“Why an Apple a day keeps the doctor away!”

William T. Cefalu, M.D.
Pennington Biomedical Research Center
The “apple” Story!
What food is required *for* me?

- Nutritional deficiency:
  - Iron - Anemia
  - Iodine – Thyroid goiter
  - Vitamin D - Rickets

- Identifying essential nutrients required for promoting growth and sustaining life.
  - Vitamins
  - Essential minerals – Calcium
  - Essential amino acids
Changing Nutrition/Health Paradigm

1950s-1990s

◊ What does food do to me?

- Nutritional excess and imbalances
  - Calories - obesity
  - Fiber – Colon cancer
- Identifying nutrients and components that contribute to premature death
  - Saturated fat
  - Cholesterol
  - Sodium
Seven Countries Study: CHD Events are Correlated with Saturated Fat

Keys, 1970
Changing Nutrition/Health Paradigm

1990s-Today!

- What does food do for me?

**Functional Foods**

- Nutritional optimization of quality of life
- Identification of physiological active components to prevent or delay premature onset of chronic disease
  - Phytochemicals
  - Pre/Probiotics
  - Fiber
Functional Foods

- **Phytochemicals**
  - “Phyto” - Plant or “botanical” source

- **Making a food “functional”**
  - *Increase Phytochemicals*
  - *Add Phytochemicals*
  - *Replace phytochemicals*
Polyphenols

- **Epicatechin**
- **Epigallocatechin**
- **Epigallocatechin gallate**

**Source:** Green tea, grapes, red wine

**Benefits:** Anti-cancer, CHD protective

**Function:** Inhibit chemical carcinogenesis and tumor formation; inhibit cancer cell growth; antioxidant; reduces free radical/oxidative damage
Carotenoids

- Lycopene
- β-carotene
- β-cryptoxanthin
- Lutein

- Source: Tomatoes, carrots, yams, cantaloupe, spinach, sweet potatoes; citrus fruits
- Benefits: Anti-cancer; CHD protective
- Function: Antioxidant; free radical scavenger; induction of cell-cell communication and growth control; inhibit tumor growth
Isoflavones

- Genistein
- Daidzein

**Source:** Soybean, flaxseed

**Benefits:** Relieves menopausal symptoms; prevents osteoporosis; anti-cancer; CHD protective

**Function:** Estrogen-like activity; inhibit growth of breast cancer cells; stimulate Ca absorption; lower cholesterol levels
Flavonoids

- Quercetin
- Apigenin
- Luteolin
- Myricetin

- **Source:** Citrus fruits; vegetables
- **Benefits:** Heart protection; Increase stamina
- **Function:** Antioxidant; inhibit platelet aggregation; inhibit cancer cell growth and proliferation; cytotoxic to cancer cells
The Promise of Functional Foods

- Better health through improved nutrition can:
  - Increase quality of life
  - Enhance productivity
  - Reduce health-care costs

Health claims need to be verified with carefully controlled studies
Botanical (Natural) Supplements

29,000 supplements available to American consumer
Diabetes: the growing global burden

IDF: 2%

- Diabetes currently affects 246 million people worldwide
- It is expected to affect 380 million by 2025
Complications of Diabetes

Large Blood Vessel
- Brain
  - Cerebrovascular disease
    - Transient ischemic attack
    - Cerebrovascular accident
    - Cognitive impairment
- Heart
  - Coronary artery disease
    - Coronary syndrome
    - Myocardial infarction
    - Congestive heart failure
- Extremities
  - Peripheral vascular disease
    - Ulceration
    - Gangrene
    - Amputation

Small Blood Vessel
- Eye
  - Retinopathy
  - Cataracts
  - Glaucoma
- Kidney
  - Nephropathy
    - Microalbuminuria
    - Gross albuminuria
    - Kidney failure
- Nerves
  - Neuropathy
    - Peripheral
    - Autonomic
Prevalence of Diagnosed Diabetes in Adults 2003
**Insulin receptor**

"SWITCH"

Plasma membrane

Blood Sugar enters body

Chemical Signals

Glucose carriers move to the surface

Glucose carriers insert into cell surface

Insulin "Efficiency"

Insulin Action ("Sensitivity") in Muscle and Fat

GLUT4=glucose transporter 4

"Pre-Diabetes" (Insulin "inefficiency")
Natural History of Type 2 Diabetes

Progressive β-Cell Failure

Years from diagnosis

-10
-5
0
5
10
15

Onset
Diagnosis

Pancreas function

Insulin “inefficiency

Insulin secretion

Post-Meal glucose

Fasting glucose

Pre-diabetes

Type 2 diabetes

PLASMA GLUCOSE

Normal: 99 mg/dl or less
Pre-Diabetes: 100-125 mg/dl
Diabetes: > 126 mg/dl fasting);
> 200 mg/dl (PostPrandial)

Cardiovascular Risk in Pre-diabetes

Non-Diabetic

Diabetes

Relative Risk of MI or Stroke

Nondiabetic Throughout

>15 Yr Before Dx

10-14.9 Yr Before Dx

<10 Yr Before Dx

Diabetic Throughout

1.0

2.4

3.19

3.64

5.02

“Metabolic” Syndrome

Obesity

Physical Inactivity

Aging

Insulin inefficiency ("resistance")

Abnormal Lipids

Elevated Blood Pressure

High Blood Sugar

Heart Disease

Blood Vessel Dysfunction

Modified from S. Grundy MD
Body Shape Matters!!!
“Central” obesity

An Index of Abdominal vs Peripheral Obesity

High Waist/Hip
(≥0.95 in men)
(≥0.80 in women)

Low Waist/Hip
(<0.95 in men)
(<0.80 in women)
Visceral Fat Distribution: Normal vs Type 2 Diabetes

Normal

Type 2 Diabetes
Risk of diabetes mellitus during 13 years in relation to WHR at baseline. Comparison between these in upper and lower 10% of WHR distribution.

Death Increases with Metabolic Syndrome

Heart Disease Deaths

Cumulative hazard (%)

Follow-up (y)

YES

NO

Metabolic Syndrome

Death Increases with Metabolic Syndrome
Natural History of Type 2 Diabetes

Years from diagnosis:
-10  -5  0  5  10  15

Onset  Diagnosis

Insulin “Inefficiency”

“Pre-Diabetes”

Nutrition and Exercise
Reduces progression to diabetes by 60%

Pre-diabetes  Type 2 diabetes

Natural History of Type 2 Diabetes

Years from diagnosis

-10  -5  0  5  10  15

Onset  Diagnosis

Insulin “Inefficiency”

Increased Consumption of “Functional Foods”

Nutrition and Exercise Reduces progression to diabetes by 60%

Pre-diabetes  Type 2 diabetes

Blueberries Improved the Ability of Insulin to Work

\[ \Delta \text{insulin Sensitivity} = \text{ability of insulin to work from week 0 to week 6} \]
Louisiana Agriculture and Diabetes

Sugar Cane can fight Diabetes?

Tarragon and Diabetes

- Extract of *Artemisia dracunculus* with antidiabetic properties
- Produced from hydroponically grown plants under controlled conditions
Potential Lifetime Impact for Pre-Diabetes Intervention

Aroda VR, Ratner R. JCEM 93(9):3259-65, 2008
Life Expectancy: Increase by 0.5 Years

Potential Lifetime Impact for Pre-Diabetes Lifestyle Intervention

Macrovascular

- Stroke ↓ 9%
- Coronary Heart Disease ↓ 8%

Microvascular

- Blindness ↓ 39%
- End Stage Renal Disease ↓ 38%
- Amputations ↓ 35%

Aroda VR, Ratner R. JCEM 93(9):3259-65, 2008
### Summing it all up

#### COLOR-CODING YOUR VEGETABLES AND FRUITS

<table>
<thead>
<tr>
<th>COLOR</th>
<th>PHYTOCHEMICAL ANTIOXIDANT</th>
<th>VEGETABLE AND FRUIT SOURCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red</td>
<td>lycopene (lie-co-pee)</td>
<td>tomatoes, red raspberries, watermelon, strawberries, red peppers</td>
</tr>
<tr>
<td>Yellow-green</td>
<td>lutein zeaxanthin (lou-te-in, ze-ah-zan-thun)</td>
<td>leafy greens, avocado, honeydew melon, kiwi fruit</td>
</tr>
<tr>
<td>Red-purple</td>
<td>anthocyanins (antho-sigh-ah-nin)</td>
<td>grapes, berries, wine, red apples, plums, prunes</td>
</tr>
<tr>
<td>Orange</td>
<td>beta-carotene</td>
<td>carrots, mangos, papayas, apricots, pumpkins, yams</td>
</tr>
<tr>
<td>Orange-yellow</td>
<td>flavonoids (fla-von-oids)</td>
<td>oranges, tangerines, lemons, plums, peaches, cantaloupe</td>
</tr>
<tr>
<td>Green</td>
<td>glucosinolates (glu-co-sin-oh-lates)</td>
<td>broccoli, brussels sprouts, kale, cabbage</td>
</tr>
<tr>
<td>White-green</td>
<td>allyl sulfides (al-lill sulf-ides)</td>
<td>onions, leeks, garlic</td>
</tr>
</tbody>
</table>

2005 Wadsworth - Thomson
“Eat and Drink the Rainbow”