Stone Agers in the Fast Lane: Chronic Degenerative Diseases in Evolutionary Perspective

S. BOYD EATON, M.D.
MELVIN KONNER, Ph.D., M.D.
MARJORIE SHOSTAK
Atlanta, Georgia

From a genetic standpoint, humans living today are Stone Age hunter-gatherers displaced through time to a world that differs from that for which our genetic constitution was selected. Unlike evolutionary maladaptation, our current discordance has little effect on reproductive success; rather it acts as a potent promoter of chronic illnesses: atherosclerosis, essential hypertension, many cancers, diabetes mellitus, and obesity among others. These diseases are the results of interaction between genetically controlled biochemical processes and a myriad of biocultural influences—lifestyle factors—that include nutrition, exercise, and exposure to noxious substances. Although our genes have hardly changed, our culture has been transformed almost beyond recognition during the past 10,000 years, especially since the Industrial Revolution. There is increasing evidence that the resulting mismatch fosters "diseases of civilization" that together cause 75 percent of all deaths in Western nations, but that are rare among persons whose lifeways reflect those of our preagricultural ancestors.

In today's Western nations, life expectancy is over 70 years—double what it was in preindustrial times. Infant death rates are lower than ever before and nearly 80 percent of all newborn infants will survive to age 65 or beyond. Such vital statistics certify that the health of current populations, at least in the affluent nations, is superior to that of any prior group of humans. Accordingly, it seems counterintuitive to suggest that, in certain important respects, the collective human genome is poorly designed for modern life. Nevertheless, there is both epidemiologic and pathophysiologic evidence that suggests this may be so.

In industrialized nations, each person's health status is heavily influenced by the interaction between his or her genetically controlled biochemistry and a collection of biobehavioral influences that can be considered lifestyle factors. These include nutrition, exercise, and exposure to harmful substances such as alcohol and tobacco. This report presents evidence that the genetic makeup of humanity has changed little during the past 10,000 years, but that during the same period, our culture has been transformed to the point that there is now a mismatch between our ancient, genetically controlled biology and certain important aspects of our daily lives. This discordance is not genetic maladaptation in the terms of classic evolutionary science—it does not affect differential fertility. Rather, it promotes chronic degenerative diseases that have their main clinical expression in the post-reproductive period, but that together account for nearly 75 percent of the deaths occurring in affluent Western nations.

From the Department of Anthropology, the School of Medicine, and the Institute of Liberal Arts, Emory University, Atlanta, Georgia. Requests for reprints should be addressed to Dr. S. Boyd Eaton, Department of Anthropology, Emory University, Atlanta, Georgia 30322. Manuscript submitted December 11, 1987, and accepted in revised form February 5, 1988.

THE HUMAN GENOME

The gene pool from which current humans derive their individual genotypes was formed during an evolutionary experience lasting over a billion years. The almost inconceivably protracted pace of genetic evolution is indicated by paleontologic findings that reveal that an average species of late cenozoic mammals persisted for more than a million years [1], by biomolecular evidence indicating that humans and chimpanzees now differ genetically by just 1.6 percent even though the hominid-pongid divergence occurred seven million years ago [2], and by dentochronologic data showing that current Europeans are genetically more like their Cro-Magnon ancestors than they are like 20th-century Africans or Asians [3]. Accordingly, it appears that the gene pool has changed little since anatomically modern humans, Homo sapiens sapiens, became widespread about 35,000 years ago and that, from a genetic standpoint, current humans are still late Paleolithic preagricultural hunter-gatherers.

THE IMPACT OF CULTURAL CHANGES

It has been proposed that chronic degenerative disorders, sometimes referred to as the "diseases of civilization," are promoted by discordance between our genetic makeup (which was selected over geologic eras, ultimately to fit the life circumstances of Paleolithic humans) and selected features of our current bioenvironmental milieu. The rapid cultural changes that have occurred during the past 10,000 years have far outpaced any possible genetic adaptation, especially since much of this cultural change has occurred only subsequent to the Industrial Revolution of 200 years ago.

The increasing industrialized affluence of the past two centuries has affected human health both beneficially and adversely. Improved housing, sanitation, and medical care have ameliorated the impact of infection and trauma, the chief causes of mortality from the Paleolithic era until 1900, with the result that average life expectancy is now approximately double what it was for preagricultural humans. The importance of these positive influences can hardly be overstated; their effects have not only increased longevity, but also enhanced the quality of our lives in countless ways. But, on the other hand, the past century has accelerated the biologic estrangement that has increasingly differentiated humans from other mammals over the entire two-million-year period since Homo habilis first appeared. Despite the increasing importance of culture and technology during this time, the basic lifestyle elements of Homo sapiens sapiens were still within the broad continuum of general mammalian experience until recently. However, in today's Western nations, we have so little need for exercise, consume foods so different from those available to other mammals, and expose ourselves to such harmful agents as alcohol and tobacco that we have crossed an epidemiologic boundary and entered a watershed in which disorders such as obesity, diabetes, hypertension, and certain cancers have become common in contrast to their rarity among remaining preagricultural and other traditional humans.

METHODS

Pertinent data on fitness, diet, and disease prevalence in non-industrial societies were reviewed, tabulated, and contrasted with comparable data from industrialized nations. The literature cited is based on studies of varied traditional groups: pastoralists, rudimentary horticulturalists, and simple agriculturalists, as well as technologically primitive hunter-gatherers. We would have preferred to present data derived solely from studies of pure hunter-gatherers, since they are most analogous to Paleolithic humans. Unfortunately, only a few such investigations have been performed, so that inclusion of selected non-foraging populations constitutes a necessary first approximation. However, there is a continuum of human experience with regard to lifestyle factors that now affect disease prevalence, and on this continuum, traditional peoples occupy positions much closer to those of our preagricultural ancestors than to those of affluent Westerners. In each case, the groups analyzed resemble late Paleolithic humans far more than ourselves with respect to factors (such as exercise requirements and dietary levels of fat, sodium, and fiber) considered likely to influence the prevalence of the disease entity under consideration.

THE LATE PALEOLITHIC LIFESTYLE

The Late Paleolithic era, from 35,000 to 20,000 B.P., may be considered the last time period during which the collective human gene pool interacted with bioenvironmental circumstances typical of those for which it had been originally selected. It is because of this that the diet, exercise patterns, and social adaptations of that time have continuing relevance for us today.

Nutrition. The diets of Paleolithic humans must have varied greatly with latitude and season just as do those of recently studied hunter-gatherers; undoubtedly, there were periods of relative plenty and others of shortage; certainly there was no one universal subsistence pattern. However, the dietary requirements of all Stone Age men and women had to be met by uncultivated vegetables and wild game exclusively; from this starting point, a number of logically defensible nutritional generalizations can be extrapolated [4]. (1) The amount of protein, especially animal protein, was very great. The mean, median, and modal protein intake for 58 hunter-gatherer groups studied in this century was 34 percent [4] and protein intake in the Late Paleolithic era may have been higher still [5,6]. The current American diet derives 12 percent of its energy from protein (**Table I**). (2) Because game animals are extremely lean, Paleolithic humans ate much less fat than do 20th-century Americans and Europeans, although more than is consumed in most Third-World countries. (3) Stone Age hunter-gatherers generally ate more polyunsaturated than saturated fat. (4) Their cholesterol intake would ordinarily have equaled or exceeded that now common in industrialized nations. (5) The amount of carbohydrate they obtained would have varied inversely with the proportion of meat in their diet, but (6) in almost all cases they would have obtained much more dietary fiber than do most Americans. (7) The availability of simple sugars, especially honey, would have varied seasonally. For a two- to four-month period, their intake could have equaled that of current humans, but for the remainder of the year it would have been minimal. (8) The amounts of ascorbic acid, folate, vitamin B_{12}, and iron available [7,8] to our remote ancestors equaled, and likely exceeded, those consumed by today's Europeans and North Americans; probably this reflects a general abundance of micronutrients (with the possible exception of iodine in inland locations). (9) In striking contrast to the pattern in today's industrialized nations [9], Paleolithic humans obtained far more potassium than sodium from their food (as do all other mammals). On the average, their total daily sodium intake was less than a gram—barely a quarter of the current American average. (10) Because they had no domesticated animals, they had no dairy foods; despite this, their calcium intake, in most cases, would have far exceeded that generally consumed in the 20th century.

TABLE I Late Paleolithic, Contemporary American, and Currently Recommended Dietary Composition

	Late Paleolithic Diet	Contemporary American Diet	Current Recommendations
Total dietary energy (percent)			
Protein	33	12	12
Carbohydrate	46	46	58
Fat	21	42	30
Alcohol	~0	(7–10)*	—
P:S ratio	1.41	0.44	1.00
Cholesterol (mg)	520	300–500	300
Fiber (g)	100–150	19.7	30–60
Sodium (mg)	690	2,300–6,900	1,100–3,300
Calcium (mg)	1,500–2,000	740	800–1,600
Ascorbic acid (mg)	440	87.7	60

Updated from Eaton and Konner [4]. Data base now includes 43 species of wild game and 153 types of wild plant food.
* Inclusion of calories from alcohol would require concomitant reduction in calories from other nutrients—mainly carbohydrate and fat.
P:S = polyunsaturated-to-saturated fat.

Physical Exercise. The hunter-gatherer way of life generates high levels of physical fitness. Paleontologic investigations and anthropologic observations of recent foragers [10] document that among such people, strength and stamina are characteristic of both sexes at all ages.

Skeletal remains can be used for estimation of strength and muscularity. The prominence of muscular insertion sites, the area of articular surfaces, and the cortical thickness and cross-sectional shape of long bone shafts all reflect the forces exerted by the muscles acting on them. Analyses of these features consistently show that preagricultural humans were more robust than their descendants, including the average inhabitants of today's Western nations. This pattern holds whether the population being studied underwent the shift to agriculture 10,000 [11] or only 1,000 [12] years ago, so it clearly represents the results of habitual activity rather than genetic evolution. The fact that hunter-gatherers were demonstrably stronger and more muscular than succeeding agriculturalists (who worked much longer hours) suggests that the intensity of intermittent peak demand on the musculoskeletal system is more important than the mere number of hours worked for the development of muscularity.

The endurance activities associated with both hunting and gathering involve considerable heat production. The long-standing importance of such behaviors for humankind is apparently reflected in the unusual mechanisms for heat dissipation with which evolution has endowed us: we are among the very few animal species that can release heat by sweating; also, our hairless, exposed skin allows heat to escape readily, especially during rapid movement, like running, when airflow over the skin is increased. These physiologic adaptations suggest the importance of endurance activities in our evolutionary past [13], and evaluation of recent preliterate populations confirms that their daily activities develop superior aerobic fitness (**Tables II** and **III**). Whereas actual measurements of maximal oxygen uptake capacity have been made almost exclusively on men, anthropologic observations suggest commensurate aerobic fitness for women in traditional cultures as well [15].

Alcoholic Beverages. Honey and many wild fruits can undergo natural fermentation, so the possibility that some preagricultural persons had alcoholic beverages cannot be excluded. However, widespread regular use of alcohol must have been a very late phenomenon: of 95 preliterate societies studied in this century [16], fully 46, including the San (Bushmen), Eskimos, and Australian Aborigines, were unable to manufacture such beverages. It is estimated that 7 to 10 percent of the average adult American's daily energy intake is provided by alcohol; such levels are far in excess of what Late Paleolithic humans could have conceivably obtained.

In general, native alcoholic beverages are prepared periodically and drunk immediately [17]. Their availability is subject to seasonal fluctuation, and as products of natural fermentation, their potency is far less than that of distilled liquors. Their consumption is almost invariably

TABLE II Aerobic Fitness

Subsistence Pattern	Population	Average Age	Maximal Oxygen Uptake (ml/kg/minute)	Fitness Category*
Hunter-gatherers	Canadian Igloolik Eskimos	29.3	56.4	Superior
	Kalahari San (Bushmen)	Young men	47.1	Excellent
Rudimentary horticulturists	Venezuelan Warao Indians	Young men	51.2	Excellent
	New Guinea highland Lufas	25	67.0	Superior
Simple agriculturists	Mexican Tarahumara Indians	29.8	63.0	Superior
Pastoralists	Finnish Kautokeino Lapps	25–35	53.0	Superior
	Tanzanian Masai	32–43	59.1	Superior
Industrialized Westerners	Canadian Caucasians	20–29	40.8	Fair
	Canadian Caucasians	30–39	38.1	Fair
	Canadian Caucasians	40–49	34.9	Fair

* From [14].

TABLE III Fitness Classification for American Males*

Age	Maximal Oxygen Uptake (ml/kg/minute)					
	Very Poor	Poor	Fair	Good	Excellent	Superior
20–29	<33.0	33.0–36.4	36.5–42.4	42.5–46.4	46.5–52.4	>52.5
30–39	<31.5	31.5–35.4	36.5–40.9	41.0–44.9	45.0–49.4	>49.5
40–49	<30.2	30.2–33.5	33.6–38.9	39.0–43.7	43.8–48.0	>48.1

* Data modified from [14].

subject to strong societal conventions that limit the frequency and place of consumption, degree of permissible intoxication, and types of behavior that will be tolerated. In small-scale traditional preliterate societies, drinking tends to be ritualized and culturally integrated [18]. Solitary, addictive, pathologic drinking behavior does not occur to any significant extent; such behavior appears to be a concomitant of complex, modern, industrialized societies [17].

Tobacco Abuse. Recent hunter-gatherers such as the San (Bushmen), Aché, and Hadza had no tobacco prior to contact with more technologically advanced cultures, but the Australian Aborigines chew wild tobacco, so seasonal use by Paleolithic humans in geographically limited areas cannot be excluded. However, widespread tobacco usage began only after the appearance of agriculture in the Americas, perhaps 5,000 years ago. With European contact, the practice spread rapidly throughout the world. Pipes and cigars were the only methods employed for smoking until the mid-19th century, when cigarettes first appeared. Cigarettes had three crucial effects: they dramatically increased per capita consumption among men; after World War I, they made smoking socially acceptable for women; and they made inhalation of smoke the rule rather than the exception. Although the hazards of chewing tobacco, snuff, pipes, and cigars are not insignificant, the major impact of tobacco abuse is a post-cigarette phenomenon of this century.

HOW ALTERED LIFESTYLE FACTORS AFFECT DISEASE PREVALENCE

In many, if not most, respects, the health of humans in today's affluent countries must surpass that of typical Stone Agers. Infant mortality, the rate of endemic infectious disease (especially parasitism), and the prevalence of post-traumatic disability were all far higher 25,000 years ago than they are at present. Still, pathophysiologic and epidemiologic research conducted over the past 25 years supports the concept that certain discrepancies between our current lifestyle and that typical of preagricultural humans are important risk factors for the chronic degenerative diseases that account for most mortality in today's Western nations. These "diseases of civilization" are not new: Aretaeus described diabetes 2,000 years ago, atherosclerosis has been found in Egyptian mummies, paleolithic "Venus" statuettes show that Cro-Magnons could be obese, and the remains of 500-year-old Eskimo burials reveal that cancer afflicted hunter-gatherers isolated from contact with more technologically ad-

TABLE IV Triceps Skinfold Measurements in Males*

Subsistence Pattern	Population	Age	Thickness (mm)
Hunter-gatherers	Australian Aborigines	25–29	4.7
	Kalahari San (Bushmen)	Young men	4.6
	Canadian Igloolik Eskimos	20–29	4.4
	Congo Pigmies	20–29	5.5
	Tanzanian Hadza	25–34	4.9
Rudimentary horticulturists	New Guinea Tukisenta	16–37	5.0
	Venezuelan Warao Indians	Young men	5.9
	New Guinea Biak	25	5.3
	Solomon Islanders	19–70	5.4
	New Guinea Lufa	21–35	5.1
	Surinam Trio Indians	21 and over	6.0
Simple agriculturists	Peruvian Quechua Indians	35	4.0
	Japanese Ainu	Young men	5.3
	Tarahumara Indians	21 and over	6.3
	Rural Ethiopean peasants	20–30	5.3
Mean			5.2
Industrialized Westerners	Canadian Caucasians	20–29	11.2
	American Caucasians	18–24	9.0
Mean			10.1

* As initially submitted, the manuscript included 236 supportive references. A copy of the original manuscript can be obtained by sending a stamped ($1.80), addressed envelope (to accommodate 47 8½ X 11″ pages) to: Eaton/Konner/Shostak, Department of Anthropology, Emory University, Atlanta, Georgia 30322.

vanced cultures [19]. However, the lifestyle common in 20th-century affluent Western industrialized nations has greatly increased the prevalence of these and other conditions. Before 1940, diabetes was rare in American Indians [20], but now the Pimas have one of the world's highest rates [21]; hypertension was unknown in East Africans before 1930, but now it is common [22]; and in 1912, primary malignant neoplasms of the lungs were considered "among the rarest forms of disease" [23]. It is not only because persons in industrialized countries live longer that these illnesses have assumed new importance. Young persons in the Western world commonly harbor developing asymptomatic atherosclerosis [24], whereas youths in technologically primitive cultures do not [25,26]; the age-related rise in blood pressure so typical of affluent society is not seen in unacculturated groups [27]; and older members of preliterate cultures remain lean [28–30] in contrast to the increasing proportion of body fat that is almost universal among affluent Westerners [31].

Obesity. Obesity is many disorders: its "causes"—genetic, neurochemical, and psychologic—interact in a complex fashion to influence body energy regulation. Superimposed upon this underlying etiologic matrix, however, are salient contrasts between the Late Paleolithic era and the 20th century that increase the likelihood of excessive weight gain (**Table IV**). (1) Most of our food is calorically concentrated in comparison with the wild game and uncultivated fruits and vegetables that constituted the Paleolithic diet [4]. In general, the energy-satiety ratio of our food is unnaturally high: in eating a given volume, enough to create a feeling of fullness, Paleolithic humans were likely to consume fewer calories than we do today [32]. (2) Before the Neolithic Revolution, thirsty humans drank water; most beverages consumed today provide a significant caloric load while they quench our thirst. (3) The low levels of energy expenditure common in today's affluent nations may be more important than excessive energy intake for development and maintenance of obesity [33]. Total food energy intake actually has an *inverse* correlation with adiposity, but obese persons have proportionately even lower levels of energy expenditure [33]—a low "energy throughput" state. Increased levels of physical exercise raise energy expenditure proportionately more than caloric intake [34] and may lower the body weight "set point."

Diabetes Mellitus. Mortality statistics for New York City between 1866 and 1923 show a distinct fall in the overall death rate, but a steady, impressive rise in death rates from diabetes. For the over-45 age group, there was a 10-fold increase in the diabetic death rate during this period [35]. This pattern anticipated the more recent experience of Yemenite Jews moving to Israel [36], Alaskan Eskimos [37], Australian Aborigines [38], American Indians [39], and Pacific Islanders of Micronesian, Melanesian, and Polynesian stock [40]. In these groups, dia-

TABLE V Diabetes Prevalence*

Subsistence Pattern	Population	Prevalence (percent)
Hunter-gatherers	Alaskan Athabaskan Indians	1.3
	Greenland Eskimos	1.2
	Alaskan Eskimos	1.9
Rudimentary horticulturists	Papua, New Guinea Melanesians	0.9
	Loyalty Island Melanesians	2.0
	Rural Malaysians	1.8
Simple agriculturists	Rural villagers, India	1.2
	"New" Yemenite immigrants, Israel	0.1
	Rural Melanesians, New Caledonia	1.5
	Polynesians on Pukapuka	1.0
	Rural Figians	0.6
Pastoralists	Nomadic Broayas, North Africa	0.0
Mean		1.1
Industrialized Westerners	Australia, Canada, Japan, United States	Range 3.0–10.0†

* See footnote to Table IV.
† Data are from [41].

betic prevalence, if not the actual mortality rate, has risen rapidly and it has been observed that obesity and maturity-onset diabetes are among the first disorders to appear when unacculturated persons undergo economic development. At present, the overall prevalence of non-insulin-dependent diabetes among adults in industrialized countries ranges from 3 to 10 percent [41], but among recently studied, unacculturated native populations that have managed to continue a traditional lifestyle, rates for this disorder range from nil to 2.0 percent (**Table V**).

Like obesity, diabetes mellitus is a family of related disorders, each of which reflects the interplay of genetic and environmental influences. But again, in comparison with Paleolithic experience, the lifestyle of affluent, industrialized countries potentiates underlying causal factors to promote maturity-onset diabetes by several mechanisms. (1) A 1980 World Health Organization expert committee on diabetes concluded that the most powerful risk factor for type II diabetes is obesity [42]. The obese persons common in Western nations have reduced numbers of cellular insulin receptors. They manifest a relative tissue resistance to insulin [43], and therefore their blood insulin levels tend to be higher than those of lean persons. (2) Conversely, high-level physical fitness, characteristic of aboriginal persons, is associated with an increased number of insulin receptors and better insulin binding [44]; these effects enhance the body's sensitivity to insulin [45]. Serum insulin levels are typically low in hunter-gatherers [46] and trained athletes [44]; cellular insulin sensitivity can be improved by physical conditioning that increases cardiorespiratory fitness [47]. This effect is independent from [47], but may be augmented by, an associated effect on body weight and composition [43]. (3) Diets containing ample amounts of non-nutrient fiber and complex carbohydrate have been shown to lower both fasting and post-prandial blood glucose levels [48]. Diets with high intakes of fiber and complex carbohydrates are the rule among technologically primitive societies, but are the exception in Western nations. Their recommendation by the American Diabetes Association underscores the merit of these Paleolithic dietary practices.

Hypertension. Across the globe, there are many cultures whose members do not have essential hypertension nor experience the age-related rise in average blood pressure that characterizes populations living in industrialized Western nations. These persons are not genetically immune from hypertension since, when they adopt a Western style of life, either by migration or acculturation, they develop, first, a tendency for their blood pressure to rise with age and, second, an increasing incidence of clinical hypertension [27,49]. These normotensive cultures exist in varied climatic circumstances—in the arctic, the rain forest, the desert, and the savanna—but they share a number of essential similarities, each of which is the reciprocal of a postulated causal factor for hypertension. These include diets low in sodium and high in potassium [50]. In addition, the pastoralists and those groups still subsisting as hunter-gatherers have diets that provide a high level of calcium [51]. These persons are slender [52], aerobically fit [53], and, at least in their unacculturated state, have limited or no access to alcoholic beverages [54].

More than 90 percent of the hypertension that occurs in the United States and similar nations is idiopathic or "essential" in nature. Many theories about the origin of this hypertension have been advanced and it may represent a family of conditions that share a final common pathway resulting in blood pressure elevation. Although its

TABLE VI Serum Cholesterol Values*

Subsistence Pattern	Population	Gender	Cholesterol Value (mg/dl)
Hunter-gatherers	Tanzanian Hadza	M	114
		F	105
	Kalahari San (Bushmen)		130
	Kalahari San (Bushmen)		109
	Congo Pygmies	M	101
		F	111
	Australian Aborigines	M	146
		F	132
	Canadian Eskimos		141
Rudimentary horticulturists	Palau Micronesians	M	160
		F	170
	New Guinea Chimbu		130
	New Guinea Wabag		144
	Brazilian Xavante Indians	M	107
		F	121
	Brazalian Kren-Akorore Indians		100
	Solomon Islands Aita	M	135
		F	142
	Solomon Islands Kwaio	M	114
		F	125
	New Guinea Bomai	M	130
		F	140
	New Guinea Yongamuggl	M	139
		F	140
Simple agriculturists	Mexican Tarahumara Indians	M	136
		F	139
	Rural Samoans	M	167
		F	180
	Guatemalan Mayan Indians	M	132
		F	143
Pastoralists	Kenyan Samburu	M	166
	Kenyan Masai	F	135

* See footnote to Table IV.

"causes" remain obscure, its occurrence in most cases probably reflects the interaction between individual genetic predisposition and pertinent modifiable lifestyle characteristics. Accordingly, a promising approach to its prevention is suggested by the practices of traditional persons who are spared this disorder; the common features they share reflect components of our ancestral lifestyle.

Atherosclerosis. Clinical and postmortem investigations of arctic Eskimos [55–57], Kenyan Kikuyu [58], Solomon Islanders [59], Navajo Indians [60], Masai pastoralists [61], Australian Aborigines [62], Kalahari San (Bushmen) [30], New Guinea highland natives [63], Congo Pygmies [64], and persons from other preliterate societies reveal that, in the recent past, they experienced little or no coronary heart disease. This is presumably because risk factors for development of atherosclerosis were so uncommon in such cultures. Like our Paleolithic ancestors, they traditionally lacked tobacco, rarely had hypertension, and led lives characterized by considerable physical exertion. In addition, their serum cholesterol levels were low (**Table VI**). The experience of hunter-gatherers is of special interest in this regard: their diets are low in total fat and have more polyunsaturated than saturated fatty acids (a high polyunsaturated-to-saturated fat ratio), but contain an amount of cholesterol similar to that in the current American diet. The low serum cholesterol levels found among them suggest that a low total fat intake together with a high polyunsaturated-to-saturated fat ratio can compensate for relatively high total cholesterol intake [65]. This supposition is supported by the experience of South African egg farm workers. Their diets include a mean habitual cholesterol intake of 1,240 mg per day, but fat (polyunsaturated-to-saturated fat ratio = 0.78) provides only 20 percent of total energy and their serum cholesterol levels average 181.4 mg/dl (with high-density lipoprotein cholesterol = 61.8 mg/dl) [66].

The adverse changes that occur in atherosclerotic risk factors when persons from societies with little such disease become westernized recapitulate the pattern observed for the other diseases of civilization. The experiences of Japanese [67], Chinese [68], and Samoans [69] migrating to the United States, of Yemenite Jews to Israel [70], and of Greenland Eskimos to Denmark [71] parallel those of Kalahari Bushmen [72], Solomon Islanders [59], Ethiopean peasants [73], Canadian Eskimos [74], Australian Aborigines [38], and Masai Pastoralists [75] who have become increasingly westernized in their own countries.

Abnormalities of coagulability may contribute to both the development and the acute clinical manifestations of atherosclerosis [76]. Platelet function has received considerable attention in this respect [77]. Fibrinolytic activity is enhanced by physical exercise [78], but decreased by smoking cigarettes [79], obesity [80], and hyperlipoproteinemia [81], so it is not surprising that preliterate peoples have more such activity than do average Westerners [82,83]. Platelet aggregation is influenced by hypercholesterolemia [84], by physical exercise [85], and by blood levels of long-chain polyunsaturated omega-3 class fatty acids [86]. The latter, in turn, are related to dietary intake of fats containing these constituents; fish oils have especially high concentrations of such fatty acids. Meat from domesticated animals is deficient in this regard [87] but the wild game consumed by our ancestors contained a moderate amount [4,87], possibly enough to induce blood levels comparable to those of the Japanese [88] or Dutch [89], although almost certainly not those of the Eskimos [71].

Coronary atherosclerosis was apparently uncommon in the United States before about 1930 [90,91], but its importance thereafter rapidly increased to a peak in the 1960s, then began a gradual decline. Whereas many factors ranging from changes in the diagnostic classification codes to improvements in treatment are involved in these trends, both the "epidemic" and the decline have been linked to alterations in lifestyle—initially away from and subsequently back toward the pattern that prevailed among preagricultural humans [92].

Cancer. The perception of cancer as a disease primarily related to the environment has been progressively strengthened over the past decade [93]. International studies reveal large differences in cancer incidence rates between countries; for example, age-standardized analyses reveal that Canadian women have seven times more breast cancer than do non-Jewish women in Israel [94]. Genetic variation cannot account for these major differences, since groups migrating from an area with a characteristic pattern of cancer incidence rates acquire different rates typical of their new geographic location within a few generations. Age-standardized data show that Japanese men in Hawaii have 11 times more prostatic cancer than do Japanese men in Japan and that black Americans have 10 times more colon cancer than do black Nigerians [94]. Also, there have been large changes in incidence rates for many types of cancer within genetically stable populations: in Ireland, lung cancer mortality increased 177 percent between 1950 and 1975 [94]. In Canada, acculturation of western and central Arctic Eskimos has led to an increase in overall cancer morbidity together with marked change in the relative frequency of specific tumor types. Between 1950 and 1980, the number of proven salivary gland cancers decreased by two thirds, whereas lung cancers increased 550 percent [95]. Furthermore, tumor incidence in laboratory animals can be readily altered by manipulating external factors ranging from radiation exposure to dietary composition.

On the basis of these observations, epidemiologists have argued that it should be theoretically possible to reduce site-specific incidence for each type of cancer to the lowest rate found in any population [96]. By summing the lowest national or regional rates observed for each cancer site, basal or "naturally occurring" minimal incidence rates can be developed. When these minimal rates are compared with the rates observed in countries where each type of tumor is common, it appears that from 70 to 90 percent of cancers are the result of environmental influences and hence potentially preventable [94,96].

The factors considered most likely to affect the development of cancer are tobacco abuse [93,97] and nutritional influences [98]. Extensive tobacco usage (and the regular consumption of alcoholic beverages) postdate the Agricultural Revolution, whereas current cancer-preventive nutritional recommendations [99,100]—to avoid obesity, reduce total fat intake, consume a wide variety of fruits and vegetables (including considerable dietary fiber, vitamin C, and vitamin A or beta-carotene), and to drink alcohol only in moderation if at all—are a fairly accurate, if incomplete, summary of Paleolithic nutritional practices.

CONCLUSION

The diseases considered, as well as others ranging from dental caries to diverticulosis, share important features. In each case, the condition is uncommon, rare, or almost unknown in cultures whose pertinent essential features mimic those of our Late Paleolithic ancestors. However, in each instance, the prevalence of disease increases dramatically when the previously unaffected society adopts a Western lifestyle, whether by migration or acculturation. Furthermore, extensive pathophysiologic research has identified bioenvironmental factors that are likely etiologic agents for each condition. Such factors (e.g., caloric concentration, tobacco abuse, sedentary living, diets high in fat and salt, and so on) are pervasive in affluent industrialized society, but not in traditional cultures where the lifestyle is, in important ways, similar to that of preagricultural humans—similar to that for which the current human genome was selected. These considerations are consistent with the hypothesis that discordance between our genes and the affluent 20th-century lifestyle (defined to include diet, exercise, and exposure to harmful substances) accentuates underlying causal factors and thereby promotes the chronic "diseases of civilization."

Of course, cancer, atherosclerosis, non-insulin-dependent diabetes mellitus, and other afflictions of affluence are all disorders whose clinical manifestations become increasingly common with advancing age; might not the prevalence of these conditions in 20th-century Western nations result simply from the unprecedented life expectancy that characterizes these countries? The population's greater age must certainly be a contributing factor, but the failure of young persons in traditional cultures to exhibit the early stages of these chronic diseases [58,101] contrasts with the experience of youths in Western nations [24], indicating that age is not the primary determinant. Furthermore, those persons in traditional societies who do reach age 60 and beyond remain lean [28–30] and normotensive [27], while clinical [57] and postmortem [58] examinations reveal little or no significant coronary atherosclerosis. Findings like these suggest that chronic degenerative diseases need not be the inevitable consequence of advancing years.

Evolution has endowed Homo sapiens with the ability to adapt and thrive under an extraordinary range of conditions, and this adaptability allows us to benefit enormously from the manifold advantages of today's civilization. In 20th-century industrialized nations, parameters such as infant mortality, childhood growth rates, and average life expectancy all indicate a state of public health far exceeding that which was obtained in the Stone Age or at any time thereafter until the current century. Indeed, more than half the persons who have ever lived beyond age 65 are alive today. Nevertheless, we can still profit from the experience of our remote ancestors. We still carry their inheritance—genes selected for their way of life, not ours. Despite the achievements of science and technology, we remain collectively fearful of diseases that available evidence suggests were uncommon, rare, or unknown in the Late Paleolithic era. In order to regain relative freedom from these illnesses, we need to take a step backward in time. For each disorder, we may anticipate increasingly sophisticated and effective treatments, but the crucial corrective measure will almost certainly be prevention. This will entail reintroduction of essential elements from the lifestyle of our Paleolithic ancestors.

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