Dairy, Sugar and Red Meat - What If Macrobiotics Was Right All Along?

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DISCLOSURE

• No financial disclosure to reveal
• I have lived with a macrobiotic chef for the past 17 years!

Macrobiotics

• Based on teachings of Japanese physician, Sagen Ishizuka (1850-1910)
• Saw food as basis of health and illness
• Saw changing food habits as the cause of physical and moral decline of Japan
• Modern era ushered in meat, dairy, potatoes, eggs, white bread, refined sugar
  – Perhaps appropriate for cold, dry climates
  – For warm, moist island climate, proper diet is rice, vegetables and sea products

Macrobiotics

• Introduced to the US by Georges Oshawa
• Published *Zen Macrobiotics: The Art of Rejuvenation and Longevity* in 1960
• Mishio Kushi established the Kushi Institute in Brookline in 1977
• Diet promoted as prevention as well as therapy for serious diseases esp. heart disease and cancer


Macrobiotics

• Macro=great bios=life
• Diet emphasizes whole grains and fresh vegetables
• Avoids meat, dairy foods and processed foods
• Goal is to provide the body with essential nutrients to function efficiently without taxing it with toxins or excesses that must be eliminated or stored
• A body not burdened by excesses or toxins can heal better

Macrobiotics

- All things – our bodies, our food and everything else – are composed of yin and yang energies.
- Yin energies are outward moving, yang inward.
- Most American foods have strong yin and yang energies and tend to be acid-forming.
- Macrobiotics emphasizes two food groups – grains and vegetables – that have the least extreme yin and yang qualities – hence easier to achieve balance.


ACS and WCRF/AICR Guidelines

- Maintain a healthy weight throughout life
  - Balance caloric intake with physical activity
  - Avoid excessive weight gain throughout the life cycle
  - Achieve & maintain a healthy weight if currently overweight or obese

Be as lean as possible without becoming underweight

WEIGHT GUIDELINES

Obesity-Associated Malignancies

AICR report estimates that obesity-related excesses of these 7 cancers account for approx 105,000 preventable deaths a year in the US

Body Fat Increases CA Risk

- Body fat secretes cytokines that promote inflammation
- Too much body fat triggers insulin resistance, raising levels of insulin and growth factors that promote cancer
- Fat increases estrogen production
- Increase in body fat may impair immunity
Overweight and Breast Cancer

- Aromatization of adrenal androgens in adipose tissue generates estrogens
- SHBG levels lower in overweight women resulting in more bioavailable estrogen
- Losing weight after menopause can reduce circulating estrogens and ↑ SHBG
- Nurses Health Study suggests 15% breast CA associated with adulthood weight gain
- Risks stronger in women never using HRT

Linos and Willett, JNCCN, 2007

ENERGY DENSE FOODS GUIDELINES

Choose foods and beverages in amounts that help achieve & maintain a healthy weight

- Avoid sugary drinks
- Limit consumption of energy dense foods
- Particularly processed foods high in added sugar, low in fiber or high in fat

Glycemic Load and Colon CA

- Study of 131,000 people to determine effect of dietary glycemic load, GI, CHO, fructose and sucrose on colon CA
- In Nurse’s Health Study cohort– no association found
- In Health Professional’s Follow-Up Study men, 27-37% increased CA risk with increasing intake of CHO, GL, sugars

Michaud CA Epi Bio Prev 2006

Mortality in CA with Diabetes

- Systematic review and metaanalysis comparing overall survival in cancer pts with and without preexisting diabetes
- 8-18% newly dx’ed CA pts with DM (7% US)
- Equivocal data on impact of DM on CA death
- This analysis evaluates longterm, all-cause mortality
- 23 articles of 7858 titles met all criteria

Barone et al, JAMA, 2008
Meta-analysis and Pooled Hazard Rate of Long-term All-Cause Mortality in 23 Studies Comparing Cancer Patients With and Without Preexisting Diabetes Mellitus

- Endometrial (HR 1.76), breast (1.61) and colorectal (1.32)

Mortality in CA with Diabetes

- Explanations for observed association
  - Increased proliferation and metastases with hyperinsulinemia, hyperglycemia and ↑ ROS
  - Less aggressive CA treatment offered DM pts
  - DM pts may have poorer response to CA Rx
  - Pts with DM may present with later stage dz b/o suboptimal screening
  - Dx and Rx of CA may distract from glycemia mx
  - Excess mortality may be independent of CA & Rx

Barone et al, JAMA, 2008

Insulin Like Growth Factor-I

- Substantial evidence implicates IGF-I signaling in the development and progression of many cancers, including breast
  - High IGF-I levels predict increased risk
  - Antiestrogens reduce IGF-I levels
  - IGF-IR hyperactive and overexpressed in many breast cancers
  - IGF-I caused gene expression changes in breast CA cells associated with cell proliferation, metabolism and DNA repair

Creighton et al JCO 2008

RED MEAT GUIDELINES

- Limit consumption of processed and red meats

- Limit consumption of red meats (beef, pork and lamb) and avoid processed meats

Meat Intake and Colon Cancer

- NIH-AARP Diet and Health Study is an analytic cohort of 300,948 Americans aged 50-71 from 6 states
  - Completed a 124-tem FFQ
  - 2719 incident colorectal cases after 7.2 yrs
  - Red meat [HR 1.24, 1.09, 1.42; p=0.001] and total processed meat [HR 1.18, 1.01, 1.32; p=0.017] both positively associated with CRC

Cross et al, Cancer Res 2010
Meat and Colorectal Cancer

- Total iron intake and dietary iron both inversely associated, although the more bioavailable heme iron was positively associated.
- Nitrate intake from processed meat positively associated; nitrite not (p=0.055).
- Heterocyclic amine intake (MeIQx and DiMeIQx) positively associated but only associated with colon, not rectal CA.

Cross et al. Cancer Res 2010

Colorectal Cancer and Diet

- Only 1:100,000 native Africans develop colon cancer compared with 1:2000 AA's.
- Diets of 17 healthy urban Africans aged 50-65 c/w those of age matched AA's.
- Significantly increased animal protein and fat was the only major dietary difference.
- Native Africans diet high in corn meal.

Jones AICR, 2006

Colorectal Cancer and Diet

- Sulfur-reducing bacteria stimulated to grow by dietary meat's high S content.
- Bacteria produce hydrogen sulfide, toxic to colonic mucosa.
- Growth of 7-alpha-dehydroxylating bacteria stimulated by bile acids synthesized in response to dietary fat.
- Bacteria stimulate chronic inflammation.

Jones AICR, 2006

Colorectal Cancer and Diet

- 7 AA study subjects had adenomatous polyps compared to 1 native African.
- Cell proliferation rates significantly higher in all regions of the AA's colons.
- More 7-alpha dehydroxyating bacteria species found in AAs.
- AA diet typically high in beef and pork; frequently fast food, high fat, low cost.

Jones AICR 2006

Dietary Patterns in Colon CA

- Prospective observational study of 1099 pts with Stage III colon cancer enrolled in CALGB 89803 between 4/99 - 5/01.
- Pts reported on dietary intake using a ffq during and 6 months after the trial.
- Two major dietary patterns recognized.
- Two major dietary patterns identified:
  - Western pattern characterized by high intakes of meat, fat, refined grains, and dessert.
  - Prudent pattern characterized by high intakes of fruits and vegetables, poultry and fish.
- Every patient scored along the spectrum of both.
- Patients were followed up for cancer recurrence or death.

Meyerhardt et al JAMA 2007

CALGB Prospective Observational Study: Western Dietary Pattern and Cancer Outcomes

<table>
<thead>
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<th>Quintile of Western Dietary Pattern</th>
<th>Disease-free Survival (p trend&lt;0.001)</th>
<th>Recurrence-free Survival (p trend&lt;0.001)</th>
<th>Overall Mortality (p trend&lt;0.001)</th>
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F/U 5.3 years, 324 patients recurred, 223 died with recurrence and 28 died without CA.
Dietary Patterns in Colon CA

- Highest quintile in Western diet had daily median
  - 1 serving of red meat
  - 5 servings of refined grains
  - 2 sugar desserts
- Lowest quintile in Western diet had daily median
  - 0.3 serving red meat (2 per week)
  - 2 servings refined grain
  - 0.5 sugar desserts (3 per week)

“So the recommendation is more of an avoidance than an increase in diet components”

Meyerhardt Personal Communication

Western Diet and Breast Cancer

- Analysis conducted at Fox Chase, Harvard, Vanderbilt and Shanghai Cancer Institute
- 1602 women 25-64 dx’ed with breast CA 96-98 with controls selected from Shanghai
- “Meatsweet” pattern associated with > 2-fold increased risk of ER+ breast CA
- No overall association of risk with “vegetable-soy” pattern
- Association most pronounced in heavier, postmenopausal women with ER+ tumors

Tsang et al

Red Meat and Breast Cancer

- Heterocyclic amines created during high-temperature cooking of meet are estrogenic
- Iowa Women’s Health Study analysis revealed 4-fold increased risk with regular consumption of well-done and fried meats
- High iron content may also be a factor
- Exogenous hormones in cattle may promote tumor growth
- Red meat consumption viewed as possible risk for hormone-sensitive breast cancer

Linos and Willett, JNCIN, 2007

Other Red Meat Associations

- Survival disadvantage in ovarian CA for prediagnosis consumption of meats, specifically red and cured/processed subgroups [HR 2.28, 1.39 3.89; p<0.01]
  Æ Dolecek et al, J Am Dietetic Assn 2010

Dietary Fat and Pancreatic CA

- NIH/AARP study, 6.3 yrs f/u 525K→ 1337 cases
- Pancreatic cancer risk directly related to the intake of:
  - Saturated fat 51.6 vs 33.1 cases/100K py
    - HR=1.36 (1.14,1.62, P<.001)
  - Monounsaturated fat 46.2 vs 32.9 cases/100K py
    - HR=1.22 (1.02,1.46, P<.05)
  - Strongest associations for saturated fat from animal sources 52 vs 32.2 cases/100K py
    - HR=1.43 (1.20,1.70, P<.001)
  - Specifically, intakes from red meat (HR=1.27) and dairy products (HR=1.19) were both associated with increased risk

Thiebaut et al, JNCI 2009

Obesity, Diet and NHL Risk

- Overweight/obesity probably ↑ NHL risk
- Diet imposes antigenic challenges to lymphoid tissue in GI tract, can alter immune responses
- High consumption of fats, meat and dairy products may also increase NHL risk
- Several studies support inverse relationship between vegetables (esp. cruciferous) and NHL risk
- Fish intake may be inversely associated

Skibola, Cancer Epidemiol Biomarkers Prev 2007
Dietary Factors and NHL Risk

- 597 Swedish NHL cases, 467 controls
- Food frequency questionnaire completed evaluating dietary habits two years before the interview
  - Highest vs lowest quartile dairy OR for NHL 1.5 (1.1 - 2.2; p (trend) 0.003)
  - Highest vs lowest quartile fried red meat OR 1.5 (1.0 - 2.1); p (trend) 0.02)
  - Highest vs lowest quartile F&V OR of follicular lymphoma among women 0.3 (0.1 - 0.7) p0.002)

Chang et al Cancer Epidemiol Biomarkers Prev 2005

Dairy and NHL

- International correlations studies show positive association between consumption of nonfat portion of milk and NHL mortality
- Reports of ↑ risk of NHL associated with milk consumption in studies from US, Norway and Italy
- Positive associations for butter, cream soups, ice cream, milk shakes, cheese and dairy products
- Mechanisms unresolved
  - Inhibition of 1,25(OH)\textsubscript{2}D by milk calcium (Vit D protects)
  - Organochlorines in dairy fat are known carcinogens and can alter B-cell responses
  - Bovine leukemia virus?

Milk Consumption and Prostate Cancer

- Meta-analysis of 11 published case-control studies from 1984-2003
- Combined Odds Ratio was 1.68 (95% CI 1.34 - 2.12), varying little by study stratification
- All studies carried out in American and northern Europe where a milk/dairy free group is difficult to find
- Milk increases risk; possible mechanism via fat, testosterone, IGF-1,calcium, ? other factors

Qin et al Nutrition and Cancer 2004

Milk Consumption and Prostate Cancer

- Increased fat intake from animal products leads to increased testosterone
- Calcium intake (dairy major source) suppresses 1,25(OH)\textsubscript{2}D3
  - Metabolite may inhibit cellular proliferation and induce differentiation of nl and neoplastic CaP cells in vitro
- Elevated level of IGF-1 associated with increased risk of CaP

Raimondi et al, The Prostate 2010

Calcium and Prostate Cancer

- 27,293 Chinese men in Singapore, 4574 yrs old, with low dairy consumption
- Food frequency questionnaires completed
- 298 men diagnosed with prostate cancer
  - 25% increased risk of CaP when comparing those who consumed ~659 mg compared with 211 mg of total Ca/day

Butler, Cancer Res 2010
Other Dairy Associations

- Borderline positive association between cheese intake and bladder CA in Belgium
  - Brinkman et al., Eur J CA 2010
- Increased HR for death in ovarian CA observed for prediagnosis milk (all types) subgroup [HR 2.15, 1.20,3.84, p<0.05]
  - Dolecek et al., J Am Dietetic Assn 2010

PLANT-BASED GUIDELINES

- Consume a healthy diet, with an emphasis on plant sources
- Eat 5 or more servings of a variety of fruits and vegetables each day; every meal and snacks
- Choose whole grains in preference to refined

Eat more of a variety of vegetables, fruits, whole grains and legumes

U.S. Diets Fall Short on F&Vs

- CDC reports only 14% of adults eat recommended number of servings/day
  - 33% eat 2 or more servings of fruit a day
  - 27% eat 3 or more servings of vegetables
- DC 20.1%, VT, ME, HI, MA top 5
- WV, SD, AL, OK/SC, MS 8.8% rank last
- Only 9.5% of high school students meet recommendations (32% fruit, 13% veg)
- Healthy People 2010 objective was to have 75% meet fruit and 50% vegetable

The Macrobiotic Diet

- Precursor to whole foods/natural foods movement
- Precursor to the local/seasonal movement
- Precursor to the alkaline diet movement
- Overall the diet appears to be very consistent with AICR/WCRF and ACS guidelines

Centers for Disease Control 2008