

This work is licensed under a [Creative Commons Attribution-NonCommercial-ShareAlike License](https://creativecommons.org/licenses/by-nc-sa/4.0/). Your use of this material constitutes acceptance of that license and the conditions of use of materials on this site.



Copyright 2006, The Johns Hopkins University and Benjamin Caballero. All rights reserved. Use of these materials permitted only in accordance with license rights granted. Materials provided "AS IS"; no representations or warranties provided. User assumes all responsibility for use, and all liability related thereto, and must independently review all materials for accuracy and efficacy. May contain materials owned by others. User is responsible for obtaining permissions for use from third parties as needed.



JOHNS HOPKINS  
BLOOMBERG  
SCHOOL *of* PUBLIC HEALTH

## *Antioxidant Nutrients*

---

Benjamin Caballero, MD, PhD  
Johns Hopkins University



JOHNS HOPKINS  
BLOOMBERG  
SCHOOL *of* PUBLIC HEALTH

## *Section A*

---

Antioxidant Nutrients

# *Antioxidant Nutrients*

- Ascorbic acid
- Alpha-tocopherol
- Beta-carotene
- Selenium
- Manganese

# *Oxidants and Antioxidants*

## *Pro-Oxidants*

- Substrate oxidation
- Antimicrobial defense
- Radiation
- Sunlight
- Ionized compounds
- Aging
- Oxygen

## *Antioxidants*

- Free radical scavengers:
  - Extracellular/  
circulating
  - Cellular
    - ▶ Cytosolic
    - ▶ Membrane-bound

# What Is a Free Radical?

- An unbound compound (i.e., free) having one or more unpaired electrons



Hydroxyl group

(good guy)



Hydroxyl radical

(bad guy)

## Examples of Free Radicals and their Half-Lives

Hydroxyl radical		$\text{HO}\cdot$	$1 \times 10^{-9}$ sec.
Singlet oxygen		$^1\text{O}_2$	$1 \times 10^{-6}$
Alkoxyl radical	$\text{RO}\cdot$		$1 \times 10^{-6}$
Peroxyl radical		$\text{ROO}\cdot$	7
Semiquinone radical	$\text{Q}\cdot-$		days

# *Free Radical Formation*

- Oxidation of substrates with high oxygen affinity (for example, fatty acids)
- Microbial lysis
- Environmental exposure (sunlight, radiation, high-oxygen levels)

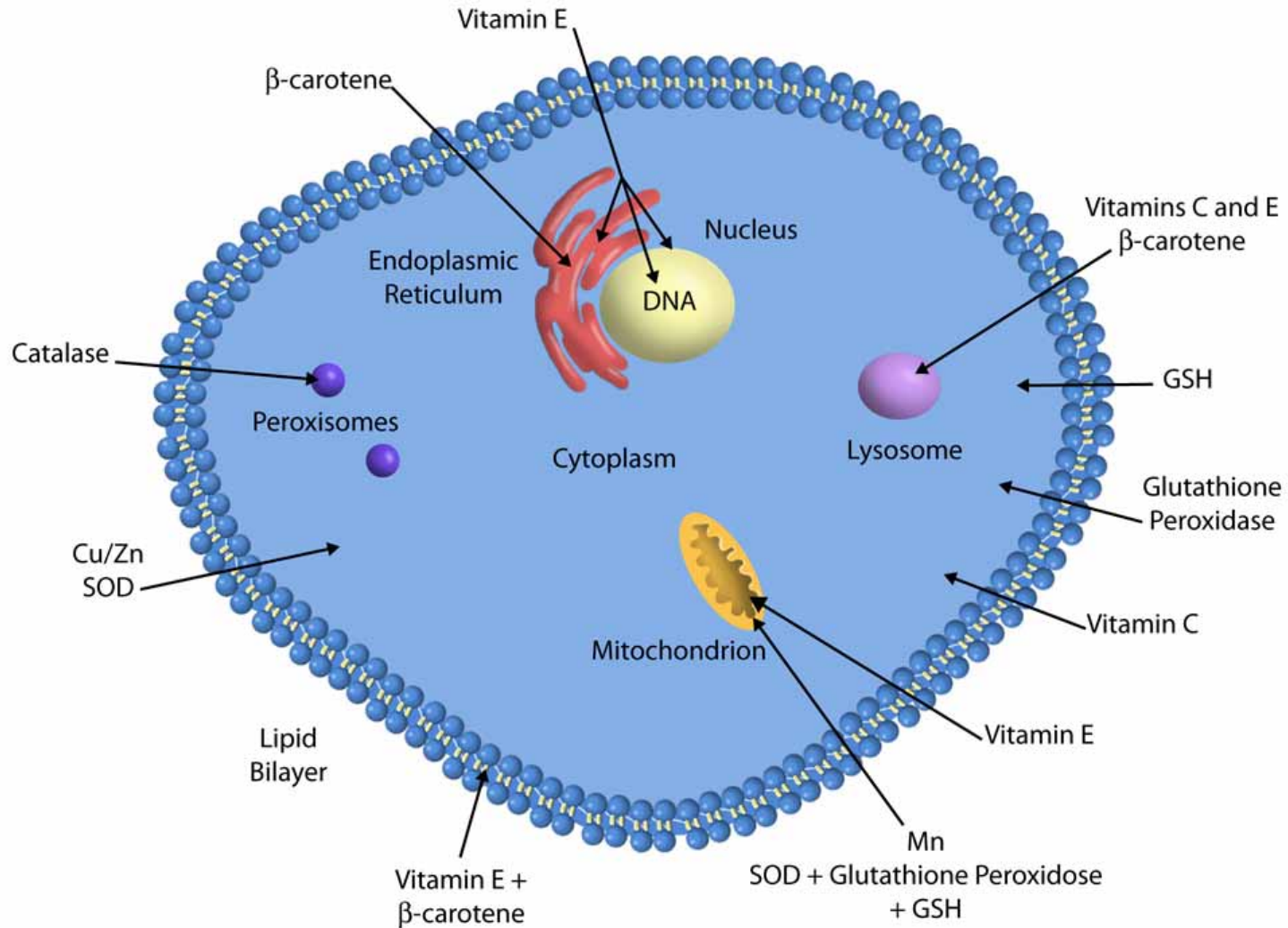


- **Water-Soluble**
  - Ascorbate
  - Glutathione
  - Urate
  - Bilirubin

## ■ **Lipid-soluble**

- Alpha-tocopherol
- Beta-carotene
- Lycopene
- Lutein
- Zeaxanthin
- Ubiquinol-10

# Antioxidant Systems in Cells



# *Antioxidant Defense Processes*

- **Prevention**—Balance between oxidative load and antioxidant function
- **Interception**—Local antioxidant levels
- **Repair**—Mostly enzymatic

# *Antioxidant Defense Processes*

- **Prevention**—Vitamin E, ascorbic acid, beta-carotene
- **Interception**—Vitamin E, glutathione, superoxide dismutase
- **Repair**—DNA repair system, reductases

# *Role of Nutrients in Antioxidant Systems*

## ■ **Vitamin E**

- Protects lipids from the cell membrane bilayer from attack by free radicals

## ■ **Vitamin C**

- Quenches  $^1\text{O}_2$  in cytosol
- Recycles vitamin E after it captures free radicals

## ■ **Carotenoids**

- Beta-carotene quenches  $^1\text{O}_2$ ; may also inhibit free-radical-generating reactions
- Autoregenerate with release of thermal energy

# *Role of Nutrients in Antioxidant Systems*

## ■ **Selenium**

- Constituent of glutathione peroxidase

## ■ **Manganese**

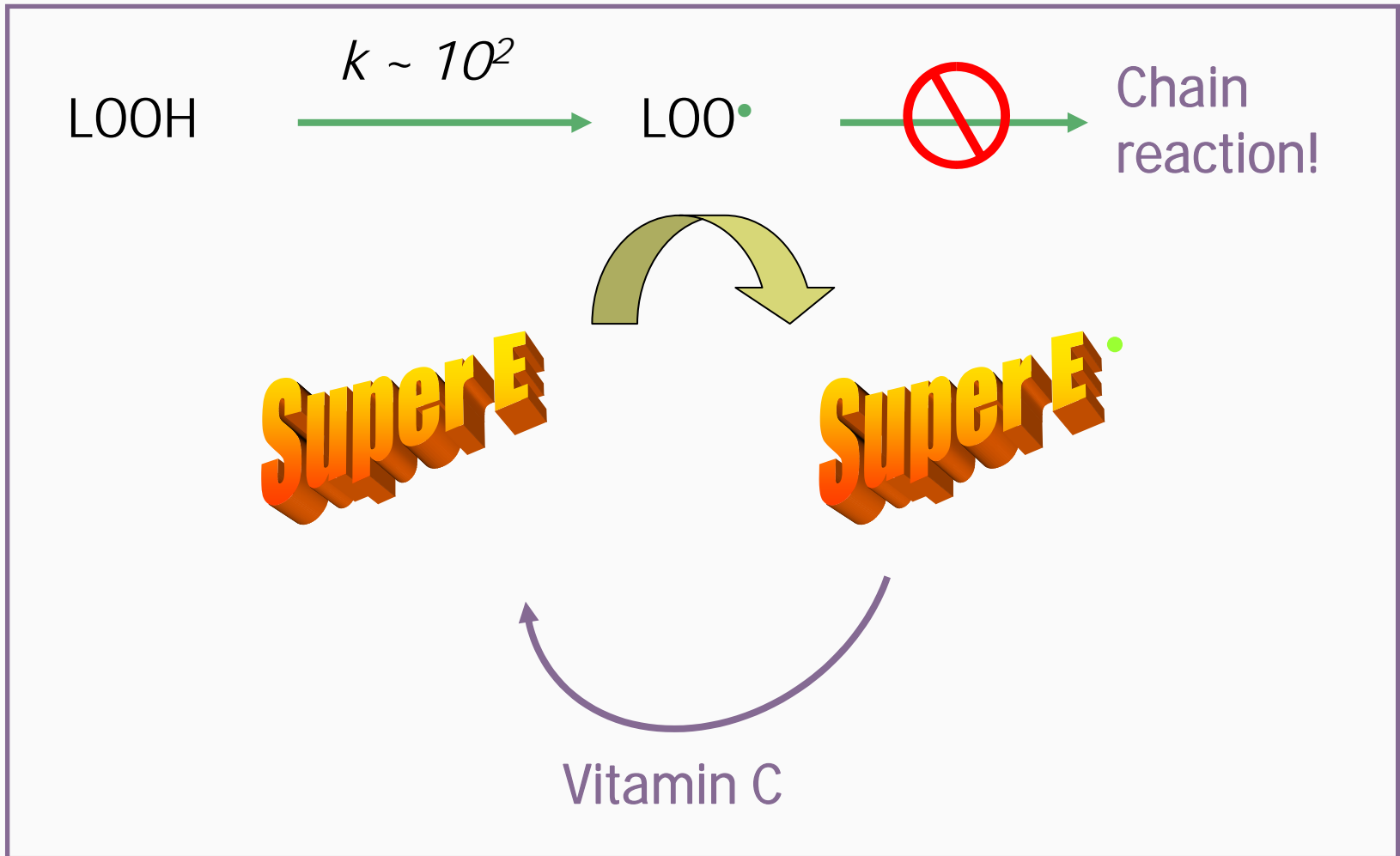
- Constituent of superoxide dismutase (MnSOD)

## ■ **Copper, zinc**

- Constituents of superoxide dismutase (CuZnSOD)



# Antioxidant Mechanism of Vitamin E



# *“Protective” Intake Levels of Antioxidant Nutrients*

	<b>Protective level*</b>	<b>RDA</b>
Vitamin C	>600 mg	60
Vitamin E	>200 IU	10
Selenium	70–120 µg	70

*\* Daily intakes associated with a risk reduction of 25% or more*



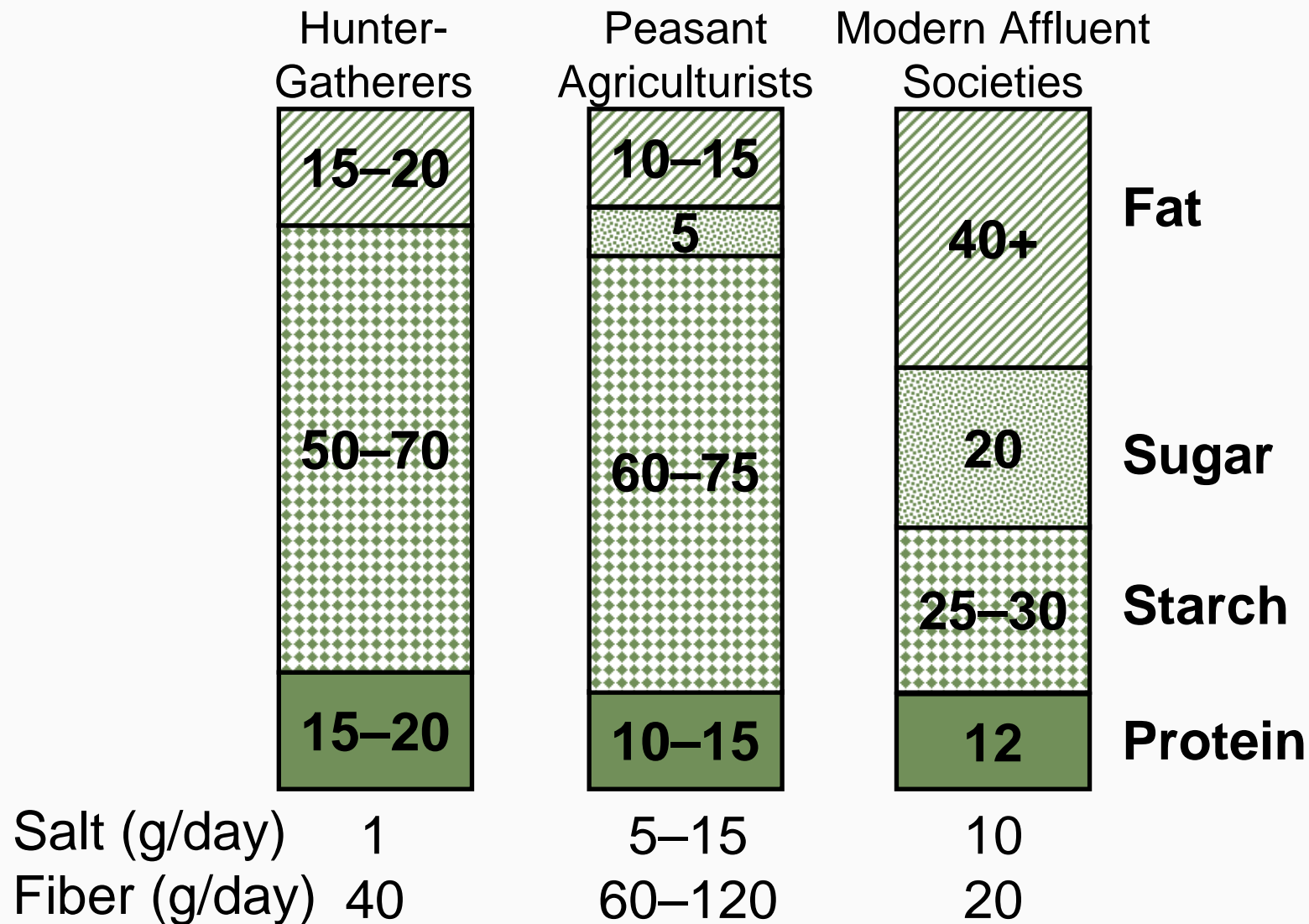
JOHNS HOPKINS  
BLOOMBERG  
SCHOOL *of* PUBLIC HEALTH

## *Section B*

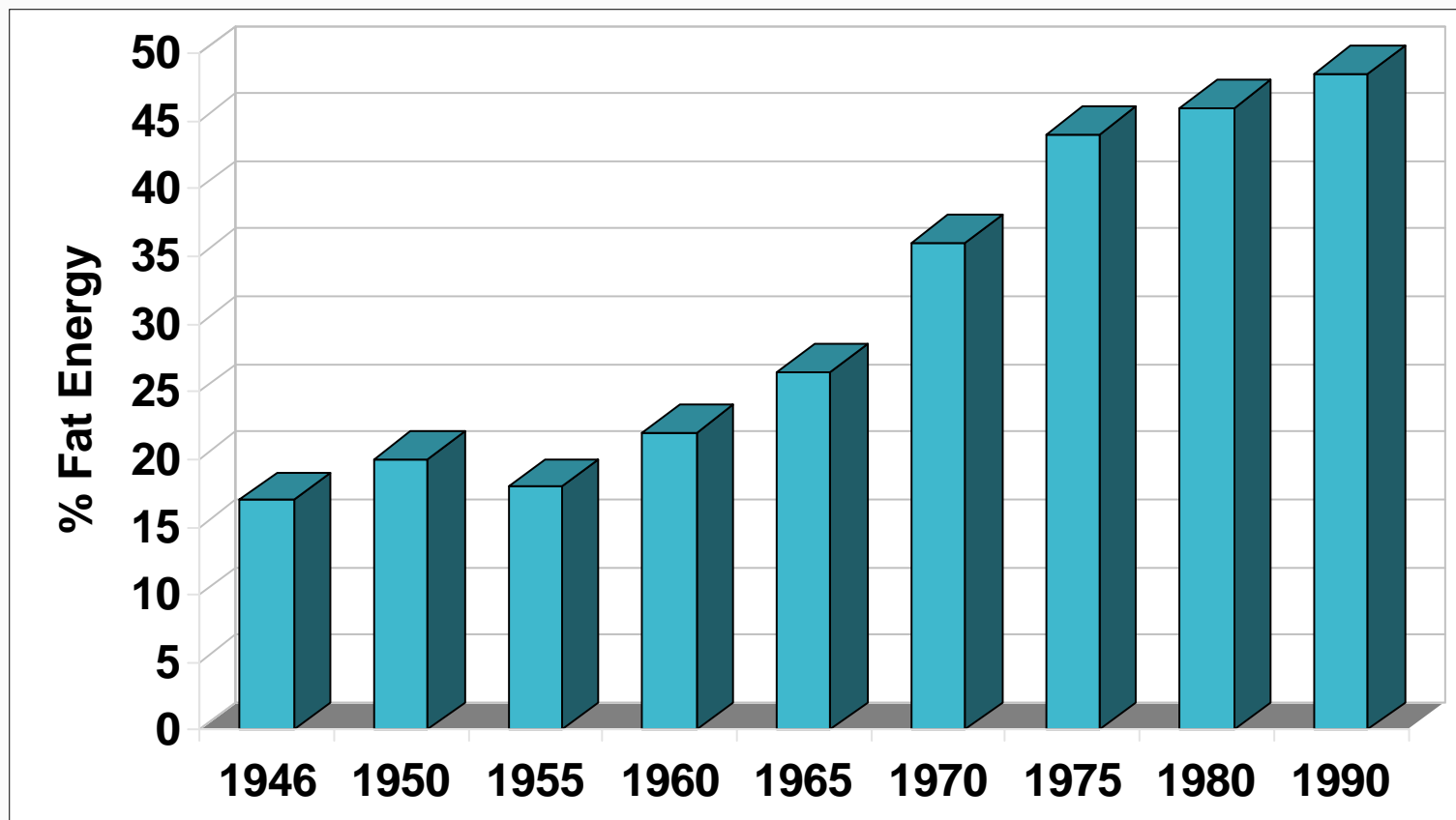
---

Diet and Chronic Diseases

# Evolution of the Human Diet



# *Nutrition Transition Fat Consumption Patterns—Japan*



# *Diet Constituents Implicated on Disease Risk*

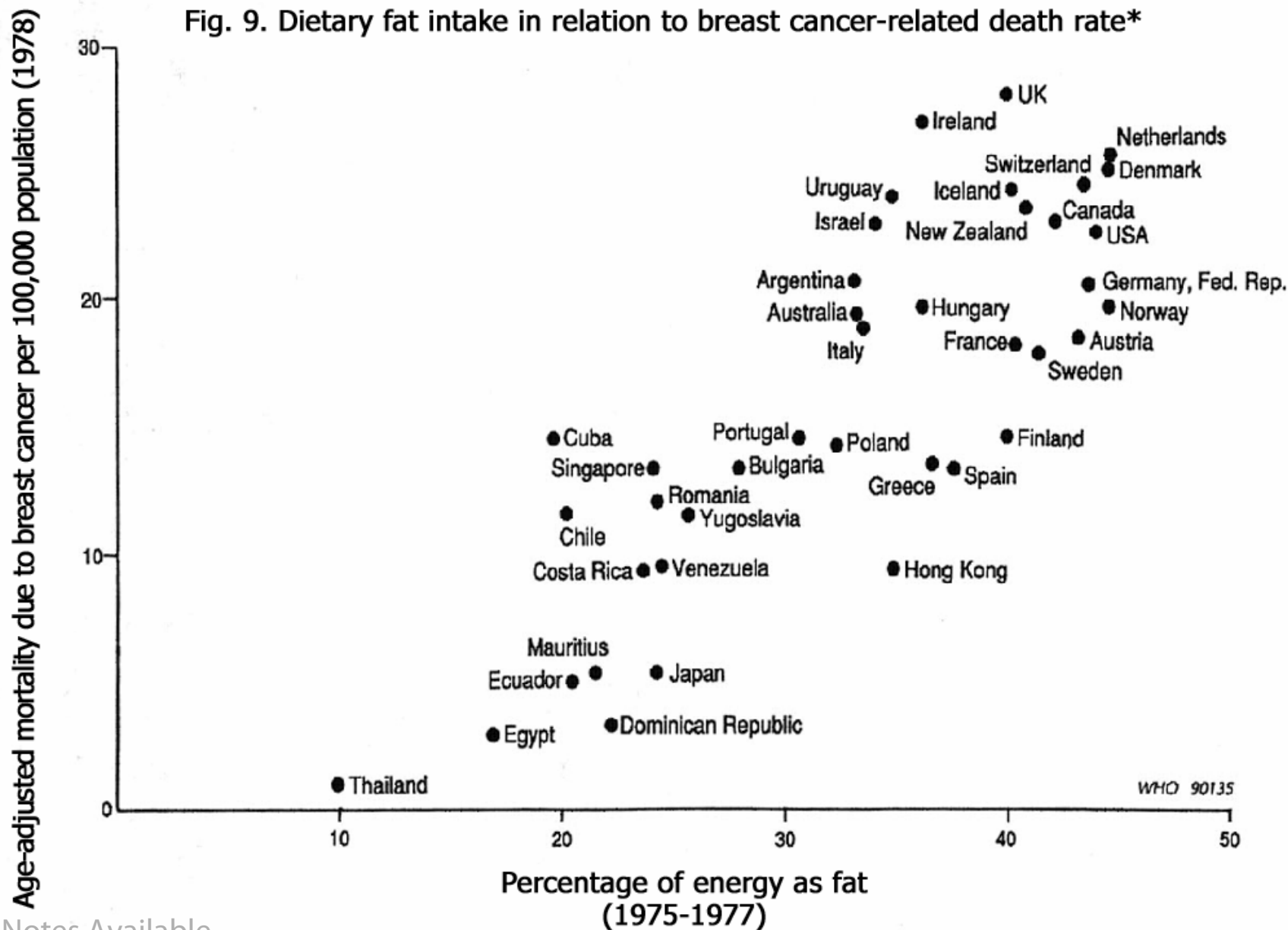
- Fats
- Cholesterol
- Fiber
- Antioxidant vitamins and minerals
- Sugar
- Protein
- Calcium and vitamin D
- Folic acid
- Iron

# *Criteria for Diet-Disease Relationships*

- Strength of association
- Dose-response relationship
- Temporally correct association
- Consistency of association
- Specificity of association
- Biological plausibility

# Dietary Fat Intake and Breast Cancer-Related Deaths

Fig. 9. Dietary fat intake in relation to breast cancer-related death rate\*





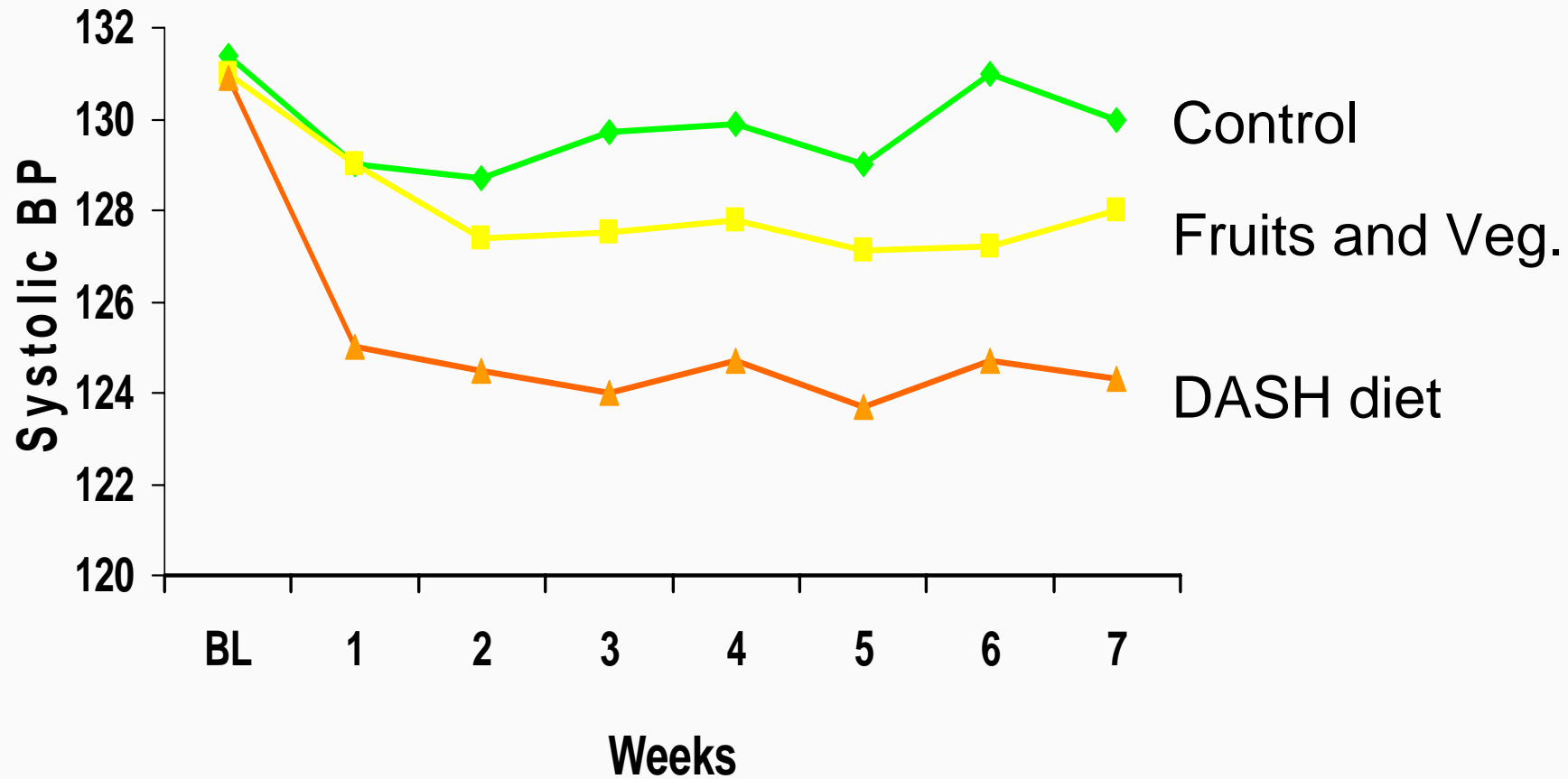
# Fish Consumption and Risk of CVD

	Fish Consumption, g/day			
	0	<18	18–34	>35
MI	1.0	0.88	0.76	0.56
CHD	1.0	0.88	0.84	0.62
CVD	1.0	0.94	0.89	0.74
All causes	1.0	1.02	0.98	0.85

# *Diet and Blood Pressure*

- Sodium
- Calcium
- Potassium
- Magnesium
- Alcohol

# The DASH Study



## *Dietary Patterns and Blood Pressure: The DASH Diet*

	Control	F & V	DASH
Fat (% cal)	36	36	26
Cholesterol (mg)	233	184	150
Fiber (g)	9	31	31
Potassium (mg)	1752	4101	4415
Magnesium (mg)	176	423	480
Calcium (mg)	443	534	1265
Sodium (mg)	3028	2816	2859



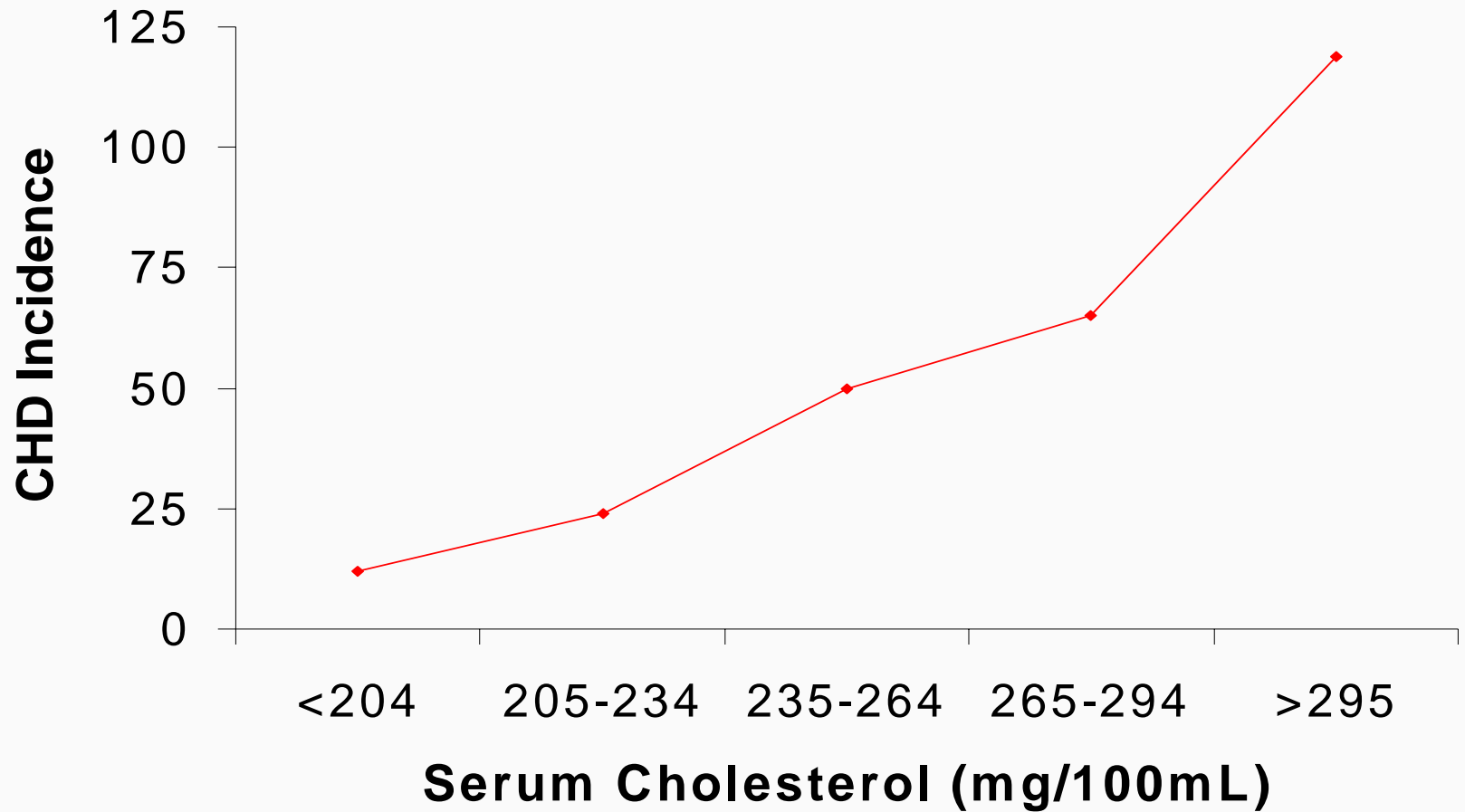
JOHNS HOPKINS  
BLOOMBERG  
SCHOOL *of* PUBLIC HEALTH

## *Section C*

---

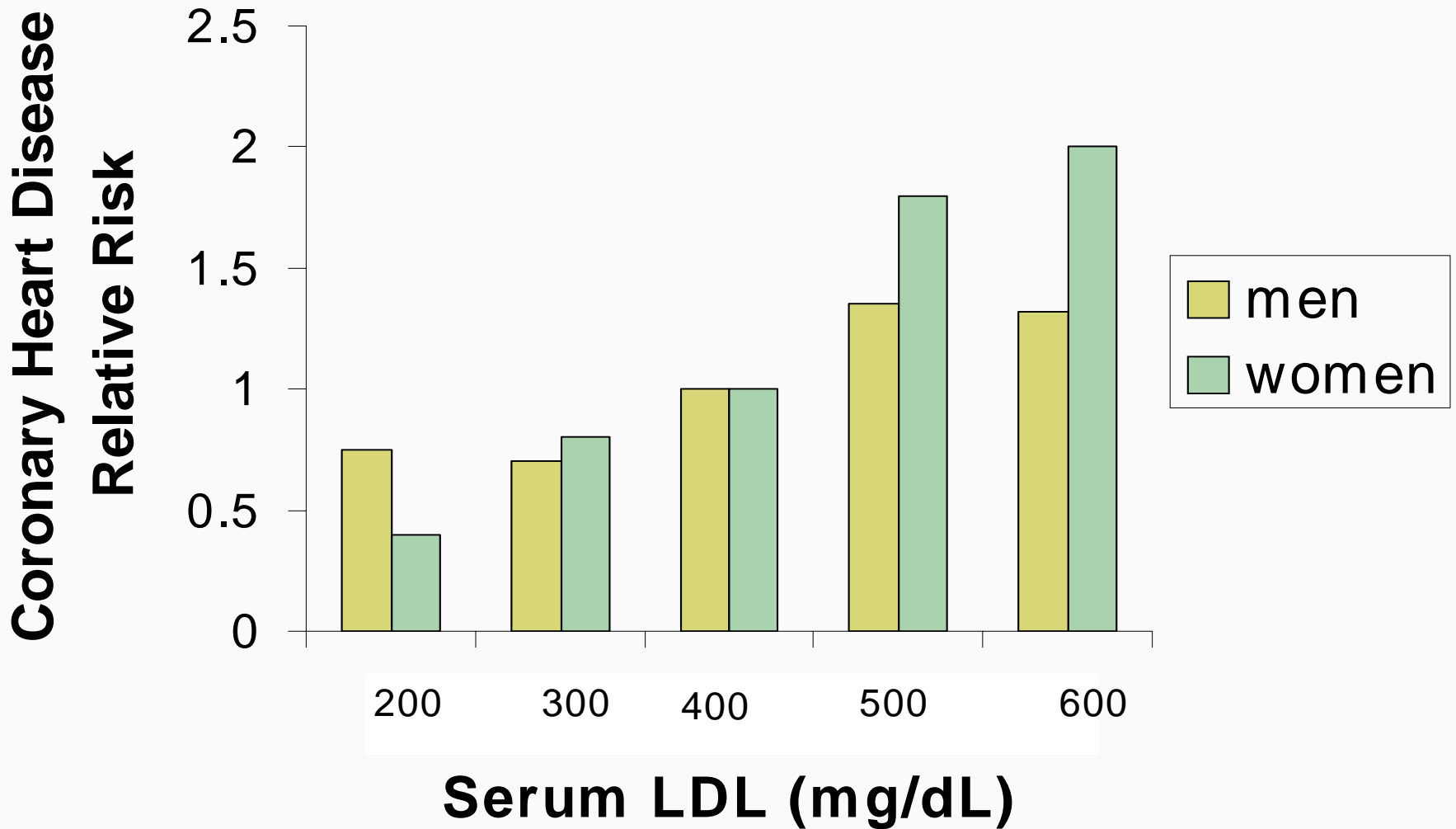
Fats and Cardiovascular Disease

# *Serum Cholesterol and Coronary Heart Disease*



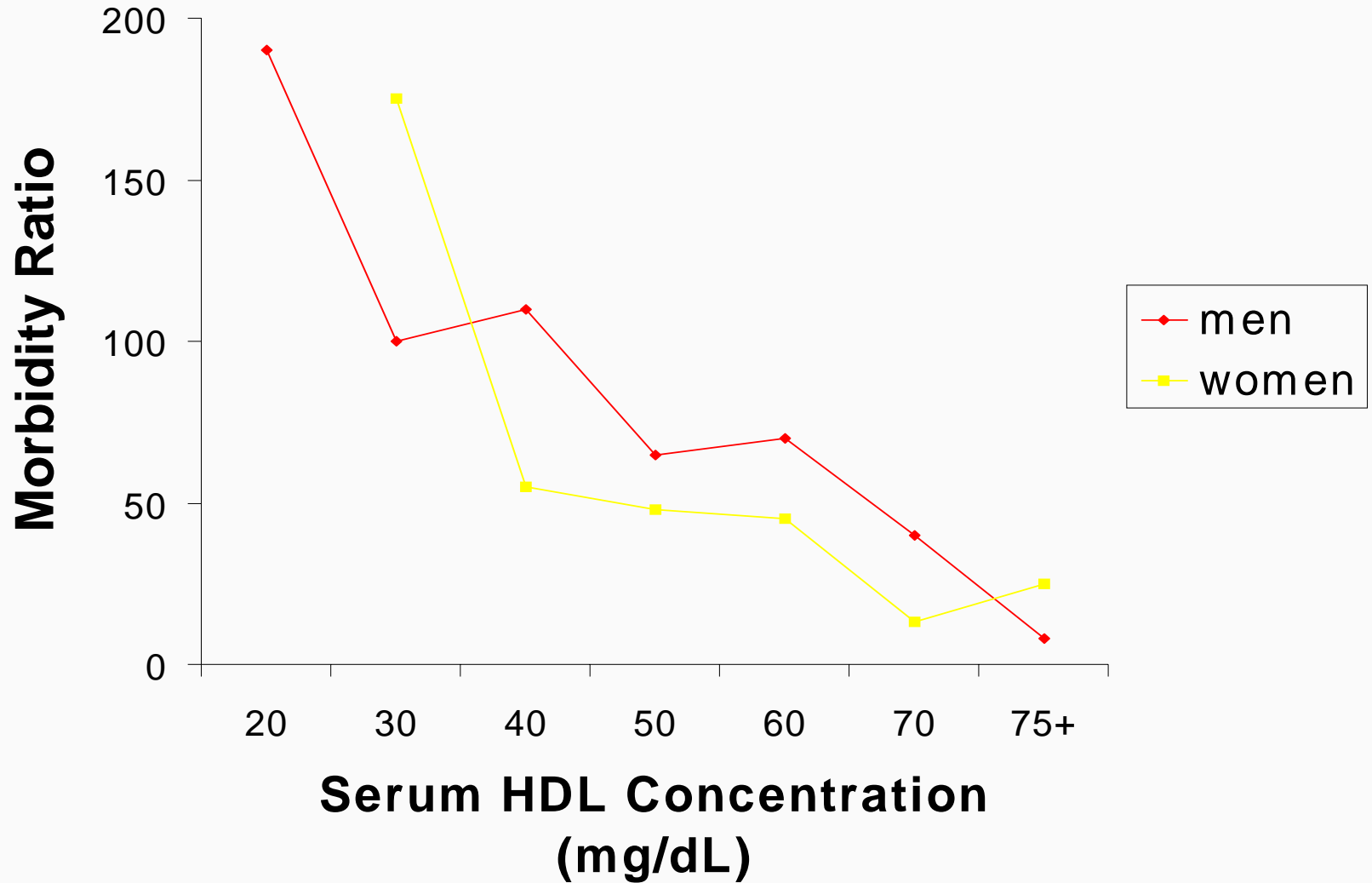
- The cholesterol hypothesis of coronary heart disease
- Dietary cholesterol, blood cholesterol, and atherosclerosis
- Dietary factors affecting blood cholesterol levels
- Non-dietary factors affecting blood cholesterol levels

# Serum LDL and CHD Risk





# Serum HDL and CHD



- **Low-fat diets**
  - Lower blood cholesterol but also tend to lower LDL and HDL
- **Low-saturated, high-monounsaturated diets**
  - Lower blood cholesterol and LDL, tend to increase HDL

## ■ **High-carbohydrate diets**

- Modest lowering effect on all lipid fractions, but rise in TG

## ■ **Fish oils**

- Strong lowering effect on blood TG, but minor effect of lipoprotein fractions

# *Dietary Factors Affecting Blood Cholesterol*

## ■ **Increase**

- Saturated fat
- Cholesterol
- Trans fatty acids

## ■ **Decrease**

- Monounsaturated fat
- PUFA (fish oil)
- Fiber

# *Non-Dietary Factors Affecting Blood Cholesterol*

## ■ **Increase**

- Smoking
- Excess body fat
- Alcohol

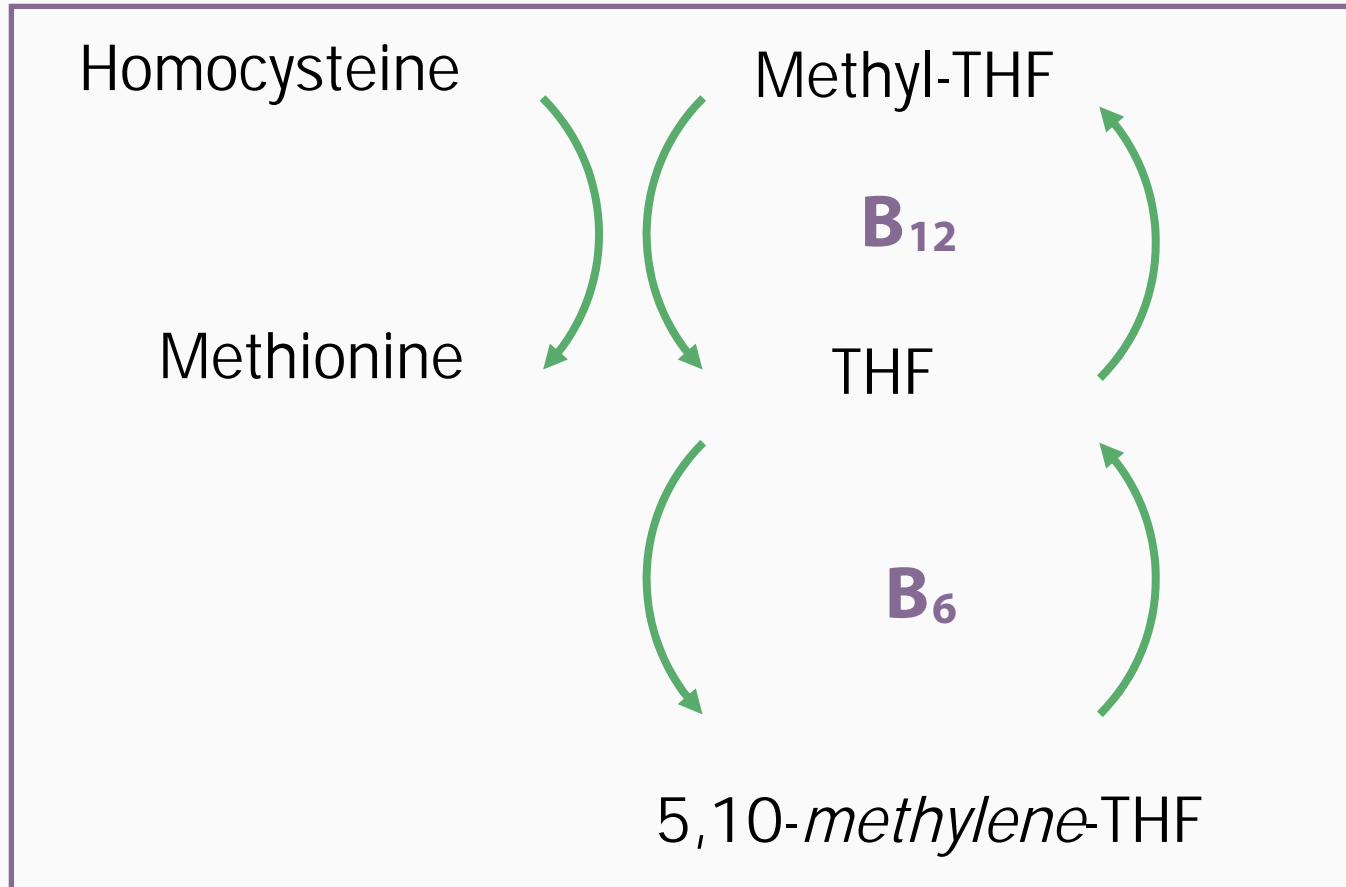
## ■ **Decrease**

- Exercise
- Estrogens

## *Other Nutrients Associated with Risk of CHD*

- Folic acid
- Vitamins B<sub>6</sub> and B<sub>12</sub>
- Iron

# Folate and Vitamin B: Interrelationships



Copyright 2005, Benjamin Caballero and The Johns Hopkins University. All rights reserved. Use of these materials permitted only in accordance with license rights granted. Materials provided "AS IS"; no representations or warranties provided. User assumes all responsibility for use, and all liability related thereto, and must independently review all materials for accuracy and efficacy. May contain materials owned by others. User is responsible for obtaining permissions for use from third parties as needed.