

Chronic Disease:

Adaptation Gone Awry?

Chronic Disease

- Chronic diseases are those of long duration as opposed to short-term, acute, mostly infectious diseases
 - Our focus is on non-infectious diseases associated with the adoption of modern lifestyles
- Little impact on natural selection since mortality clusters in post-reproductive years
 - However, many of these conditions have their roots in the adaptive patterns of our Pleistocene and Neolithic populations

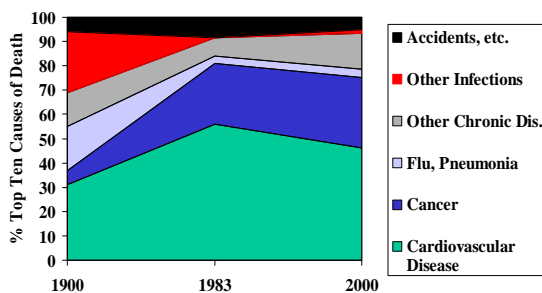
Chronic Diseases

- Cardiovascular Diseases
- Cancer
- Chronic Obstructive Pulmonary Disease
- Diabetes
- Cirrhosis of the liver
- Osteoarthritis

Leading Causes of Death in the United States in 1900, 1983, and 2000

1900 (e ₀ = 46)		1983 (e ₀ = 74)		2000 (e ₀ = 76.9)	
Cause of Death	% Top 10	Cause of Death	% Top 10	Cause of Death	% Top 10
CVD + Stroke	31.0	CVD + Stroke	56.0	CVD	37.4
Influenza, pneumonia	18.0	Cancer	25.0	Cancer	29.0
Tuberculosis	17.0	Accidents	5.0	Stroke	8.9
Stomach/intestine probs	13.0	CCPD, emphysema	4.0	CCPD, emphysema	6.4
Accidents	6.0	Influenza, pneumonia	3.0	Accidents	5.1
Cancer	6.0	Diabetes mellitus	2.0	Diabetes mellitus	3.6
Diphtheria	4.0	Suicide	1.5	Influenza, pneumonia	3.4
Typhoid, paratyphoid	3.0	Cirrhosis of the liver	1.5	Alzheimer's Disease	2.6
Measles	1.0	Homicide	1.0	Nephritis	2.0
Cirrhosis of the liver	1.0	Neonatal diseases	1.0	Septicemia	1.6

Top Causes of Death, U.S.



Etiology

- Mostly multifactorial models:
 - Genetics
 - Diet
 - Physical activity
 - Alcohol and tobacco consumption
 - Psychosocial stress
 - Lifestyle

Cardiovascular Diseases

- Circulatory problems primarily based on narrowing of the lumen of blood vessels from multiple causes
 - Primary sites of damage include the arteries supplying the heart (Coronary Artery Disease or CAD) and brain (stroke)
 - Occlusion of blood supply to the heart results in a heart attack, whereas occlusion of brain blood supply results in a stroke

Atherosclerosis

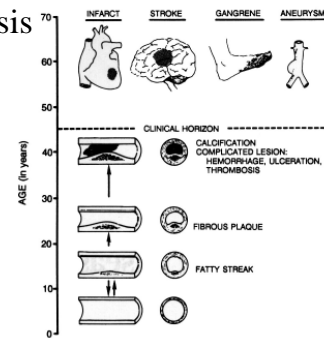


FIGURE 19-1 Natural history of atherosclerosis, showing progressive arterial occlusion and resultant health effects. From McGill et al. (1963).

CVD Risk Factors

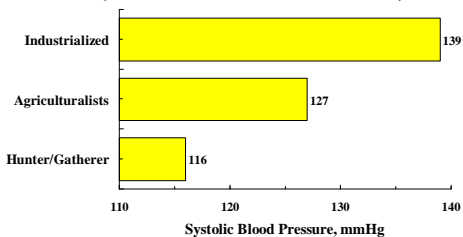
- Hyperlipidemia
 - Cholesterol > 200 mg/dl
 - TG > 150 mg/dl
 - HDL < 45 mg/dl
 - LDL > 130 mg/dl
- Hypertension
 - Systolic > 140
 - Diastolic > 90
- Psychosocial Stress
- Cigarette Smoking
- Low activity
- Low estrogen
- Inflammation
 - C-reactive protein (CRP) > 3.0 mg/L

Hyperlipidemia

- Reflects an evolutionary adaptation in our lipolytic pathways to low fat intake
 - Proto-hominid ancestors were likely frugivores
 - Once meat eating was added to our diet, game provided relatively low fat intakes
- Compare to habitual meat-eaters
 - It is almost impossible to generate atherosclerosis in dogs because of their carnivorous metabolism

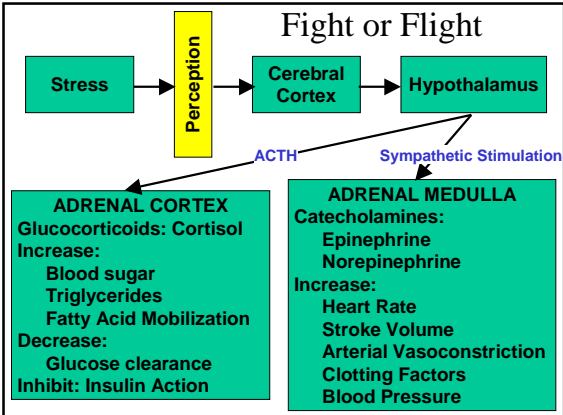
Average Systolic Blood Pressure of Adults

(Modified from Waldron et al. 1982)



Evolutionarily our bodies are not adapted to an age related blood pressure increase

Fight or Flight



Cigarette Smoking “The Red Man’s Revenge”

- We are not adapted to smoking tobacco
- Nicotine stimulates the sympathetic nervous system
 - Increases blood pressure, heart rate, circulating fatty acids, clotting factors
- Over-ventilation (drawing) increases peripheral vasoconstriction, blood pressure
- CO damages arterial wall

Tobacco Mortality

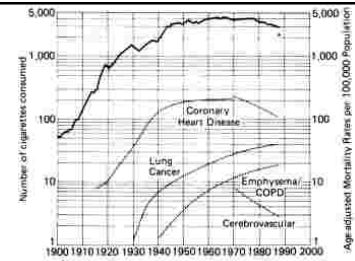


Figure III.8.2. Cigarette consumption and tobacco-related mortality in the United States, 1900–87. The asterisk indicates that the population exposure to tobacco tars is decreasing faster than the cigarette curve. (From Economic Research Service, U.S. Department of Agriculture; Vital Statistics of the United States; WCHSA Archives (personal communication); Ravenholt 1962; Walker and Brin 1988; U.S. Department of Health and Human Services.) (From Ravenholt 1993)

Causes of Death

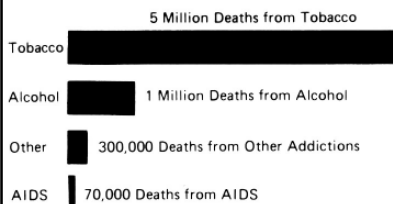


Figure III.8.3. The price of pleasure: deaths from addictive substances and AIDS in the United States, 1980s. (From Ravenholt 1984 and Centers for Disease Control.) (From Ravenholt 1993)

Activity

- We are evolutionarily accustomed to substantial activity
- High levels of caloric expenditure through physical activity improves lipid profiles
 - Combats hyperinsulinemia by making peripheral cells more sensitive to insulin
 - Reduces triglycerides, LDL-Cholesterol
 - Increases HDL-Cholesterol

Low Estrogen

- Estrogen and the estrogen synthesis pathways buffer from hyperlipidemia
 - Men and post-menopausal women have relatively low estrogen levels
 - Lipid metabolism is more likely in these groups to produce fatty streaks in arteries

Cancer

- Abnormal malignant growth of cells that invade nearby tissues and often spread to other sites in the body, interfering with normal function of the affected sites
 - Symptoms of different malignancies are dependent on the affected tissues
 - Populations have different susceptibilities, due to differing environmental exposures and varying genetic backgrounds

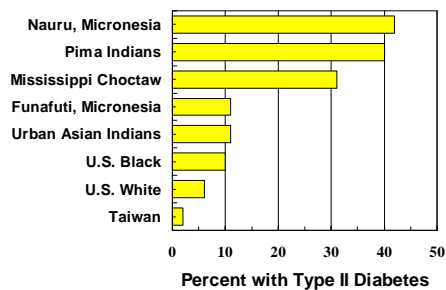
Cancer Patterns

- Lung cancer is high in the U.S., U.K.
 - Environmental exposure to tobacco smoke
- Stomach cancer high in Iceland, Japan
 - Environmental exposure to smoked fish, meat
- Breast cancer high in Ashkenazi Jews
 - BrCa1 gene at relatively high frequencies

Diabetes

- Disorder of carbohydrate metabolism due to either a partial or total failure to manufacture insulin or to an inability of insulin to function normally, resulting in an impaired ability to remove glucose from the blood

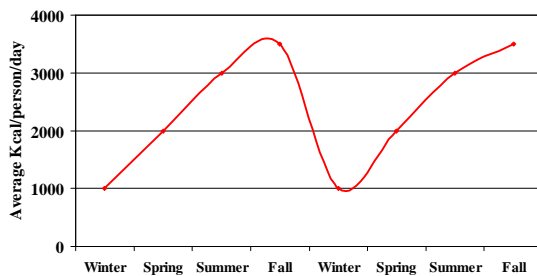
Diabetes Rates among Adults of Various Populations



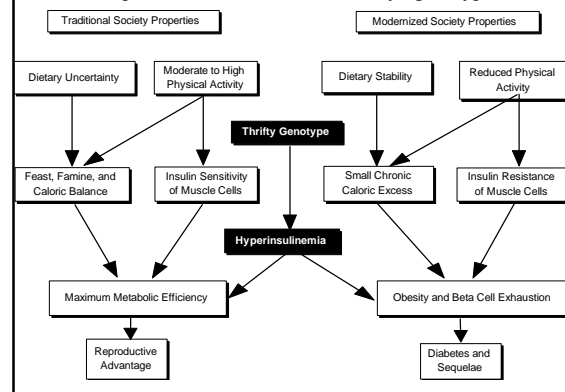
Thrifty Genotype (TG) Model

- Neel (1962) noted that Type II diabetes was unequally distributed across human populations
- He reasoned that the populations with the highest diabetes prevalence were likely to have undergone cyclic episodes of severe resource deprivation
- He postulated a model of natural selection favoring energetic efficiency for these populations

Feast and Famine



A speculative model of the “thrifty” genotype



Thrifty Genotype in Feast

- High caloric intake, relatively low activity expenditure
- TG individuals more efficient at handling excess calories due to hyperinsulinemia
 - Circulating insulin activates lipoprotein lipase on the capillary surfaces which hydrolyzes triglycerides in the plasma to facilitate transfer into adipose cells
 - Insulin also inhibits hormone sensitive lipase which is instrumental in hydrolyzing triglycerides stored in adipose tissue and releasing fatty acids into plasma
 - Leaves them better adapted to undergo subsequent deprivation and cold stress

Thrifty Genotype in Famine

- Low caloric intake, relatively higher activity expenditure
- TG individuals have higher energy stores in adipose tissue to draw on to meet needs
- Negative effects of TG such as reduced insulin sensitivity in peripheral cells and excess adiposity are counteracted by reduced caloric availability

Thrifty Genotype in Energy Balance

- Moderate to high caloric intake and expenditure
- No excess energy to process
 - TG individuals not at a selective advantage or disadvantage
- High levels of activity normal for pre-modern societies counteract insulin resistance in peripheral tissues

Thrifty Genotype in Small Chronic Excess

- Low to moderate caloric intake and expenditure
 - Intake exceeding expenditure by as little as 10 Kcal/day or one bite of apple
- TG individuals efficiently process excess calories due to chronic hyperinsulinemia
 - Predisposed to obesity (lipogenesis)
 - Type II diabetes (insulin resistance)
 - Cardiovascular diseases (hypertension)

Sources

- Bindon JR, and Baker PT (in press) Bergmann's rule and the thrifty genotype. *American Journal of Physical Anthropology*.
- McGill HC, Jr, Geer JC, and Strong JP (1963) Natural history of human atherosclerotic lesions. In Sandler M, and Bourne GH, eds. *Atherosclerosis and Its Origin*. Academic Press, New York, pp. 39-65.
- Neel JV (1962) Diabetes mellitus: a "thrifty" genotype rendered detrimental by "progress"? *American Journal of Human Genetics*, 14:353-362.
- Ravenholt RT (1993) *Tobaccosis*. In Kiple KP, ed. *The Cambridge World History of Human Disease*. Cambridge, Cambridge University Press, pp. 176-186.

Sources, 2

- Trowell HC, and Burkitt DP (1981) *Western Diseases: Their Emergence and Prevention*. Cambridge, MA, Harvard University Press. (Excellent coverage of the diseases of modernization: cardiovascular disease, diabetes, gallstones, cancer. Chapters on Inuit, North American Indians, Australian Aborigines, Pacific Islanders, and others)
- Waldron I, Nowotarski M, Freimer M, Henry JP, Post N, and Witten C (1982) Cross-cultural variation in blood pressure: a quantitative analysis of the relationships of blood pressure to cultural characteristics, salt consumption, and body weight. *Social Science and Medicine*, 16:419-430.
- Weiss ML, and Mann AE (1990) *Human biology and Behavior: An Anthropological Perspective*. Glenview, IL, Scott, Foresman, and Co.