




**Preparing for Pregnancy:
Pre-conception Nutritional Advice**



Victoria Maizes MD
Executive Director
Arizona Center for Integrative Medicine
Professor of Medicine, Family Medicine and Public Health
University of Arizona

 THE UNIVERSITY
OF ARIZONA.
College of Medicine


 ARIZONA CENTER FOR
Integrative Medicine

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Nothing to disclose.

Is fertility declining?

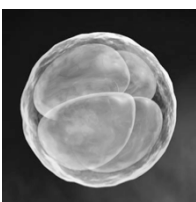
- ⌘ Delayed child bearing
- ⌘ Obesity
- ⌘ Dietary changes
- ⌘ Environmental pollutants
- ⌘ Psychological stress



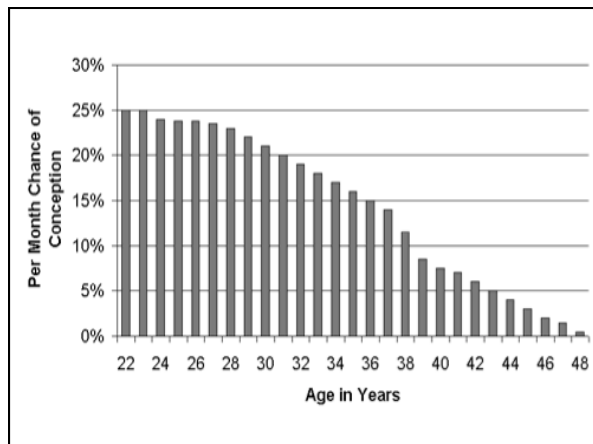
Human Reprod Update 13(3) 209-223 2007

Definitions:

- ⌘ Fertility = the capacity to produce offspring
- ⌘ Clinical infertility = the inability to become pregnant after 12 months of unprotected intercourse
- ⌘ Affects approx. 15% of the population in industrialized nations

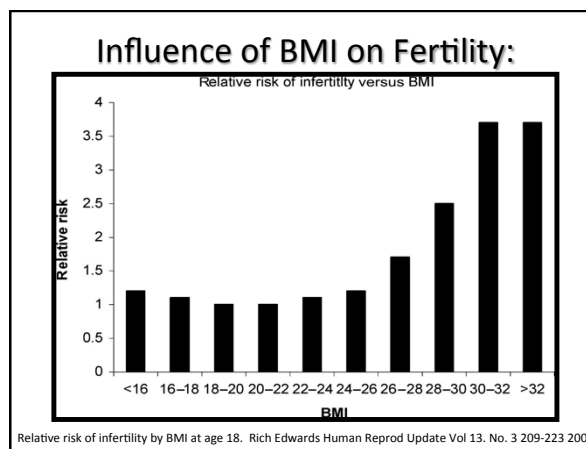
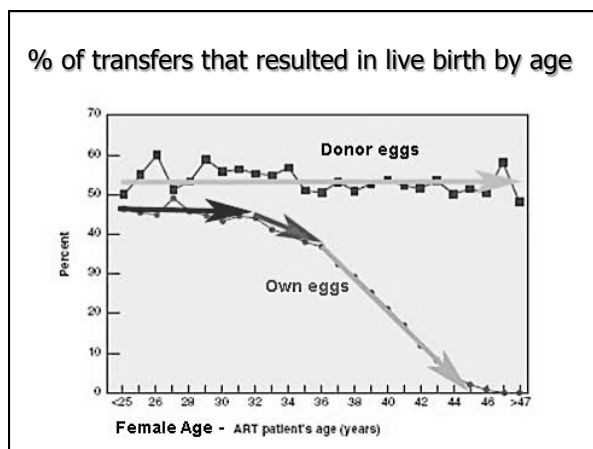
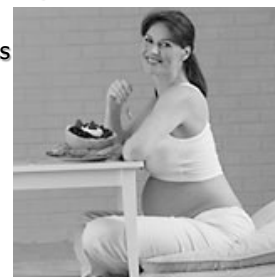


Human Reprod Update 13(3) 209-223 2007



Can ART solve all?

- ☞ IVF was 47% effective overall in women who received three IVF cycles
- ☞ Women in their twenties: 58% success
- ☞ Women aged 40-44: 22% success



The Nurse's Health Study II on Fertility:

- ⌘ Onset 1989
- ⌘ 116,000 female registered nurses ages 24–42
- ⌘ Followed every 2 years
- ⌘ Diet first measured in 1991 and updated every 4 years
- ⌘ 18,555 married women attempting to conceive; 438 women reported ovulatory infertility

Epidemiology • Volume 20, Number 3, May 2009

Carbohydrates and Infertility

Total carb intake not related to ovulatory infertility

- ⌘ High glycemic index (GI) foods

↑ risk: RR was 1.92
(CI =1.26-2.92)

- ⌘ Low GI foods associated with ↓ risk

- ⌘ Specific foods: only cold breakfast cereal intake statistically significant (P = 0.02)



A prospective study of dietary carbohydrate quantity and quality in relation to risk of ovulatory infertility. Chavarro JE. et al. European J of Clin Nutrition. 63(1):78-86, 2009 Jan.

Protein and Fertility:

- ⌘ Protein type matters in ovulatory infertility:
 - ⌘ RR comparing highest and lowest quintiles of animal protein intake was 1.39 (1.01 to 1.90; 0.03)
 - ⌘ RR for vegetable protein intake was 0.78 (0.54 to 1.12; 0.07)
 - ⌘ Consuming 5% of total energy intake as vegetable protein rather than as animal protein was associated with >50% lower risk (P =.007)

Chavarro JE. et al, Protein intake and ovulatory infertility. Amer J of Ob Gyn. 198(2) :2008

Age Matters

- ⌘ For women <32 years, consuming 5% of energy as vegetable protein rather than as carbs was unrelated to ovulatory infertility
- ⌘ For women >32 years,
 - ⌘ 50% lower risk if eating vegetable protein rather than carbs (RR 0.48; CI 0.27-0.86; P .01).
 - ⌘ lower risk if 5% of energy consumed as vegetable protein instead of animal protein

Insulin Sensitivity:

- ⌘ High glycemic index/load increases insulin
- ⌘ Insulin decreases SHBG
- ⌘ SHBG preferentially binds testosterone – less SHBG means more free testosterone



Protein intake and ovulatory infertility. Chavarro JE. et al Amer J of Ob Gyn. 198(2) 2008

Dairy and Fertility



- ⌘ Hormone free
 - ⌘ Full fat vs low-fat
 - ⌘ Hormones separate
 - ⌘ Lipophilic hormones
 - ⌘ Water-soluble hormones
- ⌘ Milking pregnant cows

*J Am Acad of Derm 2005;53:207-214
www.cornucopia.org/dairysurvey*

Dairy and Fertility:

- ⌘ Inverse relationship between dairy fat intake and ovulatory infertility (P, trend = 0.05).
 - ⌘ women consuming low-fat dairy foods ≥ 2 servings per day compared to ≤ 1 serving per week was 1.85 (1.24-2.77; 0.002)
 - ⌘ Intakes of lactose, calcium, phosphorus and vitamin D were unrelated to ovulatory infertility.
- ⌘ RR comparing women consuming ≥ 1 serving per day of high-fat dairy foods to those consuming ≤ 1 serving per week was 0.73 (0.52-1.01; 0.01).

Chavarro JE. Et al A prospective study of dairy foods intake and anovulatory infertility. Human Reproduction. 22(5):1340-7, 2007

Caffeine:

- ⌘ Multiple trials and data is mixed
 - ⌘ Retrospective trials – recall bias?
- ⌘ Caffeine improves insulin sensitivity which improves ovulatory function in women with PCOS



Epidemiology 20(3) May 2009

Soda and Fertility:

- ⊗ NHS: Intake of caffeinated soft drinks, was associated with a higher risk of ovulatory infertility among women consuming ≥ 2 caffeinated soft drinks per day
 - ⊗ 47% greater risk than women who consumed < 1 caffeinated soft drink per week
- ⊗ Similar associations were observed for noncaffeinated, sugared, diet, and total soft drinks
- ⊗ Mechanism: impaired fasting glucose and metabolic syndrome?



Epidemiology 20(3) May 2009

Fat and fertility:

- ⊗ Trans fat reduce PPAR-gamma –
 - ⊗ PPAR-gamma responsible for activating insulin
 - ⊗ The average amount of trans fat in American's diets (6 g) cuts PPAR-gamma in half
- ⊗ Trans fats increase inflammation in the body which interferes with ovulation, conception, and early embryonic development

Nutrition Facts	
Serving Size 1 bag 7 oz 198g (198 g)	
Amount Per Serving	
Calories 972	Calories from Fat 555
% Daily Value*	
Total Fat 64g	99%
Saturated Fat 16g	80%
Trans Fat	
Cholesterol 0mg	0%
Sodium 1485mg	62%
Total Carbohydrate 105g	35%
Dietary Fiber 9g	35%
Sugars	
Protein 15g	
Vitamin A 9% • Vitamin C 112%	
Calcium 10% • Iron 21%	

Mozaffarian D, Cao H, King IB, et al. Trans-palmitoleic acid, metabolic risk factors, and new-onset diabetes in U.S. adults: a cohort study. *Ann Intern Med* 2010;153:790–799

Trans fats and Ovulatory Infertility:

- ⊗ NHS: Trans fat vs Carbs: each 2% increase in energy intake from trans fats as opposed to carbs was associated with a 73% greater risk of infertility
- ⊗ Trans fat vs mono unsat: obtaining 2% of energy from trans fats rather than monounsaturated fats was associated with $>$ double risk of infertility (RR = 2.31; 95% CI: 1.09, 4.87).



Dietary fatty acid intakes and the risk of ovulatory infertility. Chavarro JE, et al. *American Journal of Clinical Nutrition*. 85(1):231-7, 2007

Alcohol:

- ⊗ NHS: positive association between alcohol intake of ≥ 1 drink per day and ovulatory infertility
 - ⊗ Association disappeared after accounting for parity and other factors
 - ⊗ Drinking < 1 drinking per day was unrelated to ovulatory infertility in all analyses
- ⊗ 16 studies on association between alcohol intake and fertility
 - ⊗ Only 5 of the studies prospective
 - ⊗ Divided between null and positive studies



Epidemiology 20(3) May 2009

2004 EPA warning

- ⌘ Do not eat shark, swordfish, king mackerel, or tilefish because they contain high levels of mercury.
- ⌘ Eat up to 12 ounces (2 average meals) a week of fish and shellfish that are lower in mercury.
 - ⌘ Shrimp, canned light tuna, salmon, pollock, and catfish.
 - ⌘ Albacore ("white") tuna max of 6 ounces per week.
- ⌘ Check local advisories about the safety of fish caught in local lakes, rivers, and coastal areas.

If no advice is available, eat up to 6 ounces per week but don't consume any other fish during that week.



Fish facts

Avon Longitudinal Study of Parents and Children (ALSPAC) - 11,875 pregnant women FFQ assessing seafood consumption at 32 weeks' gestation.

- ⌘ Compared developmental, behavioral, and cognitive outcomes of the children (aged 6 mos - 8 yrs) in women consuming none, some (1-340 g per week), and >340 g per week.
- ⌘ Maternal seafood intake during pregnancy <340 g per week associated with children in the lowest quartile for verbal IQ
 - ⌘ (no seafood consumption, odds ratio 1.48, CI 1.16-1.90; some, 1.09, 0.92-1.29; overall trend, $p=0.004$)



Hibbeln JR, et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. *Lancet*. 2007 Feb 17;369(9561):578-85

Fish Facts continued

- ⌘ The Seychelles Child Development Study
 - ⌘ 779 mother-infant pairs recruited in 1989-1990 on the island of Ma'he followed to age 9
 - ⌘ Selected because fish consumption in mothers averaged 12 fish meals a week
- ⌘ No consistent adverse developmental effects in the children
- ⌘ Presumption: protective nutrients in fish including long-chain polyunsaturated fatty acids, iodine, iron, and choline

Myers GJ et al. Nutrient and Methyl Mercury Exposure from Consuming Fish. *Journal of Nutrition* 137:2805-2808, 2007

Politics and Food Policy

- ⌘ The 2010 U.S. Dietary Guidelines for Americans recommend at least eight ounces of seafood per week
- ⌘ Yet, seafood consumption has dropped to 1.89 ounces per week (2008 FDA survey)
- ⌘ Senator Kirsten Gillibrand (D-New York) joined Senator Tom Coburn, M.D. (R-Oklahoma) in urging the FDA to raise the maximum amount of seafood it recommends for young children and pregnant or nursing mothers

Mercury Levels			
Highest	Higher	Low	Lowest
AVOID	Eat no more than three 6-oz servings a MONTH	Eat no more than six 6-oz servings per MONTH	Enjoy two 6-oz servings each WEEK
Kajiki (swordfish) Saba (mackerel) Shark Tilefish	Ahi (yellowfin tuna) Buri (adult yellowtail) Hamachi (young yellowtail) Inada (very young yellowtail) Kanpachi (very young yellowtail) Katsuo (bonito) Maguro (bigeye, bluefin or yellowfin tuna) Makiki (blue marlin) Masu (trout) Meji (young bigeye, bluefin* or yellowfin tuna) Shiro (albacore tuna) Toro (bigeye, bluefin or yellowfin tuna)	Kani (crab) Seigo (young sea bass) Suzuki (sea bass)	Aji (horse mackerel) Akagai (ark shell) Anago (conger eel) Aoyagi (round clam) Awabi (abalone) Ayu (sweetfish) Ebi (shrimp) Hamaguri (clam) Hamo (pike conger, sea eel) Hatahata (sandfish) Himo (ark shell) Hokkigai (surf clam) Hotategai (scallop) Ika (squid) Ikura (salmon roe) Kaibashira (shellfish) Kaiware (daikon-radish sprouts) Karei (flatfish) Kohada (gizzard shad)

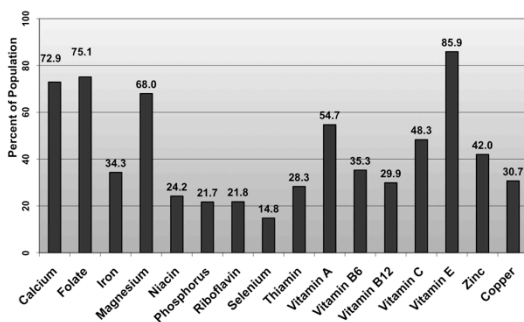
Multi-vitamin use

- ⊕ NHS: compared with women who did not take multi-vitamins, RR of ovulatory infertility was:
 - ⊗ 0.88 for women consuming ≤ 2 tabs/week
 - ⊗ 0.69 for 3-5 tabs/week,
 - ⊗ 0.59 for ≥ six tabs/week,
- ⊕ Micronutrients impact fertility, embryogenesis and placentation



Use of multivitamins, intake of B vitamins, and risk of ovulatory infertility. Chavarro JE. et al. Fertility & Sterility. 89(3):668-76, 2008 Mar. Role of micronutrients in the periconceptional period. Cetin I. et al Human Reproduction Update. 16(1):80-95, 2010 Jan-Feb.

Percent of U.S. Population Not Meeting the DRI For Specific Nutrients



<http://www.ba.ars.usda.gov/cnrg/services/cnmapfr.html>

Are women supplementing appropriately?

- ⊕ Pilot study: 176 pregnant women's use of omega-3, multivitamin, and other supplements
 - ⊗ Surveyed women in prenatal clinics
 - ⊗ 6 women in first trimester, 82 in the second trimester, and 87 were in the third trimester
 - ⊗ 159 respondents (90.3%) reported taking a multivitamin - none were taking a supplement that contained omega-3
 - ⊗ only 20 (11.4%) were taking omega-3

Grigoriadis S. et al J of OBGYN Canada: JOGC. 32(3):209-16, 2010 Mar.

Fertility Blend

- ⌘ A proprietary combination of chasteberry, green tea extracts, L-arginine, vitamins E, B₆, B₁₂, folate, iron, magnesium, zinc, and selenium
- ⌘ Two RCTs
 - ⌘ 2004 pilot -30 women, aged 24 - 46 who were unsuccessful at conceiving over 6 - 36 months, Fertility Blend tid vs placebo for three cycles
 - At 5 months, 5 women in the treatment group were pregnant 0 in control (33% versus 0%, $P < .01$).
 - Four of the five women had healthy live births
 - ⌘ 2006 - 93 women, aged 24-42
 - At 6 months, 17 vs 10 women pregnant. ($P < .01$)

Westphal LM, et al A nutritional supplement for improving fertility in women. J Reprod Med 2004;49:289
Westphal LM, et al Double-blind, placebo-controlled study of Fertility blend: a nutritional supplement for improving fertility in women. Clinical & Experimental Obstetrics & Gynecology. 33(4):205-8, 2006.

Folic Acid

- ⌘ NHS: women who consumed >700 mcg /day from food and supplements were 40% more likely to get pregnant
- ⌘ Methyl donor needed during DNA replication
- ⌘ Folate helps metabolize homocysteine into methionine
 - ⌘ Women with high homocysteine are more likely to miscarry and to have preeclampsia
- ⌘ Folic acid may stimulate ovulation (more dizygotic twins)
- ⌘ Methylene tetrahydrofolate reductase genetic variant associated with poorer response to IVF

Thaler, C. J., Budiman, H., Ruebsamen, H., Nagel, D. and Lohse, P. Effects of the Common 677C-T Mutation of the 5,10-Methylenetetrahydrofolate Reductase (MTHFR) Gene on Ovarian Responsiveness to Recombinant Follicle-Stimulating Hormone. American Journal of Reproductive Immunology, 55(4): 251-258 April 2006.

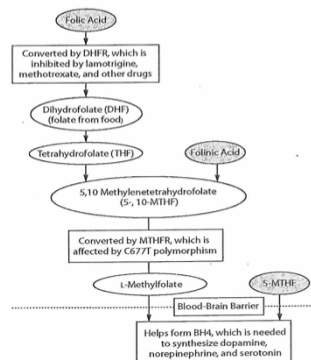
Folate

3 commercially available forms



Fava M et al. Folate in Depression. J Clin Psychiatry 2009; 70(suppl):18-2

Figure 1. Metabolic Steps Required for 3 Folate Formulations to Cross the Blood-Brain Barrier



Abbreviations: BH4 = tetrahydrobiopterin, DHFR = dihydrofolate reductase, MTHFR = methylenetetrahydrofolate reductase.

Vitamin C

- ⌘ RCT of 150 women with luteal phase defects
 - ⌘ 750 mg/day of vitamin C vs placebo
 - ⌘ After 6 months of treatment fertility in the vitamin C group was significantly higher than in the placebo group (25% versus 11%, $P = .045$).
 - ⌘ Progesterone levels were also significantly increased in the treatment group (52.6% versus 21.7%, $P < .01$).
 - ⌘ Potential Mechanism: effects of oxidative stress in oocyte maturation and fertilization

Henmi H, et al. Effects of ascorbic acid supplementation on serum progesterone levels in patients with luteal phase defect. Fertil Steril 2003;80:459-61.

Iron and Fertility:

- ⌘ NHS: Women who consumed iron supplements had a significantly lower risk of ovulatory infertility than those who did not (RR 0.60, CI 0.39-0.9)
- ⌘ Ideal dose appears to be 40-80 mg of iron
- ⌘ Heme iron intake did not reduce ovulatory infertility



Chavarro JE. Et al. Iron intake and risk of ovulatory infertility. *Obstetrics & Gynecology*.108(5):1145-52, 2006 Nov.

Iodine intake recommendations:

- ⌘ WHO: 150 mcg/d for adults & adolescents, 200 mcg/d for pregnant or lactating women
- ⌘ IOM recommends 150 mcg/d for adults, 220 mcg/d for pregnant women, and 290 mcg/d for lactating women
- ⌘ Historical levels:
 - ⌘ NHANES I (1971-1974) - median urine iodine was 320 mcg/L, reflecting adequate dietary iodine intake
 - ⌘ NHANES III (1988-1994) - median urinary iodine had fallen to 145 mcg/L
 - ⌘ NHANES 2001-2002 iodine intake 167.8 mcg/L
- ⌘ The risk for insufficient dietary iodine intake in reproductive-aged women (15-44 y) increased 3.8-fold
 - ⌘ 11.7% of adult women are iodine deficient
 - ⌘ 7% of pregnant women in 1994 were deficient (compared to 1% in 1974)

Iodine

- ⌘ Not all multivitamins contain iodine. Those that do typically contain 150 mcg of iodine per tablet.
- ⌘ Replacement of iodine
 - ⌘ use iodized salt in cooking and at the table
- ⌘ Food sources include:
 - ⌘ Milk
 - ⌘ egg yolks
 - ⌘ Saltwater fish
 - ⌘ Garlic
 - ⌘ Lima beans and soybeans
 - ⌘ Mushrooms
 - ⌘ Seaweed, dulse and kelp
 - ⌘ Sesame seeds
 - ⌘ Asparagus, spinach, summer squash, Swiss chard, Turnip greens



Flax seed

Pilot trial: 18 normally cycling women, randomized cross-over design.

- ⌘ **Methods:**
 - ⌘ Each woman consumed her usual omnivorous, low fiber (control) diet for 3 cycles and her usual diet supplemented with flax seed for another 3 cycles.
 - ⌘ 2nd and 3rd flax cycles compared to 2nd and 3rd control cycles.
- ⌘ **Results:**
 - ⌘ 3 anovulatory cycles occurred during the 36 control cycles - none during the 36 flax seed cycles.
 - ⌘ ovulatory flax cycles were consistently associated with longer luteal phase (LP) (12.6 vs. 11.4 days; P = 0.002).
 - ⌘ No significant differences between flax and control cycles for estradiol or estrone during the early follicular phase, midfollicular phase, or LP.
 - ⌘ The LP progesterone/estradiol ratios were significantly higher during the flax cycles.

Phipps WR. et al Effect of flax seed ingestion on the menstrual cycle. *J Clinical Endocrinology & Metabolism*. 77(5):1215-9, 1993 Nov.

Male Factors



Fertility in men

⌘ Obesity

- ⌘ alterations in hormonal profiles (reduced inhibin B and androgen levels accompanied by elevated estrogen levels)
- ⌘ increased scrotal temperature
- ⌘ contributes to erectile dysfunction
- ⌘ reduces semen quality
- ⌘ changes sperm proteomes



*Cabler S. et al Asian Journal of Andrology. 12(4):480-9, 2010 Jul.
Du Plessis SS. Et al Nature Reviews Urology. 7(3):153-61, 2010 Mar.*

BMI in men

- ⌘ Despite major differences in reproductive hormone levels with increasing body weight, only extreme levels of obesity influence male reproductive potential
- ⌘ Obesity in father does predicts obesity in pre-menarchal daughter

*Chavarro JE. et al. Fertility & Sterility. 93(7):2222-31, 2010
Ng Nature Oct 2010*

Fertility in men

- ⌘ 80% of men don't get 5 servings of fruits and vegetables per day
- ⌘ Vitamin D and autism



*Cabler S. et al Asian Journal of Andrology. 12(4):480-9, 2010 Jul.
Du Plessis SS. Et al Nature Reviews Urology. 7(3):153-61, 2010 Mar.*

Cochrane Review of Anti-oxidants in Men

- ⌘ 30-80% of male subfertility due to effects of oxidative stress on sperm.
- ⌘ 34 RCTs, 2876 couples
 - ⌘ antioxidant supplements (single or combined) taken by the male partner of a couple seeking fertility assistance compared with placebo, no treatment, or another antioxidant
- ⌘ Outcomes:
 - ⌘ live birth, pregnancy, miscarriage, stillbirth, sperm DNA damage, sperm motility, sperm concentration and adverse effects.
 - ⌘ *Live birth*: 3 trials. Antioxidant use associated with increase in live birth rate (OR 4.85, 95% CI 1.92 to 12.24; P = 0.0008)
 - ⌘ *Pregnancy rate*: 15 trials. 96 pregnancies in 964 couples. Antioxidant use was associated with increased pregnancy rate (OR 4.18, 95% CI 2.65 to 6.59; P < 0.00001)

Showell MG, et al. Antioxidants for male subfertility
Cochrane Database of Systematic Reviews 2011, Issue 1

Paternal age and autism

- ⌘ Increases genetic mutations – increases risk for autism
- ⌘ Autism Spectrum Disorder 5.75 times more common for fathers >40 rather than <30



Environmental influences

- ⌘ Endocrine disruptors
 - ⌘ Pesticides
 - ⌘ Plastics
 - ⌘ BPA
 - ⌘ Phthalates
- ⌘ Environmental Working Group – ewg.org
- ⌘ UCSF – Program on Reproductive Health and the Environment:
prhe.ucsf.edu/prhe/pubs/shapingourlegacy.html



Does changing your diet help?

- ⌘ 25 people, 5 days, vegetarian diet, at a Buddhist temple
- ⌘ Measured levels of urinary excretion of antibiotic residues, phthalate metabolites and oxidative stress biomarkers
- ⌘ Reduction in antibiotics and phthalates and oxidative stress biomarker

Ji, K, et al. 2010. Influence of a five-day vegetarian diet on urinary levels of antibiotics and phthalate metabolites: Environmental Research. 2010

Eat more

- ⌘ Vegetable protein
- ⌘ Foods with rich amounts of omega 3
- ⌘ Vitamin D foods
- ⌘ Whole dairy products
- ⌘ Low glycemic index carbohydrates



Eat less

- ⌘ Trans fats
- ⌘ High mercury fish
- ⌘ Animal protein
- ⌘ Sodas (eliminate)
- ⌘ Pesticide laden
- ⌘ Alcohol



Supplement Wisely:

- ⌘ Multivitamin
- ⌘ Iron
- ⌘ Folic acid
- ⌘ Vitamin C
- ⌘ Iodine
- ⌘ Vitamin D
- ⌘ Omega 3



Integrative Approaches

