Numerous epidemiology studies support the concept that diets rich in plant foods are associated with a reduced risk for vascular disease.

**Fruits/Vegetables**

- Multivariate adjusted* RR for >=3 times/day vs. <1 time/day
  - Ischemic heart disease mortality
    RR=0.76 (95% CI: 0.56, 1.03)
  - CVD mortality
    RR=0.73 (95% CI: 0.58, 0.92)
  - All cause mortality
    RR=0.85 (95% CI: 0.72, 1.00)

*adjusted for age, sex, race, energy, physical activity, alcohol consumption, smoking, plus others
Numerous epidemiology studies support the concept that diets rich in plant foods are associated with a reduced risk for vascular disease.

Hertog et al., Arch Intern Med, 1995;155: 381-6

Flavonoids

- C\textsubscript{15} (C\textsubscript{6} -C\textsubscript{3} -C\textsubscript{6}) basic skeleton
- 3 most common classes

Anthocyanins  
Flavonols  
Flavan-3-ols
Flavanol Profiles

- Cocoa and Chocolate
  - B-type procyanidins
- Cranberries
  - A- and B-type procyanidins
  - few monomers
- Peanuts
  - A- and B-type procyanidins
  - few monomers
- Tea
  - Procyanidins and Prodelphinidins
  - few oligomers
- Apple
  - B-type procyanidins
- Blueberries
  - B-type procyanidins
- Almond
  - B-type procyanidins
- Wine
  - B-type procyanidins
- Grape Seeds
  - B-type procyanidins
  - Galloylated

Lazarus et al., J. Ag. Food Chem., 47, 3693-3701

Can common foods provide significant amounts of flavonoids?

- Healthy volunteers, 25-56 y.
- Asked to refrain from taking vitamin supplements, and food rich in flavonoids for 24 h, and fasted overnight.
- Subjects ingested a flavonoid-rich chocolate food (0, 35, 70, and 105 g) and bread.
- Blood was drawn at 0 h, 2 h and 6 h.
- The chocolate contained 1.3 mg/g of epicatechin and 5.3 mg/g of total procyanidins.
Plasma Concentrations of Cocoa Flavanols and Dimeric Procyanidins After Consuming 0.375 g/kg of Cocoa

Holt et al. AJCN 2002; 76: 798

Platelet Activation

Resting

Activated

Fibrinogen Receptor PAC1-FITC binding

ADP-Epinephrine

GPIb-IX complex

CD42a-PerCP binding

GPIb-lla

P-Selectin

GPIb-lla

GPIb-IX

Surface P-Selectin

CD62-PE binding
Flavonoids: Platelet Reactivity

Consumption of cocoa beverage increases closure time (time to clot)

- Baseline
- 2 hour
- 6 hour

Caffeine
Cocoa

Wine, Grape Products, and Cocoa Reduce Platelet Function

Pelligrini et al., 1996
Pace-Asciak et al., 1996
Rein et al., 2000

Osman et al., 1998
Keevil et al., 2000
Freedman et al., 2001

Rein et al., 2000
Pearson et al., 2002
Holt et al., 2002
Murphy et al., 2003
Innes et al., 2003
Endothelium Dependent Vasorelaxing Activity of Flavanols

Changes in RNO and FMD after Flavanol-Rich Cocoa Consumption

Heiss et al. JAMA 2003; 290: 1030
Peripheral Arterial Tone (PAT)

Pathogenesis of Atherothrombotic Disease

**Risk Factors**
- Hypertension
- Diabetes
- Dyslipidemia
- Estrogen Withdrawal
- Homocysteine

**Oxidative Stress**
- NO
- Endothelin, AngII, TXA₂
- Superoxide anion, Catecholamines
- Smooth muscle cell proliferation

**Endothelial Dysfunction**
- Thrombosis
  - t-PA
  - PAI-1
- Platelet adhesion & aggregation

**Vascular Lesion Progression**
- Plaque Rupture
- Thrombosis and Vasospasm

**Coronary Events**

**Local mediators:**
- Endothelin, AngII, TXA₂
- Superoxide anion, Catecholamines

**Smooth muscle cell proliferation**

Changes in food processing and food storage

Changes in agricultural practices

**Improved nutrient profiles in plants and animals**

- Conventional genetics
- GMO
Improved nutrient profiles in plants and animals

Improved food products

Food safety

Economic viability

Acceptability

Palatability

Health Optimization

Health Agencies

Identification of new targets for improved quality of life

Identification of new targets for disease prevention

Risk-Benefit Analysis
Potential Health Impacts of Excessive Flavonoid Intake

“....the fetus may be exposed to high circulating levels of flavonoids, which may elicit toxic responses that may otherwise be innocuous to the mother.”


...“Perhaps pregnant women should restrict their intake of fruits”  Paul Harvey, 2003

Who do we protect?

Will future legislation require food industries to educate susceptible populations on the putative “risks”, as well as the putative “benefits”, of modified foods?

Will the expectation be that “foods” are optimized for the “general” population (eg non-smokers; non-pregnant women), or that they be optimized for “susceptible” populations (eg smokers; pregnant women)?
Adversity presents danger, as well as opportunity.

The “omics” revolution provides a path through which food can be tailored to significantly enhance health. The above requires the teams with diverse backgrounds, and an education program that targets the public, as well as regulatory and government officials.

Nutrition education programs that ignore the concept of risk-benefit set the stage for public confusion and anger at the food industry. However, education programs that include this concept will result in more realistic expectations of what food can provide to the “individual”, the family, and the general population.