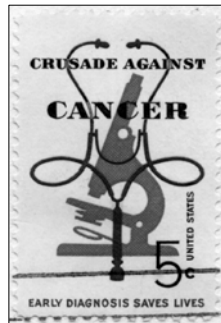


## “Cancer Prevention in the 21<sup>st</sup> Century”



Tieraona Low Dog, MD

Director: Medicine Lodge  
 Author of *National Geographic's*  
*“Fortify Your Life”*  
*“Healthy At Home”* and  
*“Life Is Your Best Medicine”*

www.DrLowDog.com

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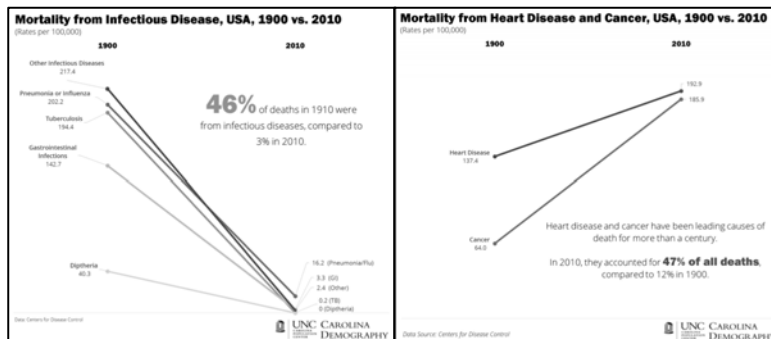
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2

## The Times They Are A-Changing



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3

## Epigenetics



- The mapping of **human genome** one of the greatest scientific undertakings of past century, **detailing with incredible accuracy the blueprint of our species.**
- It paved the way for field of **epigenetics**, showing that when it comes to our genes, **nurture** is inextricably linked with **nature**.
- That it is the **way we live our lives - from the moment of conception to our last breath - that influences the expression of our genes.**

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## Fast Facts

- In 2010, 1.6 million people were diagnosed with cancer.
- In 2030, estimated to increase to 2.3 million.
- Cancer rates are increasing globally, people diagnosed at younger ages.
- In US, one in four people will die from cancer.
- But *many people survive the disease*.
- >12 million people have survived cancer treatment and are looking to prevent cancer recurrence.

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## Recommendations for Cancer Prevention WCRF/AICR

- Do not smoke or use tobacco products.
- Body Fatness – be as lean as possible within normal range of body wt.
- Physical Activity – be physically active as part of everyday life
- Foods and Drinks that Promote Weight Gain – limit consumption of energy-dense foods. Avoid sugary drinks
- Plant Foods – eat mostly foods of plant origin
- Animal Foods - limit intake of red meat, avoid processed meat
- Alcoholic Drinks – limit 2 serving/d men, 1 serving/d women
- Preservation, Processing, Preparation - limit consumption of salt
- Breastfeeding – mothers to breastfeed, children to be breastfed

*Cancer Survivors* – follow recommendations above

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## Smoking Cessation

- Tobacco smoking accounts for 21% of global cancer deaths.
- Smoking cessation dramatically reduces risk for oral cancers.
- Survey 1,802 dentists: > 90% of dental providers routinely ask patients about tobacco use, 76% counsel patients, and 45% routinely offer cessation assistance: cessation counseling, cessation prescription, or both.
- Patients are **twice as likely to try quitting** with advice from a clinician
- ADA certified online course for smoking cessation:  
<https://healthcareinnovation-mcdph.talentlms.com/catalog/info/id:238>
- Check [www.smokefree.gov](http://www.smokefree.gov) for your state quit line number



Lee YC, et al. *Ann Glob Health* 2014; 80(5):378-383.

Jannat-Khah DP, et al. *Prev Chronic Dis* 2014; 6:11:E196.

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## Cancer Prevention Knowledge Quiz (AICR)



Alcohol has been shown to increase the risk for which cancers?

1. Esophageal cancer
2. Prostate cancer
3. Mouth cancer
4. Breast cancer
5. Lung cancer
6. None of the above

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## Alcohol and Cancer



- **LACE** study women drinking **>half-serving** alcohol/day: 35% increased risk of recurrence and 51% increased risk of death due to **breast cancer**, especially if **postmenopausal and obese**.
- Women drinking ~1 serving alcohol/d had **increased survival from colorectal cancer** compared to non-drinkers.
- **No direct link between alcohol and prostate cancer** (do not exceed 2 servings per day)

Kwan ML, et al. *J Clin Oncol* 2010; 28(29):4410-6.; Fung TT, et al. *PLoS One* 2014; Dec 15;9(12):e115377

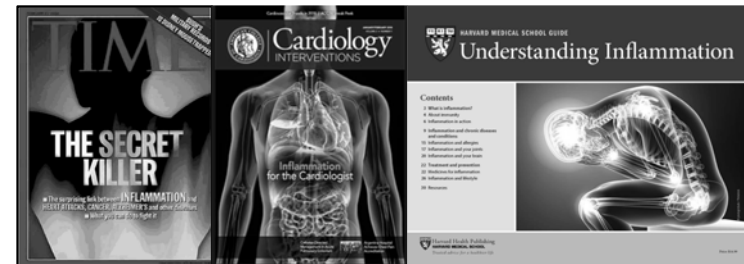
Artero A, et al. *Maturitas* 2015; Jan;80(1):3-13

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## Inflammation.....



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## Inflammation and Cancer

- Hallmark of cancer - **plays an essential role in development and progression of most cancers.**
- Nuclear factor- $\kappa$ B (**NF- $\kappa$ B**) is one of the most important molecules **linking chronic inflammation to cancer**
- Activation of NF- $\kappa$ B primarily initiated by bacterial endotoxins such as **lipopolysaccharide (LPS)** and **pro-inflammatory cytokines** such as TNF and IL-1. NF- $\kappa$ B activation occurs in **cancer cells and in tumor microenvironments of most solid cancers.**

Taniguchi K, et al. NF- $\kappa$ B, inflammation, immunity and cancer: coming of age. *Nature Reviews Immunology* 2018; 18: 309–324

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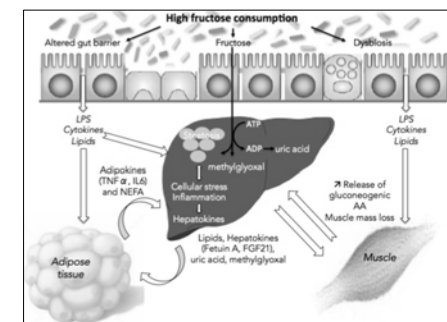
11

- **High fructose diet increases intestinal permeability.**
- **Bacterial endotoxin (LPS)** enters bloodstream, **inflammation is activated** by changing **insulin signaling** and triggering **inflammatory mediators.**

Jin R, et al. *Nutrients* 2014; 6:3187–3201

Boroni Morcira AP, et al. *Nutr Hosp* 2012; 27(2):382-90

Jegatheesan P, et al. *Nutrients* 2017; Mar 3;9(3)



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## Probiotics

- Regulate/modulate immune functions, reduce risk intestinal infection.
- Improve **intestinal barrier functions**, reduce **endotoxemia**
- Induce hypo-responsiveness to **food antigens**
- Improve glucose control and **reduce inflammatory cytokines**.
- Inhibit tumorigenesis and **may inhibit cancer progression**
- 81 obese postmenopausal women randomized to high or low dose multi-strain probiotics or placebo for 12 weeks. Statistically significant differences in **LPS, uric acid, glucose, insulin** found for both doses compared to placebo.

Gianotti L. et al. *World J Gastroenterol*. 2010;16:167–175

Szulinska M, et al. *Nutrients* 2018, 10(6), 773; <https://doi.org/10.3390/n10060773>

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## Clinical Resource Tool: [www.usprobioticguide.com](http://www.usprobioticguide.com)

Clinical Guide to Probiotic Products Available in USA Indications, Dosage Forms and Clinical Evidence to Date - 2019 Edition					
INDICATIONS FOR PEDIATRIC HEALTH					
Brand Name	Probiotic Strain	Dosage Form	CFU/Dose	No. of Doses/Day	Indications (Level of Evidence)
Bio-Rad InfanPro <sup>®</sup>	L. casei P1008 327M L. rhamnosus P1008 327M Bifidobacterium P1008 327M L. acidophilus P1008 327M B. infantis P1008 327M	Sachet	100MCFU	1/1 sachet	CEAD - Childhood exanthematous allergic dermatitis (I) Colic - Colic (I) HF - Helicobacter pylori - Adjunct to standard eradication therapy (I)
BioRad Probiotic Baby Drops with Vitamin D <sub>3</sub>	L. reuteri DSM 17928	Drops	100MCFU	5 drops	AAD - Antibiotic associated diarrhea - Prevention (I) C - Constipation (I) CEAD - Childhood exanthematous allergic dermatitis (I) CDI - Clostridium difficile infection - community acquired (I) CDI - Clostridium difficile infection - hospital acquired (I) BSPAP - Infantile bowel syndrome/Functional abdominal pain (I) D - Infectious diarrhea (I) Regurg (I) - Reduces regurgitation improves gastrointestinal motility (I)
BioRad Probiotic Baby Drops	L. reuteri DSM 17928	Chewable Drops	100MCFU	1 tab 5 drops	AAD - Antibiotic associated diarrhea - Prevention (I) C - Constipation (I) CEAD - Childhood exanthematous allergic dermatitis (I) CDI - Clostridium difficile infection - community acquired (I) CDI - Clostridium difficile infection - hospital acquired (I) BSPAP - Infantile bowel syndrome/Functional abdominal pain (I) D - Infectious diarrhea (I) Regurg (I) - Reduces regurgitation improves gastrointestinal motility (I)
Garden of Eatin' Probiotic Baby Drops	L. reuteri DSM 17928	Powder	100MCFU	1/1 sachet	AAD - Antibiotic associated diarrhea - Prevention (I) C - Constipation (I) CEAD - Childhood exanthematous allergic dermatitis (I) CDI - Clostridium difficile infection - community acquired (I) CDI - Clostridium difficile infection - hospital acquired (I) BSPAP - Infantile bowel syndrome/Functional abdominal pain (I) D - Infectious diarrhea (I) Regurg (I) - Reduces regurgitation improves gastrointestinal motility (I)
Garden of Eatin' Probiotic Baby Drops	L. reuteri DSM 17928	Drops	100MCFU	5 drops	AAD - Antibiotic associated diarrhea - Prevention (I) C - Constipation (I) CEAD - Childhood exanthematous allergic dermatitis (I) CDI - Clostridium difficile infection - community acquired (I) CDI - Clostridium difficile infection - hospital acquired (I) BSPAP - Infantile bowel syndrome/Functional abdominal pain (I) D - Infectious diarrhea (I) Regurg (I) - Reduces regurgitation improves gastrointestinal motility (I)

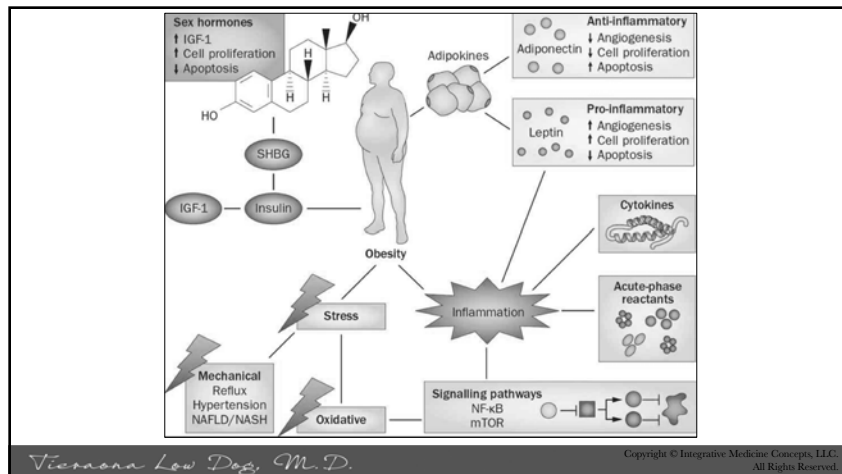
15

Table 1   Examples of foods, nutrients, and dietary patterns that influence human health linked to their effect		
Dietary element	Effect on gut microbiome	Effect on health outcomes mediated by gut microbiome
Low FODMAP diet	Low FODMAP diet increased Actinobacteria; high FODMAP diet decreased abundance of bacteria involved in gas consumption <sup>58</sup>	Reduced symptoms of irritable bowel syndrome <sup>59</sup>
Cheese	Increased <i>Bifidobacteria</i> <sup>57,58</sup> which are known for their positive health benefits to their host through their metabolic activities. <sup>59</sup> Decrease in <i>Bacteroides</i> and <i>Clostridia</i> , some strains of which are associated with intestinal infections <sup>58</sup>	Potential protection against pathogens. <sup>100</sup> Increased production of SCFA and reduced production of TMAO <sup>59</sup>
Fibre and prebiotics	Increased microbiota diversity and SCFA production <sup>22,101,102</sup>	Reduced type 2 diabetes <sup>22</sup> and cardiovascular disease <sup>103</sup>
Artificial sweeteners	Overgrowth of Proteobacteria and <i>Escherichia coli</i> . <sup>104</sup> <i>Bacteroides</i> , <i>Clostridia</i> , and total aerobic bacteria were significantly lower, and faecal pH was significantly higher <sup>27</sup>	Induced glucose intolerance <sup>105</sup>
Polyphenols (eg, from tea, coffee, berries, and vegetables such as artichokes, olives, and asparagus)	Increased intestinal barrier protectors ( <i>Bifidobacteria</i> and <i>Lactobacillus</i> ), butyrate producing bacteria ( <i>Faecalibacterium prausnitzii</i> and <i>Roseburia</i> ) and <i>Bacteroides vulgatus</i> and <i>Akkermansia muciniphila</i> . <sup>107</sup> Decreased lipopolysaccharide producers ( <i>E coli</i> and <i>Enterobacter cloacae</i> ) <sup>106</sup>	Gut micro-organisms alter polyphenol bioavailability resulting in reduction of metabolic syndrome markers and cardiovascular risk markers <sup>108</sup>
Vegan	Very modest differences in composition and diversity in humans and strong differences in metabolomic profile compared with omnivore diet in humans <sup>50</sup>	Some studies show benefit of vegetarian over omnivore diet, <sup>109</sup> others fail to find a difference <sup>110</sup>

Valdes AM, et al. Role of gut microbiota in nutrition and health. *British Medical Journal* 2018;361:j2179

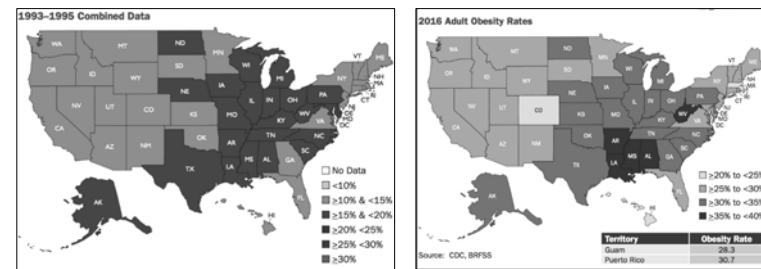
16





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## The Changing Landscape of Adult Weight



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## Mechanisms?

- **Fat tissue produces excess estrogen**, high levels are associated with increased risks of breast, endometrial, ovarian, and some other cancers.
- Obese people often have increased blood levels of **insulin and insulin-like growth factors (IGF-1)**. High levels of insulin and IGF-1 may promote the development of **colon, kidney, prostate, and endometrial cancers**.
- **Obesity** strongly linked with **chronic inflammation**, which can damage DNA
- Fat cells produce adipokines. **Leptin promotes cell proliferation**. Adiponectin less abundant in obese than normal weight—may have **anti-proliferative effects**.

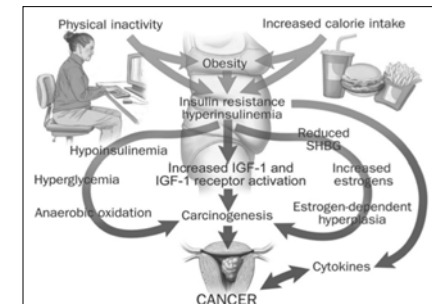
[www.cancer.gov/about-cancer/causes-prevention/risk/obesity/obesity-fact-sheet](http://www.cancer.gov/about-cancer/causes-prevention/risk/obesity/obesity-fact-sheet)

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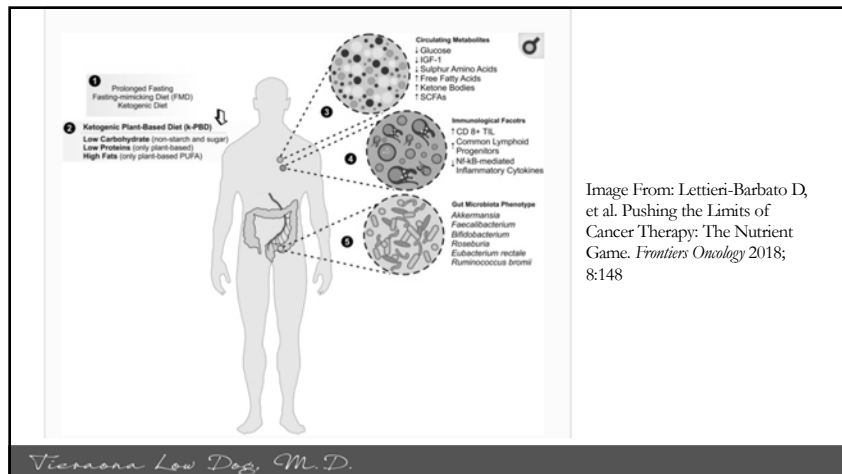
## Obesity and Insulin Growth Factors

- **Increase cancer risk** and cancer-related **mortality** via **insulin resistance, high blood sugar and insulin-growth factors (IGF)**.
- **Elevated insulin** increases tumor growth and aggressiveness.
- **IGF-1, IGF-2** identified as **tumor promoters** in multiple studies.

Belardi V, et al. *J Mammary Gland Biol Neoplasia* 2013; 18(3-4):277-89




24



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## “Cancer Loves Sugar”



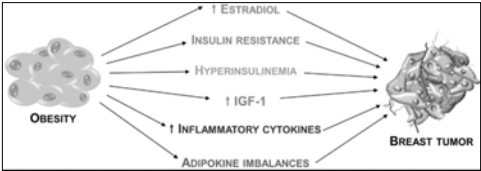
- Tumor cells have remarkable **up regulation of glucose transporter molecules on surface**. Predominant use of **glucose** anaerobically by cancer cells (Warburg effect) important characteristic cancer cells have in common.
- **Ketogenic diet** is very promising, but inconsistent results in small studies. It could be a metabolic intervention. Some tumor types may be more responsive.

Oliviera CL, et al. A Nutritional Perspective of Ketogenic Diet in Cancer: A Narrative Review. *J Acad Nutr Diet* 2018; 118(4):668-688.

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## Women's Healthy Eating and Living (WHEL)



- Carbohydrate restriction associated with striking five-fold reduction in breast cancer recurrence in 50% of subjects, specifically those whose tumors expressed the **IGF-1 receptor**.

Edmond JA, et al. *Cancer Epidemiol, Biomarkers Prev* 2014  
Image from: Mauro L, et al. *Front. Oncol* 2015; doi.org/10.3389/fonc.2015.00157

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## Ask for Advanced Tumor Testing

- FDA approved companion testing for cancer. Understanding what mutations and biomarkers you have can help choose the best therapy.
  - Comprehensive genomic testing
  - Molecular profiling
  - Immunotherapy biomarkers
- Also covered by Medicare, Medicaid.

[www.foundationmedicine.com](http://www.foundationmedicine.com)

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## Keto Diet: Clinical Trial

- **RCT** women with **ovarian or endometrial cancer** randomly assigned to ketogenic diet (**70:25:5** energy from fat, protein, and carbohydrate) or American Cancer Society diet (high-fiber, low-fat).
- **Body composition, fasting serum insulin and IGF-I** obtained at baseline and at end of 12 weeks.
- Those on keto diet **had statistically significant reduction in fasting insulin and IGF-1 levels, and greater reduction in visceral fat.**

Cohen CW, et al. A Ketogenic Diet Reduces Central Obesity and Serum Insulin in Women with Ovarian or Endometrial Cancer. *J Nutr* 2018; 148(8):1253-1260.

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SCIENTIFIC  
AMERICAN.

PUBLIC HEALTH

## The Hunger Gains: Extreme Calorie-Restriction Diet Shows Anti-Aging Results

A new study shows five days of hunger a month may reduce risk factors for aging and age-related diseases

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## Caloric Restriction?



Canto is 27 year old monkey on CR diet, Owen is 29 year old on unrestricted diet.

[news.wisc.edu/monkey-caloric-restriction-study-shows-big-benefit-contradicts-earlier-study/](https://news.wisc.edu/monkey-caloric-restriction-study-shows-big-benefit-contradicts-earlier-study/); Ravussin E, et al. *J Gerontol A Biol Sci Med Sci*. 2015;70(9):1097-104

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- 25 year study: **76 rhesus monkeys (7-14 years)**, fed 30% reduced calorie diet.
- **Disease 3 fold greater in control group. No evidence of diabetes** in any caloric-restricted animal.
- **2-year** study randomized 218 non-obese people to current diet or 25% caloric restriction (**11.7% on average**).
- **Statistically significant reduction in inflammatory markers, weight loss, improved mood, sleep duration, etc.**

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## Fasting-Mimicking Diets (FMD)



Wei M, et al. Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. *Sci Transl Med* 2017; 9(377).

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- **100 healthy participants** 2 study arms tested FMD 5 consecutive days each month for 3 months.
  - **1100 calorie first day, 700 calories for 4 days (plant based, multivitamin).** Ate whatever they wanted rest of the month.
- Three FMD cycles reduced **body weight and total body fat; lowered blood pressure, cholesterol, triglycerides and IGF-1.** Lean muscle mass remained unchanged.
- Note: **25% drop-out rate**
- **Effects noted 3 months AFTER study ended.**

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## Mediterranean Diet and Cancer

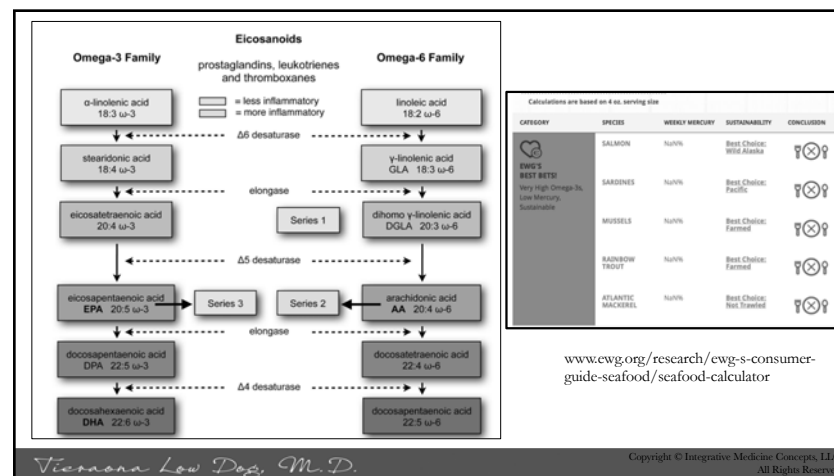


- Study > 2000 women confirmed “Western” diet increases breast cancer risk, while Med diet lowered risk all **breast cancer** subtypes, particularly triple-negative tumors.
- Strong evidence beneficial role MD on **oral and pharyngeal cancer**.
- High adherence to MD associated with **significant reduction in risk of overall cancer mortality (10%), colorectal cancer (14%), prostate cancer (4%) and aerodigestive cancers (56%)**.

Castello A, et al. *Br J Cancer* 2014; 111(7):1454-62; Filomeno M, et al. *Br J Cancer* 2014; 111(5):981-6.  
Schwingshackl L, et al. *Int J Cancer* 2014; 135(8):1884-97.

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## Omega 3 and Prostate Cancer?

- **SELECT trial raised concerns** about potential link between omega 3s and **increased prostate cancer/aggressive cancer**.
- European Food Safety (EFSA) concluded, “**there is no evidence for a role of EPA and/or DHA intake in the development of prostate cancer.**”
- Also, “**supplemental intake of EPA and DHA combined at doses up to 5 g/d does not give rise to safety concerns for adults.**”

EFSA Journal 10(7): doi:10.2903/j.efsa.2012.2815

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## Dietary Fat and Cancer: Systematic Review

- **No associations** found for prostate, esophageal, gastric, renal, bladder, lung, skin, or postmenopausal breast cancer by **total intake or types of dietary fat**.
- **May be an association** between total dietary fat and premenopausal breast cancer.
- Limited-suggestive evidence positive association for **ovarian CA** with intake of saturated fats.



Schwab U, et al. *Food Nutr Res* 2014; 10:58. doi: 10.3402/fnr.v58.25145.

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## Red and Processed Meats: Colorectal CA

- Data from Sister Study, women 35-74 years old from U.S. Puerto Rico with sister diagnosed with breast cancer.
- Red and processed meat consumption, meat cooking practices, and intake of common meat products collected at baseline (N=48,704).
- 4% increased risk of colorectal cancer in those with highest intake of red meat. Risk increased to 46% for bacon and 85% for breakfast sausages; and highest risk with grilled/barbequed red meats.
- Mehta SS, et al. A prospective analysis of red and processed meat consumption and risk of colorectal cancer in women. *Cancer Epidemiol Biomarkers Prev* 2019 Oct 1. pii: cebp.0459.2019.



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## Tips for Grilling

- **Grilling meat at high temperatures** produces polycyclic aromatic hydrocarbons and heterocyclic amines (HCAs).
- Studies show **marinating meat, poultry and seafood for 30 minutes** reduces formation of HCAs. Vinegar, lemon, wine + herbs and spices.
- Cook meat over **low flame to reduce burning and charring**. **Precooking** reduces formation of carcinogens from grilling.
- **Grilled veggies and fruits do not produce HCAs.**
- It's **WHAT** you cook, however, more than **HOW** you cook it!

<http://www.aicr.org/can-prevent/what-you-can-do/quiz-grilling-and-cancer-risk.html>

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## Red and Processed Meat: Gastric Cancer

- Meta-analysis: **43 studies** included in analysis (11 cohort studies and 32 case-control studies with 16,572 cases).
- **RRs of gastric cancer** were:
  - **1.26** (95% CI: 1.11-1.42) for every 100 g/d increment in **red meat**
  - **1.72** (95% CI: 1.36-2.18) for every 50 g/d increment in **processed red meat**
  - **0.86** (95% CI: 0.64-1.15) for every 100 g/d increment in **white meat**

Kim SR, et al. Effect of Red, Processed, and White Meat Consumption on the Risk of Gastric Cancer: An Overall and Dose Response Meta-Analysis. *Nutrients* 2019; 2019 Apr 11;11(4). pii: E826. doi: 10.3390/nu11040826.

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## The Uncertainty of Science

- Recent review: 118 articles, 56 cohorts, >6 million participants
- Possible absolute effects of **red and processed meat consumption on cancer mortality and incidence are very small**; certainty of evidence is low to very low.

Han MA, et al. Reduction of Red and Processed Meat Intake and Cancer Mortality and Incidence: A Systematic Review and Meta-analysis of Cohort Studies. *Ann Intern Med*. 2019. DOI: 10.7326/M19-0699



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## Turmeric (*Curcuma longa*)

- Family: Zingiberaceae (ginger family)
- Part Used: Rhizome
- Perennial plant tropical areas, most grown in India, they consume 80% of crop. Used in meat, fish and vegetable curries.
- Long history of medicinal use ~4,000 years.
- In ancient Ayurvedic literature, called Jayanti, meaning “one who is victorious over disease.”



[www.ncbi.nlm.nih.gov/books/NBK92752/](http://www.ncbi.nlm.nih.gov/books/NBK92752/). Accessed September 2, 2018

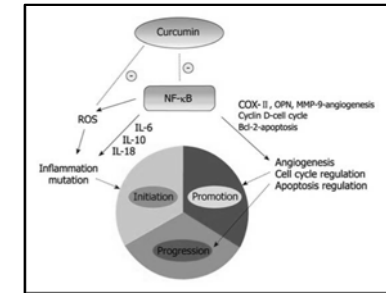
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## Turmeric: the Curcuminoids

- **Beneficial for osteoarthritis, gut inflammation, improving microbial diversity, and topically for wounds.**
- May prevent/beneficial adjunctive treatment for **colorectal cancer.**
- Acts alone/synergistically with EGCG (green tea) to **inhibit malignant changes in oral epithelium.**



Gapta S, et al. Curcumin, a Component of Turmeric: From Farm to Pharmacy. *BioFactors* 2013; 39(1):2-13  
Bannuru RR, et al. Efficacy of curcumin and Boswellia for knee osteoarthritis: Systematic review and meta-analysis. *Semin Arthritis Rheum* 2018 Mar 10; pii: S0049-0172(18)30002-7

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### Cooking Tips:

- Mix ½ teaspoon turmeric in 8 ounces plain yogurt – use as a spread on sandwich or baste for chicken
- Add ½ teaspoon to 2 cups tomato soup
- Add ½ teaspoon to 2 cups steamed rice
- Add ½ teaspoon when stir frying greens such as kale, chard or cabbage

Note: ½ tsp of turmeric powder is approximately 1.5 grams and contains roughly 80-100 mg of curcumin.

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## BENEFITS OF PHYSICAL ACTIVITY



- Enhances skeletal uptake of glucose
- American Cancer Society: exercise may reduce risk of cancer by **reducing insulin and insulin-like growth factors levels, associated with increased cell/tumor growth.**
- Review 73 studies: **25% average risk reduction for breast cancer amongst physically active women.**

Lynch, et al. *Recent Results Cancer Res* 2011; 186:13-42

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## Endocrine Society Second Scientific Statement



“Endocrine disrupting compounds contribute to **outcomes related to impaired reproduction, neurodevelopment, thyroid function, metabolism, and increased propensity for hormone-sensitive cancers.**

Unfortunately, it is difficult to directly relate chronic disease burden to exposures in humans. The **increased prevalence of such diseases underscores the need to invoke precaution in introducing new (and usually untested) chemicals into the environment.”**

**BPA may be associated breast, uterine, prostate cancer. Limit cans/plastic**

Gore AC, et al. *Endocr Rev* 2015; 36(6):E1-E150.

McGuinn LA, et al. *Environ Res* 2015; 136:381-6.

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## Phthalates

- Human made chemicals used **in toys, vinyl floor and wall coverings, detergents, lubricating oils, food packaging, pharmaceuticals, blood bags/tubing, and personal care products.**
- CDC: **84% population have >six phthalates in system. Women higher levels of urinary metabolites than men** for those phthalates that are used in soaps, body washes, shampoos, cosmetics, and similar personal care products.
- **SYNTHETIC fragrances** are a significant source of exposure.

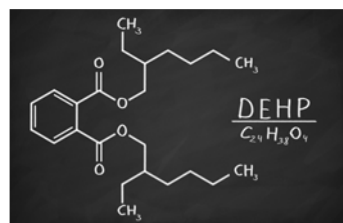
<https://www.fda.gov/cosmetics/cosmetic-ingredients/phthalates> Accessed October 6, 2019

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## Phthalates Insulin Resistance

- Systematic review by EPA researchers: phthalate exposure at levels seen in human populations may have metabolic effects.
- Association between **phthalate exposure and diabetes** should be considered.
- Other EDC implicated in type-2 DM include **BPA, PCBs, and organochlorine pesticides.**



Radke EG, et al. *Environ Int* 2019 Nov;132:104768  
Sarfis RM, et al. *Diabetologia* 2019 Oct;62(10):1811-1822.

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## Some EDCs Act As obesogens

- **Can cause weight gain** via exposure to pesticides/herbicides, industrial/household products, plastics, and personal care products.
- **Highly lipophilic**, increases fat deposition that increases capacity for own retention.
- **Animal models and epidemiological studies show especially sensitive time for exposure is *in utero* and neonatal period.**



Darbre PD. Endocrine Disruptors and Obesity. *Curr Obes Rep* 2017 Mar;6(1):18-27.

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## Reducing Exposure



- Avoid plastics with **recycling #3** on package
- Avoid foods with **plastic wrap/packaging**.
- **Don't heat food in plastic.**
- Read labels of personal care products, **avoid those with phthalates or "fragrance"**
- If water is from a well, **test for phthalates** and contact state health dept. if levels are high
- Use **activated carbon filtration system** or **reverse osmosis**

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## Insecticides and Cancer

- Meta-analysis of 16 studies found childhood exposure to **indoor residential insecticides** (nonoccupational and nonagricultural) is **associated with a significant increased risk of childhood leukemia and lymphomas**.
- Positive but not statistically significant association found for **brain tumors**.
- **Integrated pest management** recommended by **USDA, EPA, American Public Health Association, and National PTA**.



Chen M, et al. Residential Exposure to Pesticide During Childhood and Childhood Cancers: A Meta-Analysis. *Pediatrics* 2015; 136(4):719-29.

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## Glyphosate

- Introduced as **broad-spectrum herbicide** 1974.
- Glyphosate and glyphosate based herbicides have **endocrine-disrupting** effects on **male reproduction** at low doses.
- Two recent reviews of glyphosate's health hazards report conflicting results:
  - Review by International Agency for Research on Cancer (IARC) found glyphosate is a **"probable human carcinogen"**.
  - Review by the European Food Safety Agency (EFSA) **found no evidence of carcinogenic hazard**.



Pham TH, et al. Perinatal exposure to glyphosate and a glyphosate-based herbicide affect spermatogenesis in mice. *Toxicol Sci* 2019 Feb 20. pii: ktz039.

Landrigan PJ, et al. The need for independent research on the health effects of glyphosate-based herbicides. *Environ Health* 2018 May 29;17(1):51.

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## Glyphosate and Cancer

- **Agricultural Health Study:** prospective cohort of **54,251 licensed pesticide applicators** from North Carolina and Iowa, of which **44,932 (82.8%) used glyphosate**, including 5779 incident cancer cases (79.3% of all cases).
- **Glyphosate was not statistically significantly associated with cancer at any site in this study.** Applicators in **highest exposure quartile had increased risk of acute myeloid leukemia**, though didn't reach statistical significance.

Amdreotti G, et al. Glyphosate Use and Cancer Incidence in the Agricultural Health Study. *J Natl Cancer Inst* 2018; 110(5):509-516.

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## Atrazine

- Second most widely used herbicide in US and most commonly detected pesticide in surface water: *it is a pervasive water contaminant.*
- **Endocrine disruptor, inhibiting luteinizing hormone production, increasing aromatase production.** Can feminize male frogs.
- **Immunotoxic effects and potential link to lymphoma.**
- **Banned by EU in 2004.**



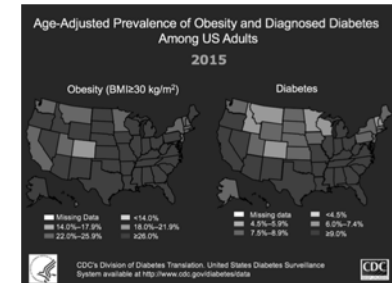
Thompson PA, et al. Environmental immune disruptors, inflammation and cancer risk. *Carcinogenesis* 2015; 36(Suppl 1): S232-S253.

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## Atrazine and Obesity

- **Agricultural Health Study: exposure during pregnancy increases risk for gestational DM.**
- Chronic administration of **low concentrations of atrazine** in drinking water of rats decreased basal metabolic rate, and increased body weight, intra-abdominal fat and insulin resistance without changing food intake or physical activity level.



Lim S, et al. Chronic exposure to the herbicide, atrazine, causes mitochondrial dysfunction and insulin resistance. *PLoS One* 2009;4(4):e5186.  
Saldana TM, et al. Pesticide exposure and self-reported gestational diabetes mellitus in the Agricultural Health Study. *Diabetes Care* 2007; 30(3):529-34

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## Lymphoma and Drinking Water

- Incidence of non-Hodgkin lymphoma increased rapidly in rural areas and has been consistently higher in Nebraska than US as a whole.
- **Nebraska water high nitrate AND atrazine.**
- Drinking water containing nitrate was associated with a **nearly three-fold increase in risk for developing NHL if atrazine** was also present.
- Example of difficulty in predicting cumulative effect of multiple chemical exposures..



Rhoades MG, et al. *Environ Health Insights* 2013; 7:15-27

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<https://www.ewg.org/tapwater/water-filter-guide.php>

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## Reducing Environmental Exposures

1. Eat **fresh** rather than processed food, when possible
2. **Organic** fruits/vegetables, dairy; **grass fed/finished** meats, **free range eggs**, when possible
3. Reduce consumption of foods/beverages **in cans and plastic containers**
4. Minimize use of personal care products containing **fragrances (skindeep.org)**
5. **Avoid** garden/household/pet pesticides or fungicides. Use **integrated pest management for home/yard**.
6. Use **water filtration system (ewgs-water-filter-buying-guide)**, consider **HEPA** filters in home



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## HPV Vaccine

- Estimated 24,600 newly diagnosed cancers attributable to **two high-risk HPV** types targeted by all currently licensed HPV vaccines
- Routine HPV vaccination age 11 or 12 years; catch-up through age 26 years; FDA approved Gardasil 9 from ages 9-45 years.
- CDC: June 2006-March 2014, ~67 million doses HPV vaccines distributed and ~25,000 adverse events reported; 92% classified as non-serious.
- After careful review, *none of these adverse events* any more common after HPV vaccination than among comparison groups.

[www.cdc.gov/vaccinesafety/vaccines/HPV/index.html](http://www.cdc.gov/vaccinesafety/vaccines/HPV/index.html)  
<https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm>

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## Hormone Therapy for Women

- **Benefits likely outweigh risks** for symptomatic women before the age of 60 years or within 10 years after menopause.
- **Transdermal estrogen less likely to cause blood clots.**
- **Unopposed estrogen** does not significantly increase risk breast CA.
- **Progesterone** associated with **lower risk of breast cancer** and clots compared to synthetic progestogens (e.g., Provera)
- If symptoms primarily urogenital, vaginal estrogen can be used with minimal systemic absorption.

Bhupathiraju SN, et al. *Endocr Pract* 2014; 20(12):1-13; L-Hermite M. *Climacteric*. 2013 Aug;16 Suppl 1:44-53.  
 Hale GE, et al. *Trends Cardiovasc Med* 2015; 25(6):540-9; deVilliers TJ, et al. *Maturitas* 2013; 391-2

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Table 1. Estimated Event Rate Difference Associated With Combined Estrogen and Progestin Use vs Placebo in Postmenopausal Women

Outcome	Absolute Event Rate Difference per 10 000 Woman-Years (95% CI)
<b>Harms</b>	
Breast cancer (invasive)	9 (1 to 19)
Coronary heart disease	8 (0 to 18)
Dementia (probable) <sup>a</sup>	22 (4 to 53)
Gallbladder disease	21 (10 to 34)
Stroke	9 (2 to 19)
Venous thromboembolism <sup>b</sup>	21 (12 to 33)
Urinary incontinence	876 (606 to 1168)
<b>Benefits</b>	
Diabetes	-14 (-24 to -3)
All fractures	-44 (-71 to -13)
Colorectal cancer	-6 (-9 to -1)

<sup>a</sup> Women aged 65 years and older.

<sup>b</sup> Includes deep vein thrombosis and pulmonary embolism.

Table 2. Estimated Event Rate Difference Associated With Estrogen Use Alone vs Placebo in Postmenopausal Women

Outcome	Absolute Event Rate Difference per 10 000 Woman-Years (95% CI)
<b>Harms</b>	
Dementia (probable) <sup>a</sup>	12 (-4 to 41)
Gallbladder disease	30 (16 to 48)
Stroke	11 (2 to 23)
Venous thromboembolism <sup>b</sup>	11 (3 to 22)
Urinary incontinence	1261 (880 to 1689)
<b>Benefits</b>	
Breast cancer (invasive)	-7 (-14 to 0.4)
All fractures	-53 (-69 to -39)
Diabetes	-19 (-34 to -3)

<sup>a</sup> Women aged 65 years and older.

<sup>b</sup> Includes deep vein thrombosis and pulmonary embolism.

**Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Women** US Preventive Services Task Force Recommendation Statement. *JAMA*. 2017;318(22):2224-2233.

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## Letting Go.....

*“Healing may not so much be about getting better, but about letting go, of all the expectations, all of the beliefs, and becoming who you are.”*

— Rachel Naomi Remen, M.D.



*Vianna Lee Do, M.D.*

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