 μmol l<sup>-1</sup>) as well as a reduced elevation of beta(2)-microglobulin excretion (25.44±3.3 vs 8.83±1.3 nmol l<sup>-1</sup>) and magnesium excretion (19.5±1.5 vs 11.16±1.5 mmol l<sup>-1</sup>). Moreover, NAC significantly improved the ifosfamide-induced glutathione depletion and the decrease of glutathione S-transferase activity, lowered the elevation of lipid peroxides and prevented typical morphological damages in renal tubules and glomeruli. Conclusions and implications: **Our results suggest a potential therapeutic role for NAC in paediatric patients in preventing ifosfamide nephrotoxicity.**
- British Journal of Pharmacology (2008) 153, 1364-1372; doi:10.1038/bjp.2008.15; published online 18 February 2008.
- PMID: 18278066 [PubMed - in process]





# GLUTATHIONE- CANCER

- Arch Physiol Biochem. 2007 Oct-Dec;113(4-5):234-58.
- **The central role of glutathione in the pathophysiology of human diseases.**
- **Franco R, Schoneveld OJ, Pappa A, Panayiotidis MI.**
- Laboratory of Signal Transduction, **National Institute of Environmental Health Sciences, National Institutes of Health**, 111 T.W. Alexander Drive, Research Triangle Park, NC 27709, USA.
- Reduced glutathione (L-gamma-glutamyl-L-cysteinyl-glycine, GSH) is the prevalent low-molecular-weight thiol in mammalian cells. It is formed in a two-step enzymatic process including, first, the formation of gamma-glutamylcysteine from glutamate and cysteine, by the activity of the gamma-glutamylcysteine synthetase; and second, the formation of GSH by the activity of GSH synthetase which uses gamma-glutamylcysteine and glycine as substrates. While its synthesis and metabolism occur intracellularly, its catabolism occurs extracellularly by a series of enzymatic and plasma membrane transport steps.  
**Glutathione metabolism and transport participates in many cellular reactions including: antioxidant defense of the cell, drug detoxification and cell signaling (involved in the regulation of gene expression, apoptosis and cell proliferation).** Alterations in its concentration have also been demonstrated to be a common feature of many pathological conditions including diabetes, cancer, AIDS, neurodegenerative and liver diseases. Additionally, GSH catabolism has been recently reported to modulate redox-sensitive components of signal transduction cascades. In this manuscript, we review the current state of knowledge on the role of GSH in the pathogenesis of human diseases with the aim to underscore its relevance in translational research for future therapeutic treatment design.
- PMID: 18158646 [PubMed - indexed for MEDLINE]





TEXAS A&M

HEALTH SCIENCE CENTER

# GLUTATHIONE- CANCER

- J Nutr. 2004 Mar;134(3):489-92. Links
- **Glutathione metabolism and its implications for health.**
- **Wu G, Fang YZ, Yang S, Lupton JR, Turner ND.**
- Collaborators (1) **Lupton JR.**
- Faculty of Nutrition, **Texas A&M University**, College Station, TX, 77843, USA. g-wu@tamu.edu
- Glutathione (gamma-glutamyl-cysteinyl-glycine; GSH) is the most abundant low-molecular-weight thiol, and GSH/glutathione disulfide is the major redox couple in animal cells. The synthesis of GSH from glutamate, cysteine, and glycine is catalyzed sequentially by two cytosolic enzymes, gamma-glutamylcysteine synthetase and GSH synthetase. Compelling evidence shows that GSH synthesis is regulated primarily by gamma-glutamylcysteine synthetase activity, cysteine availability, and GSH feedback inhibition. Animal and human studies demonstrate that adequate protein nutrition is crucial for the maintenance of GSH homeostasis. In addition, enteral or parenteral cystine, methionine, N-acetyl-cysteine, and L-2-oxothiazolidine-4-carboxylate are effective precursors of cysteine for tissue GSH synthesis. Glutathione plays important roles in antioxidant defense, nutrient metabolism, and regulation of cellular events (including gene expression, DNA and protein synthesis, cell proliferation and apoptosis, signal transduction, cytokine production and immune response, and protein glutathionylation). **Glutathione deficiency contributes to oxidative stress, which plays a key role in aging and the pathogenesis of many diseases (including kwashiorkor, seizure, Alzheimer's disease, Parkinson's disease, liver disease, cystic fibrosis, sickle cell anemia, HIV, AIDS, cancer, heart attack, stroke, and diabetes).** New knowledge of the nutritional regulation of GSH metabolism is critical for the development of effective strategies to improve health and to treat these diseases.
- PMID: 14988435 [PubMed - indexed for MEDLINE]



# GLUTATHIONE- QUALITY OF LIFE

## GSH Reduces Toxicity, Increases Quality of Life in CDDP Treated Ovarian Cancer

- 151 patients with ovarian cancer (stage I-IV) received cisplatin (CDDP) +/- reduced glutathione (GSH)
- GSH group had improved quality of life: neurotoxicity, depression, emesis, hair loss, SOB, and difficulty concentrating all decreased significantly
- GSH group had trend toward better treatment outcome (73% vs. 62%)

Smyth JF, Bowman A, et al. Glutathione reduces the toxicity and improves quality of life of women diagnosed with ovarian cancer treated with cisplatin: results of a double-blind, randomized trial. *Ann Oncol.* 1997 Jun;8(6):569-73



# GLUTATHIONE- QUALITY OF LIFE

## GSH Induces Apoptosis in Cancer Cells

- GSH induced apoptosis in human cancer cells *in vitro* without damaging healthy cells
- Cell types included small cell lung carcinoma, neuroblastoma, acute lymphoblastic leukemia, colon carcinoma
- Controlled studies showed effectiveness after 4 applications at physiological concentrations (1-2 mM)

B. Donnerstag, G. Ohlenschlager, G. Treusch, et al.  
Reduced glutathione and S-acetylglutathione as apoptosis-  
inducing agents in cancer therapy. *Cancer Letters*. 1996;  
110:63-70



# GLUTATHIONE SUPPLEMENTATION

- Glutathione must have clinical efficacy of tissue and serum absorption
- Only one oral glutathione has this efficacy
- Guaranteed quality and quantity pill to pill
- **MUST WORK WITH YOUR INDIVIDUAL TREATMENT PROGRAM**



# SELENIUM- CHRONIC DISEASE

- Nutr Clin Pract. 2008 Apr;23(2):152-60. Links
- **The role of selenium in chronic disease.**
- **Boosalis MG.**
- Address correspondence to: Maria G. Boosalis, Division of Clinical Nutrition, University of Kentucky, College of Health Sciences, 209A CTW Building, 900 South Limestone, Lexington, KY 40536-0200; e-mail: mgboos01@uky.edu.
- Selenium functions as a part of proteins known as selenoproteins. Through these selenoproteins, selenium functions as a defensive mechanism for oxidative stress, for the regulation of thyroid hormone activity, and for the redox status of vitamin C and other molecules. In several of its roles, selenium functions as a dietary antioxidant and thus has been studied for its possible role in chronic diseases. **This article reviews recent studies regarding selenium status or supplementation in** hypertension, cardiovascular disease, **cancer**, and diabetes mellitus. A few studies regarding aging and mortality are also included. What can be ascertained from this current review is that the maintenance of adequate selenium nutriture and, at minimum, **the prevention of a deficiency in selenium would be advisable for all individuals.** In addition, the indiscriminant use of selenium supplements should be approached with caution until further randomized, controlled trials monitor the effects of such supplementation, especially on a long-term basis.
- PMID: 18390782 [PubMed - in process]



# SELENIUM- PROSTATE CANCER

- Cancer Chemother Pharmacol. 2008 Apr 1 [Epub ahead of print] Links
- **Sodium selenite induces apoptosis by generation of superoxide via the mitochondrial-dependent pathway in human prostate cancer cells.**
- [Xiang N, Zhao R, Zhong W.](#)
- Department of Pathology and Laboratory Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, 53792, USA.
- PURPOSE: Studies have demonstrated that selenium supplementation reduces the incidence of cancer, particularly prostate cancer. Evidence from experimental studies suggests that apoptosis is a key event in cancer chemoprevention by selenium and reactive oxygen species play a role in induction of apoptosis by selenium compounds. The current study was designed to investigate the role of superoxide and mitochondria in selenite-induced apoptosis in human prostate cancer cells. METHODS: LNCaP cells were transduced with adenoviral constructs to overexpress four primary antioxidant enzymes: manganese superoxide dismutase (MnSOD), copper-zinc superoxide dismutase (CuZnSOD), catalase (CAT), or glutathione peroxidase 1 (GPx1). Cell viability, apoptosis, and superoxide production induced by sodium selenite were analyzed by the MTT assay, chemiluminescence, flow cytometry, western blot analysis, and Hoechst 33342 staining following overexpression of these antioxidant enzymes. RESULTS: Our study shows the following results: (1) selenite induced cancer cell death and apoptosis by producing superoxide radicals; (2) selenite-induced superoxide production, cell death, and apoptosis were inhibited by overexpression of MnSOD, but not by CuZnSOD, CAT, or GPx1; and (3) selenite treatment resulted in a decrease in mitochondrial membrane potential, release of cytochrome c into the cytosol, and activation of caspases 9 and 3, events that were suppressed by overexpression of MnSOD. CONCLUSIONS: **This study demonstrates that selenite induces cell death and apoptosis** by production of superoxide in mitochondria and activation of the mitochondrial apoptotic pathway and MnSOD plays an important role in protection against prooxidant effects of superoxide from selenite. The data suggest that superoxide production in mitochondria is, at least in part, a key event in selenium-induced apoptosis in prostate cancer cells.
- PMID: 18379781 [PubMed - as supplied by publisher]



# SELENIUM SUPPLEMENTATION

- Selenium levels should be consistent with clinical efficacy and safety data
- Guaranteed quality and quantity pill to pill
- **MUST WORK WITH YOUR INDIVIDUAL TREATMENT PROGRAM**



# HIGHLY BIOAVAILABLE DIM BREAST CANCER

- Mol Cancer Ther. 2007 Oct;6(10):2757-65. Epub 2007 Oct 3.
- **Inactivation of NF-kappaB by 3,3'-diindolylmethane contributes to increased apoptosis induced by chemotherapeutic agent in breast cancer cells.**
- **Rahman KM, Ali S, Aboukameel A, Sarkar SH, Wang Z, Philip PA, Sakr WA, Raz A.**
- Department of Pathology, Karmanos Cancer Institute, Wayne State University School of Medicine, 715 HWCRC, 4100 John R, Detroit, MI 48201, USA. kmrahman@med.wayne.edu
- Constitutive activation of Akt or nuclear factor-kappaB (NF-kappaB) has been reported to play a role in de novo resistance of cancer cells to chemotherapeutic agents, which is a major cause of treatment failure in cancer chemotherapy. Previous studies have shown that 3,3'-diindolylmethane (DIM), a major in vivo acid-catalyzed condensation product of indole-3-carbinol, is a potent inducer of apoptosis, inhibitor of tumor angiogenesis, and inactivator of Akt/NF-kappaB signaling in breast cancer cells. However, little is known regarding the inactivation of Akt/NF-kappaB that leads to chemosensitization of breast cancer cells to chemotherapeutic agents, such as Taxotere. Therefore, we examined whether the inactivation Akt/NF-kappaB signaling caused by B-DIM could sensitize breast cancer cells to chemotherapeutic agents both in vitro and in vivo. MDA-MB-231 cells were simultaneously treated with 15 to 45 micromol/L B-DIM and 0.5 to 1.0 nmol/L Taxotere for 24 to 72 h. Cell growth inhibition assay, apoptosis assay, electrophoretic mobility shift assay, and Western blotting were done. The combination treatment of 30 micromol/L B-DIM with 1.0 nmol/L Taxotere elicited significantly greater inhibition of cell growth compared with either agent alone. The combination treatment induced greater apoptosis in MDA-MB-231 cells compared with single agents. Moreover, we found that NF-kappaB activity was significantly decreased in cells treated with B-DIM and Taxotere. We also have tested our hypothesis using transfection studies, followed by combination treatment with B-DIM/Taxotere, and found that combination treatment significantly inhibited cell growth and induced apoptosis in MDA-MB-231 breast cancer cells mediated by the inactivation of NF-kappaB, a specific target in vitro and in vivo. These results were also supported by animal experiments, which clearly showed that B-DIM sensitized the breast tumors to Taxotere, which resulted in greater antitumor activity mediated by the inhibition of Akt and NF-kappaB. **Collectively, our results clearly suggest** that inhibition of Akt/NF-kappaB signaling by **B-DIM leads to chemosensitization of breast cancer cells** to Taxotere, which may contribute to increased growth inhibition and apoptosis in breast cancer cells. The data obtained from our studies could be a novel breakthrough in cancer therapeutics by using nontoxic agents, such as B-DIM, in combination with other conventional therapeutic agents, such as Taxotere.
- PMID: 17913854 [PubMed - indexed for MEDLINE]



# HIGHLY BIOAVAILABLE DIM- PANCREATIC CANCER

- Pharm Res. 2008 Apr 22 [Epub ahead of print] Links
- **Chemoprevention of Pancreatic Cancer: Characterization of Par-4 and its Modulation by 3,3' Diindolylmethane (DIM).**
- [Azmi AS](#), [Ahmad A](#), [Banerjee S](#), [Rangnekar VM](#), [Mohammad RM](#), [Sarkar FH](#).
- Department of Pathology, Karmanos Cancer Institute, Wayne State University School of Medicine, 9374 Scott Hall, 540 E Canfield, Detroit, Michigan, 48201, USA.
- **PURPOSE:** Cancer chemoprevention is defined as the use of natural, synthetic, or biological agents to suppress, reverse or prevent the carcinogenic process from turning into aggressive cancer. Prostate apoptosis response-4 (Par-4) is a unique pro-apoptotic protein that selectively induces apoptosis in prostate cancer cells. However, its role in other malignancies has not been fully explored. This study tries to identify the functional significance of Par-4 in pancreatic cancer. **METHODS:** Multiple molecular techniques such as Western blot analysis, trypan blue assay for cell viability, MTT assay for cell growth inhibition and Histone/DNA ELISA for apoptosis were used. **RESULTS:** Western blot analysis revealed that 3,3'-diindolylmethane (DIM) a chemopreventive agent, specifically its more bioavailable formulation, B-DIM, at low doses (20  $\mu\text{mol/L}$ ) induces Par-4, in L3.6pl and Colo-357 pancreatic cancer cells. At similar doses, **DIM reduced cell viability and caused cell growth inhibition and apoptosis.** Moreover, **DIM pre-treatment sensitized the cells to cytotoxic action of chemotherapeutic drug gemcitabine** through up-regulation of Par-4. **CONCLUSION:** The induction of Par-4 is indirectly related to increased sensitivity and cell death through apoptosis. To our knowledge the results reported here showed, for the first time, the induction of Par-4 by chemopreventive agents, in general, and DIM, in particular, in pancreatic cancer cells in vitro.

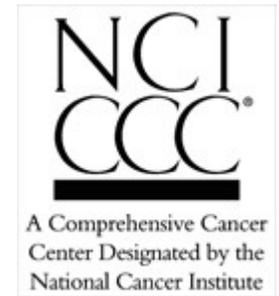


# HIGHLY BIOAVAILABLE DIM- PROSTATE CANCER

- Cancer Res. 2006 Oct 15;66(20):10064-72. Links
- **Down-regulation of androgen receptor by 3,3'-diindolylmethane contributes to inhibition of cell proliferation and induction of apoptosis in both hormone-sensitive LNCaP and insensitive C4-2B prostate cancer cells.**
- **Bhuiyan MM, Li Y, Banerjee S, Ahmed F, Wang Z, Ali S, Sarkar FH.**
- Departments of Pathology and Internal Medicine, Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, Michigan 48201, USA.
- Despite the initial efficacy of androgen deprivation therapy, most patients with advanced prostate cancer eventually progress to hormone-refractory prostate cancer, for which there is no curative therapy. Previous studies from our laboratory and others have shown the antiproliferative and proapoptotic effects of 3,3'-diindolylmethane (DIM) in prostate cancer cells. However, the molecular mechanism of action of DIM has not been investigated in androgen receptor (AR)-positive hormone-responsive and -nonresponsive prostate cancer cells. Therefore, we investigated the effects of B-DIM, a formulated DIM with greater bioavailability, on AR, Akt, and nuclear factor kappaB (NF-kappaB) signaling in hormone-sensitive LNCaP (AR+) and hormone-insensitive C4-2B (AR+) prostate cancer cells. We found that B-DIM significantly inhibited cell proliferation and induced apoptosis in both cell lines. By Akt gene transfection, reverse transcription-PCR, Western blot analysis, and electrophoretic mobility shift assay, we found a potential crosstalk between Akt, NF-kappaB, and AR. Importantly, B-DIM significantly inhibited Akt activation, NF-kappaB DNA binding activity, AR phosphorylation, and the expressions of AR and prostate-specific antigen, suggesting that B-DIM could interrupt the crosstalk. Confocal studies revealed that B-DIM inhibited AR nuclear translocation, leading to the down-regulation of AR target genes. Moreover, B-DIM significantly inhibited C4-2B cell growth in a severe combined immunodeficiency-human model of experimental prostate cancer bone metastasis. These results suggest that B-DIM-induced cell proliferation inhibition and apoptosis induction are partly mediated through the down-regulation of AR, Akt, and NF-kappaB signaling. **These observations provide a rationale for devising novel therapeutic approaches for the treatment of hormone-sensitive, but more importantly, hormone-refractory prostate cancer by using B-DIM alone or in combination with other therapeutics.**
- PMID: 17047070 [PubMed - indexed for MEDLINE]



# HIGHLY BIOAVAILABLE DIM BREAST & OVARIAN CANCER



- Cancer Lett. 2008 Mar 28
- **CXCR4 and CXCL12 down-regulation: A novel mechanism for the chemoprotection of 3,3'-diindolylmethane for breast and ovarian cancers.**
- Hsu EL, Chen N, Westbrook A, Wang F, Zhang R, Taylor RT, Hankinson O.
- Molecular Toxicology Interdepartmental Doctoral Program, University of California-Los Angeles, Los Angeles, CA 90095-1732, USA; Department of Pathology and Laboratory Medicine, University of California-Los Angeles, Los Angeles, CA 90095-1732, USA; Jonsson Comprehensive Cancer Center, University of California-Los Angeles, Los Angeles, CA 90095-1732, USA.
- Cruciferous vegetables are thought to protect against numerous types of cancer. 3,3'-Diindolylmethane (DIM) is an acid-catalyzed product generated during the consumption of cruciferous vegetables and appears to be chemoprotective for breast cancer. The interaction between the chemokine receptor, CXCR4, and its unique ligand, CXCL12, is known to mediate the progression and metastasis of breast and other cancers. Organs to which these cancers metastasize secrete CXCL12, which binds to CXCR4 expressed on the surface of primary cancer cells. This process subsequently stimulates the invasive properties of the cancer cells and attracts them to the preferred organ sites of metastases. We have found that DIM down-regulates both CXCR4 and CXCL12 in MCF-7 and MDA-MB-231 breast cancer cells as well as in BG-1 ovarian cancer cells at the transcriptional level and in an estrogen-independent manner. We demonstrate that the potential of MDA-MB-231 and BG-1 cells for chemotaxis and invasion towards CXCL12, but not towards IL-6 or fetal bovine serum, respectively, is inhibited by DIM. Furthermore, we show that DIM down-regulates CXCR4 under hypoxia and CXCL12 under estradiol-inducing conditions. Our data suggest that one mechanism whereby **DIM protects against breast, ovarian, and possibly other cancers** is through the repression of CXCR4 and/or CXCL12, thereby **lowering the invasive and metastatic potential of these cells.**
- PMID: 18378071 [PubMed - as supplied by publisher]



# DIM INHIBITS HUMAN PAPILLOMA VIRUS (HPV) GROWTH

- 
- **Absorption-enhanced 3,3'-Diindolylmethane: Human Use in HPV-related, Benign and Pre-cancerous Conditions.**
- Zeligs, M.A., Sepkovic, D.W., Manrique, C., Macsalka, M., Williams, D.E., and Bradlow, H.L
- Proc. Am. Assoc. Cancer Res. 2003, Apr; 44.
- 3,3-Diindolylmethane is a dietary indole from cruciferous vegetables that has demonstrated pre-clinical therapeutic efficacy in models of DMBA-induced mammary cancer, transplanted human breast cancer, and in models of human papilloma virus (HPV) related disease.
- Animal and human use of crystalline diindolylmethane has revealed the need for absorption-enhancing technology to allow adequate gastro-intestinal uptake. BioResponse-DIM, a patented formulation of diindolylmethane categorized and sold as a dietary supplement, utilizes solubility-enhancing micro-encapsulation technology to allow absorption of effective amounts of diindolylmethane.
- Human use of this formulation promotes a dose-responsive upward effect on the urinary ratio of 2-OH/16-OH estrone metabolites, demonstrated by ELISA testing of urine before-and-after use. In previous prospective studies, a greater 2-OH/16-OH estrone urinary ratio has been associated with a lowered risk of future breast cancer. We are able to monitor compliance by measurement of urinary diindolylmethane using gas chromatography-mass spectrometry.
- Human use of this preparation at higher doses has demonstrated treatment-related resolution of moderate and severe cervical dysplasia in preliminary open-label testing. A still higher dose, about 10 times above that possible from dietary exposure to diindolylmethane from vegetable sources, has resulted in the control of laryngeal papillomas and resolution of cutaneous and plantar warts in preliminary human testing. **The clearing of HPV-related lesions is consistent with diindolylmethane's previously described, apoptosis-promoting and chemopreventive activity.**



*American Association for Cancer Research*



## DIM SUPPLEMENTATION

- Diindoylmethane (DIM) is poorly absorbed; research demonstrates efficacy and safety with the highly bio-available form.
- Guaranteed quality and quantity pill to pill
- **MUST WORK WITH YOUR INDIVIDUAL TREATMENT PROGRAM**



# EPA & CACHEXIA

- Front Biosci. 2001 Feb 1;6:D164-74.
- **Loss of skeletal muscle in cancer: biochemical mechanisms.**
- **Tisdale MJ.**
- Pharmaceutical Sciences Research Institute, Aston University, Birmingham B4 7ET, UK.  
M.J.Tisdale@aston.ac.uk
- Patients with cancer often undergo a specific loss of skeletal muscle mass, while the visceral protein reserves are preserved. This condition known as cachexia reduces the quality of life and eventually results in death through erosion of the respiratory muscles. Nutritional supplementation or appetite stimulants are unable to restore the loss of lean body mass, since protein catabolism is increased mainly as a result of the activation of the ATP-ubiquitin-dependent proteolytic pathway. Several mediators have been proposed. An enhanced protein degradation is seen in skeletal muscle of mice administered tumour necrosis factor (TNF), which appears to be mediated by oxidative stress. There is some evidence that this may be a direct effect and is associated with an increase in total cellular-ubiquitin-conjugated muscle proteins. Another cytokine, interleukin-6 (IL-6), may play a role in muscle wasting in certain animal tumours, possibly through both lysosomal (cathepsin) and non-lysosomal (proteasome) pathways. A tumour product, proteolysis-inducing factor (PIF) is produced by cachexia-inducing murine and human tumours and initiates muscle protein degradation directly through activation of the proteasome pathway. The action of PIF is blocked by eicosapentaenoic acid (EPA), which has been shown to attenuate the development of cachexia in pancreatic cancer patients. **When combined with nutritional supplementation EPA from fish oil leads to accumulation of lean body mass and prolongs survival.** Further knowledge on the biochemical mechanisms of muscle protein catabolism will aid the development of effective therapy for cachexia.
- PMID: 11171557 [PubMed - indexed for MEDLINE]



# INHIBITION OF PROLIFERATION BY OMEGA-3 FATTY ACIDS IN CHEMORESISTANT PANCREATIC CANCER CELLS

- Ann Surg Oncol. 2007 Dec;14(12):3620-8. Epub 2007 Sep 26. Links
- **Inhibition of proliferation by omega-3 fatty acids in chemoresistant pancreatic cancer cells.**
- **Hering J, Garrean S, Dekoj TR, Razzak A, Saied A, Trevino J, Babcock TA, Espat NJ.**
- Department of Surgery, University of Illinois at Chicago, Chicago, Illinois, USA.
- **BACKGROUND:** Pancreatic cancer-gemcitabine (GEM) chemoresistance has been demonstrated to be associated with enhanced NF-kB activation and antiapoptotic protein synthesis. The well-known capacity of omega-3 fatty acids (n-3 FAs) to inhibit NF-kB activation and promote cellular apoptosis has the potential to restore or facilitate gemcitabine chemosensitivity. **METHODS:** Four pancreatic cancer cell lines (MIA PaCa-2, BxPC-3, PANC-1, and L3.6), each with distinct basal NF-kB and differing GEM sensitivity profiles, were administered: 100 uM of (1) n-3FA, (2) n-6FA, (3) GEM, (4) n-3FA + GEM, or (5) n-6FA + GEM for 24 and 48 hours. Proliferation was assessed using the WST-1 assay. To define the mechanism(s) of altered proliferation, electron mobility shift assay for NF-kB activity, western blots of phosphoStat3, phosphoI-kappaB, and poly(ADP-ribose) polymerase (PARP) cleavage were performed in the MIA PaCa-2 cell line. **RESULTS:** All cell lines demonstrated a time/dose-dependent inhibition of proliferation in response to n-3FA. For MIA PaCa-2 cells, n-3FA and n-3FA + GEM treatment resulted in reduction of I-kB phosphorylation and NF-kB activation when compared with n-6FA control. n-3FA and combination treatment also significantly decreased Stat3 phosphorylation, whereas GEM alone had no effect. n-3FAs and n-3FA + GEM groups demonstrated increased PARP cleavage, mirroring NF-kB activity and Stat3 phosphorylation. **CONCLUSIONS:** n-3 FA treatment is specifically associated with inhibition of proliferation in these four pancreatic cell lines irrespective of varied gemcitabine resistance. An experimental paradigm to screen for potential contributory mechanism(s) in altered pancreatic cancer cellular proliferation was defined, and **using this approach the co-administration of n-3 FA with GEM inhibited GEM-induced NF-kB activation and restored apoptosis** in the MIA PaCa-2 cell-line.
- PMID: 17896154 [PubMed - indexed for MEDLINE]



# OMEGA 3 BREAST CANCER

- Breast Cancer Res Treat. 2007 Jan;101(1):7-16. Epub 2006 Jul 6. Links
- **Differential effects of omega-3 and omega-6 Fatty acids on gene expression in breast cancer cells.**
- [Hammamieh R](#), [Chakraborty N](#), [Miller SA](#), [Waddy E](#), [Barmada M](#), [Das R](#), [Peel SA](#), [Day AA](#), [Jett M](#).
- Division of Pathology, Walter Reed Army Institute of Research, 503 Robert Grant Road, Silver Spring, MD 20910, USA.
- Essential fatty acids have long been identified as possible oncogenic factors. Existing reports suggest omega-6 (omega-6) essential fatty acids (EFA) as pro-oncogenic and omega-3 (omega-3) EFA as anti-oncogenic factors. **The omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), inhibit the growth of human breast cancer cells while the omega-6 fatty acids induces growth** of these cells in animal models and cell lines. In order to explore likely mechanisms for the modulation of breast cancer cell growth by omega-3 and omega-6 fatty acids, we examined the effects of arachidonic acid (AA), linoleic acid (LA), EPA and DHA on human breast cancer cell lines using cDNA microarrays and quantitative polymerase chain reaction. MDA-MB-231, MDA-MB-435s, MCF-7 and HCC2218 cell lines were treated with the selected fatty acids for 6 and 24 h. Microarray analysis of gene expression profiles in the breast cancer cells treated with both classes of fatty acids discerned essential differences among the two classes at the earlier time point. The differential effects of omega-3 and omega-6 fatty acids on the breast cancer cells were lessened at the late time point. Data mining and statistical analyses identified genes that were differentially expressed between breast cancer cells treated with omega-3 and omega-6 fatty acids. Ontological investigations have associated those genes to a broad spectrum of biological functions, including cellular nutrition, cell division, cell proliferation, metastasis and transcription factors etc., and thus presented an important pool of biomarkers for the differential effect of omega-3 and omega-6EFAs.
- PMID: 16823509 [PubMed - indexed for MEDLINE]



# OMEGA 3 – TUMOR CELL CHEMOSENSITIVITY

- Eur J Cancer Prev. 2005 Jun;14(3):263-70. Links
- **Exogenous supplementation with omega-3 polyunsaturated fatty acid docosahexaenoic acid (DHA; 22:6n-3) synergistically enhances taxane cytotoxicity and downregulates Her-2/neu (c-erbB-2) oncogene expression in human breast cancer cells.**
- **Menendez JA, Lupu R, Colomer R.**
- Department of Medicine, Breast Cancer Translational Research Laboratory, Evanston Northwestern Healthcare Research Institute, Evanston, Illinois 60201, USA. jmenendez@enh.org
- Omega-3 polyunsaturated fatty acid (PUFA), docosahexaenoic acid (DHA; 22:6n-3) and other omega-3 and omega-6 PUFAs have raised interest as novel anticancer agents by exerting selective cytotoxic effects on human cancer cells without affecting normal tissues. Here, we examined the in vitro relationship between exogenous supplementation with DHA and breast cancer chemosensitivity to taxanes. We measured cell viability in the highly metastatic human breast cancer cell line MDA-MB-231 exposed sequentially to DHA followed by paclitaxel (Taxol) or docetaxel (Taxotere). As DHA by itself showed cytotoxic effects, possible synergistic interactions between DHA and taxanes were assessed, employing the combination index (CI) method and the isobologram analysis. Both methods showed a strong synergism (CI approximately 0.5;  $P < 0.005$ ) between DHA and taxanes in MDA-MB-231 cells. When the increase in taxanes efficacy was measured by dividing the IC<sub>50</sub> values (50% inhibitory concentrations) obtained when the cells were exposed to taxanes alone by those after DHA pre-exposure, we found that DHA enhanced the cytotoxic activity of taxanes against MDA-MB-231 cells in a dose-dependent manner (up to 13- and 5-fold increase in Taxol and Taxotere efficacy, respectively). Importantly, sequential exposure to DHA followed by taxanes also yielded strong synergism in Her-2/neu (c-erbB-2)-overexpressing and taxanes-resistant SK-Br3 and BT-474 breast cancer cells. Moreover, exogenous supplementation with DHA significantly decreased the expression of Her-2/neu-codified p185(Her-2/neu) oncoprotein (up to 78% reduction in BT-474 cells). **Our results provide experimental support to the hypothesis that omega-3 PUFAs can be used as modulators of tumor cell chemosensitivity and provide the rationale for in vivo preclinical investigation.** In addition, this is the first study demonstrating that omega-3 PUFA DHA downregulates Her-2/neu oncogene expression in human breast cancer cells.
- PMID: 15901996 [PubMed - indexed for MEDLINE]



# DHA – FROM FISH OIL PRIMARY TUMOR SUPPRESSIVE OMEGA 3 FATTY ACID

- Nutr Cancer. 2007;58(2):178-87.
- **Docosahexaenoic acid (DHA), a primary tumor suppressive omega-3 fatty acid, inhibits growth of colorectal cancer independent of p53 mutational status.**
- **Kato T, Kolenic N, Pardini RS.**
- Biochemistry, College of Agriculture, Biotechnology and Natural Resources, University of Nevada, Reno, NV 89557, USA.
- Human colon carcinoma COLO 205, carrying wild type p53, grown subcutaneously in athymic mice was inhibited 80% by a high fat menhaden oil diet containing a mixture of omega-3 fatty acids compared to the low fat corn oil diet containing omega-6 fatty acids. Feeding a high fat diet of golden algae oil containing docosahexaenoic acid (DHA) as the sole long chain omega-3 fatty acid resulted in 93% growth inhibition. Similar findings were previously reported for WiDr colon carcinoma containing mutated p53 (His237). In vitro, 125 µM DHA inhibited COLO 205 growth by 81%, WiDr by 42%, while eicosapentaenoic acid (EPA) marginally inhibited growth of both lines by approximately 30%. DHA inhibited cell proliferation by 41% in WiDr but did not significantly inhibit proliferation in COLO 205. Cell cycle analysis revealed that DHA arrested cell cycle at Resting/Gap 1 (G0/G1 phase) in WiDr and at Gap 2/Mitosis (G2/M) phase in COLO 205. DHA induced apoptosis in COLO 205 but not in WiDr, and EPA did not induce apoptosis in either line. Taken together, **these findings suggest DHA is the primary tumor suppressive omega-3 fatty acid in vivo and in vitro and inhibits cancer growth by p53 dependent and independent pathways,** while the marginal inhibition by EPA is p53 independent.
- PMID: 17640164 [PubMed - indexed for MEDLINE]



# EPA DHA FISH OIL SUPPLEMENTATION

- Only one fish oil has over 120 clinical studies providing efficacy and safety.
- Fish oil must be stable or increases oxidative stress, glucose, and LDL.
- Fish oil is easily damaged in the production, concentration, and purification methods.



**Where's the  
fish oil?**



# ARE ALL SUPPLEMENTS CREATED EQUAL?

- Independent studies have shown:
  - Several supplement products contained contaminants such as lead. The levels of lead were unsafe for children and pregnant women.
  - Several did not contain the amount of ingredients listed on the label.
  - Many do not have proof of efficacy and safety testing on the actual product.



# MY CRITERIA FOR CHOICE OF SUPPLEMENTATION

- Product effectiveness and safety proven by independent testing.
- Must be manufactured to the highest of quality standard in the industry
  - FDA Drug Registered manufacturer
    - Guarantees consistency pill to pill
    - Dissolution testing to assure assimilation in the gut
    - Stability and expiration testing
    - No cross contamination
    - Assayed for impurities
- Most supplement companies are FDA Food registered, not DRUG.



# MY APPROACH - SUPPORT ALL KEY AREAS

- Cells and their membranes
- The detoxification system
  - The liver
  - The intestines
- The Immune system
  - Bone marrow
  - Liver
  - Thymus
  - Intestinal flora
  - Lymph system
- Organ affected by cancer



# PROMISES IN A BOTTLE - NO CURE ALL

- Get professional advice
  - Use Science Based approach
  - Get Experience based guidance
  - Comprehensive approach
  - TEAMWORK WITH YOUR ONCOLOGIST
- Not all dietary supplements are created equal
  - Contaminants found
  - Missing ingredient and potency



# INDIVIDUALITY

- Different cancers
- Different causes
- Different treatments
- Different responses
- *Your comprehensive approach will be as individual as you are*



# ALCOHOL & FATS

- It's a relief to know the truth after all those conflicting medical studies.
  - The Japanese eat very little fat
    - and suffer fewer heart attacks than the British or Americans.
  - The French eat a lot of fat
    - and also suffer fewer heart attacks than the British or Americans.
  - The Japanese drink very little red wine
    - and suffer fewer heart attacks than the British or Americans.
  - The Italians drink a lot of red wine
    - and also suffer fewer heart attacks than the British or Americans.
  - The Germans drink a lot of beer and eat lots of sausages and fats
    - and suffer fewer heart attacks than the British or Americans.
  - CONCLUSION: Eat and drink what you like. Speaking English is apparently what kills you.





**ALAN SIMON R.PH.**  
**INTEGRATIVERX2@INSIGHTBB.COM**  
**SIMON'S PROSPECT APOTHECARY**  
**WWW.INTEGRATIVERXPHARMACY.COM**  
**(502) 228-4161**  
**9217 US Highway 42**  
**Prospect, KY 40059**