8th Annual University of Arizona Center of Integrated Medicine Nutrition and Health Conference May 9-11, 2011

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

Donald I. Abrams, M.D.
Chief, Hematology-Oncology
San Francisco General Hospital
Integrative Oncology
UCSF Osher Center for Integrative Medicine
Professor of Clinical Medicine
University of California San Francisco

SPONSORED BY

THE UNIVERSITY OF ARIZONA®
Arizona Health Sciences Center

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

Kotzsch, Macrobiotics: Yesterday and Today, 1985

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

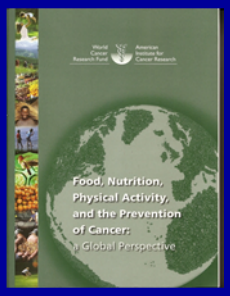
Ferre'. Pocket Guide to Macrobiotics. 1997

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

Ferre'. Pocket Guide to Macrobiotics. 1997

ACS and WCRF/AICR Guidelines



WEIGHT 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

Obesity-Associated Malignancies

Estimated Percentages of Annual US Cancers Caused by Excess Body Fat

Breast: 17% , 33,000 cases
Esophagus: 35%, 5,800 cases
Pancreas: 28%, 11,900 cases
Gallbladder: 21%, 2,000 cases
Colorectal: 9%, 13,200 cases
Endometrial: 49%, 20,700 cases
Kidney: 24%, 13,900 cases

Source: AICR/WCRF "Policy and Action for Cancer Prevention" report, 2009

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 fit 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

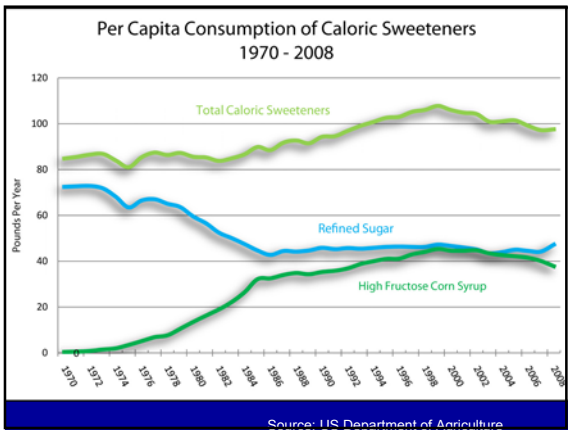
- Aromatization of adrenal androgens in adipose tissue generates estrogens
- SHBG levels lower in overweight women resulting in more bioavailable estrogen
- Losing weight after menopause can reduce circulating estrogens and↑ SHBG
- Nurses Health Study suggests 15% breast CA associated with adulthood 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



For Full Story on Sugar

Review
Sugar: The Bitter Truth
Robert Lustig, MD
Monday May 10, 2011

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

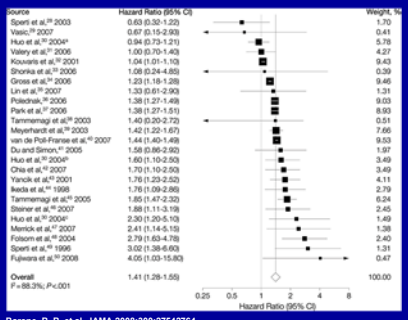
Michaud CA Epi Bio Prev 2006

Mortality in CA with Diabetes

- Systematic review and meta-analysis 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 Ratio of Long -term, All-Cause Mortality in 23 Studies Comparing Cancer Patients With and Without Preexisting Diabetes Mellitus



Barone, B. B. et al. JAMA 2008;300:27542764.

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

JAMA

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 IGFI levels
  - IGF-IR hyperactive and overexpressed in many breast cancers
  - IGF-IR being targeted in therapy
- IGF-I caused gene expression changes in breast CA cells associated with cell proliferation, metabolism and DNA repair

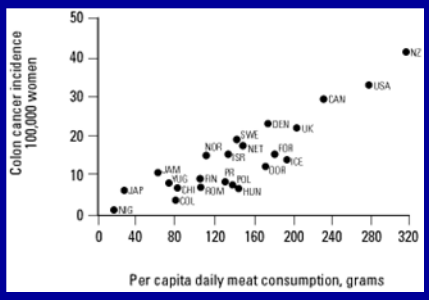
Creighton et al JCO 2008

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



Armstrong and Doll, 1975 in Willett, 1995

Meat and Colorectal 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 1.16, 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-dehydoxylating 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 dehydroxylating bacteria species found in AAs
- AA diet typically high in beef and pork; frequently fast food, high fat, low cost

Jones AICR 2006

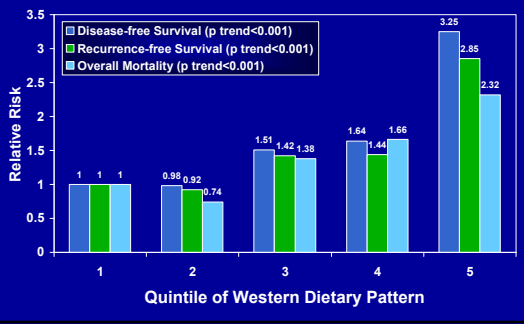
Dietary Patterns in Colon CA

- Prospective observational study of 1009 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

•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
- "Meat-sweet" 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

Tseng et al

Red Meat and Breast Cancer

- Heterocyclic amines created during high-temperature cooking of meat 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, JNCCN, 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]
  - » 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 51.5 vs 33.1 cases/100K py
    - HR= 1.36 (1.14,1.62; P_{trend}<.001)
  - Monounsaturated fat 46.2 vs 32.9 cases/100K py
    - HR= 1.22 (1.02,1.46; P_{trend}=.05)
  - Strongest associations for saturated fat from animal sources 52 vs 32.2 cases/100K py
    - HR= 1.43 (1.20,1.70; P_{trend}<.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 $1,25(OH)_2D$ 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

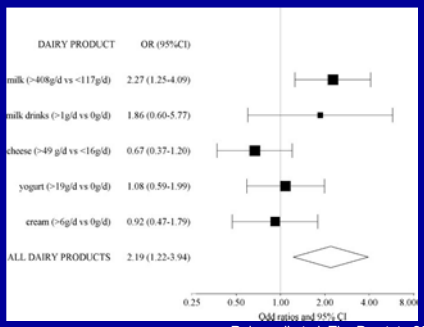
Qin et al Nutrition and Cancer 2004

Milk Consumption and Prostate Cancer

- Increased fat intake from animal products leads to increased testosterone
- Calcium intake (dairy major source) suppresses $1,25(OH)_2D_3$
  - 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

Milk Consumption and Prostate Cancer



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

Centers for Disease Control 2009

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