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DIETARY, EVOLUTIONARY, AND MODERNIZING INFLUENCES ON THE PREVALENCE OF TYPE 2 DIABETES

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Key Words obesity, Westernized diets, Syndrome X, dietary globalization, thrifty genotypes

■ **Abstract** An evolutionary perspective is used to elucidate the etiology of the current epidemic of type 2 diabetes estimated at 151 million people. Our primate legacy, fossil hominid, and hunting-gathering lifestyles selected for adaptive metabolically thrifty genotypes and phenotypes are rendered deleterious through modern lifestyles that increase energy input and reduce output. The processes of modernization or globalization include the availability and abundance of calorically dense/low-fiber/high-glycemic foods and the adoption of sedentary Western lifestyles, leading to obesity among both children and adults in developed and developing countries. These trends are projected to continue for a number of decades.

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TYPE 2 DIABETES PREVALENCE

Introduction and Overview: Definition, Diagnosis, Etiology

Diabetes is now one of the most common noncommunicable diseases and one of the most challenging health problems in the twenty-first century (38, 47, 90, 103, 104, 226, 232, 234). The World Health Organization (226) has accorded diabetes priority status and has called for the development of strategic interventions. Modernization, including urbanization, westernization of lifestyles, and economic development are the underlying cultural processes driving the escalating diabetes epidemic. Although demographic trends play a role (e.g., the increased number of elderly persons), the epidemic is reaching younger age groups of obese children and adolescents (6, 7, 215, 231). Explanatory models of the rising "diabesity" prevalence (9, 10) focus on historical trends with little or no discussion of evolutionary prehistoric mechanisms (54, 164–167). Yet, the evolution of hominids and our own species has been profoundly shaped by diet and fluctuations in energy balance (125, 130, 143–145). This article examines the evolutionary, historical, and contemporary selection factors that shape the projected diabetes pandemic (Figure 1).

Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar or hyperglycemia. Chronic hyperglycemia results from defects in insulin secretion from the pancreas and/or insufficient insulin action in muscle and adipose tissue. Both hypo- and hyperinsulinemia occur with diabetes. The criteria for the diagnosis of type 2 diabetes established by the American Diabetes Association Expert Committee on Diagnosis and Classification of Diabetes Mellitus (7) are: a random plasma glucose of $\geq$200 mg/dl (11.l mmol/l); or a fasting plasma glucose (FPG) of $\geq$126 mg/dl (7.0 mmol/l); or a two-hour oral glucose tolerance test with plasma glucose $\geq$200 mg/dl. A normal FPG is $\leq$110 mg/dl (6.1 mmol/l) and a FPG 110–126 mg/dl is defined as impaired glucose tolerance, impaired fasting glucose, or "prediabetes." The World Health Organization (226) diagnostic criterion for diabetes is set at $\geq$140 mg/dl (7.8 mmol/l) for FGP.

Diabetes is characterized by frequent urination (polyuria), hunger (polyphagia), thirst (polydipsia), weight loss, blurred vision, and skin itchiness. In children with type 1 diabetes there maybe growth impairment. Diabetes is associated with long-term damage and dysfunction of the beta cells of pancreas, eyes (retinopathy and diabetic cataracts), kidneys (nephropathy), nerves (neuropathy), heart, and blood vessels (6, 7, 38, 86). Because its complications lead to blindness, amputations, and other debilitating conditions, diabetes has an enormous impact on the economy and productivity of both developed and developing nations. Health care costs

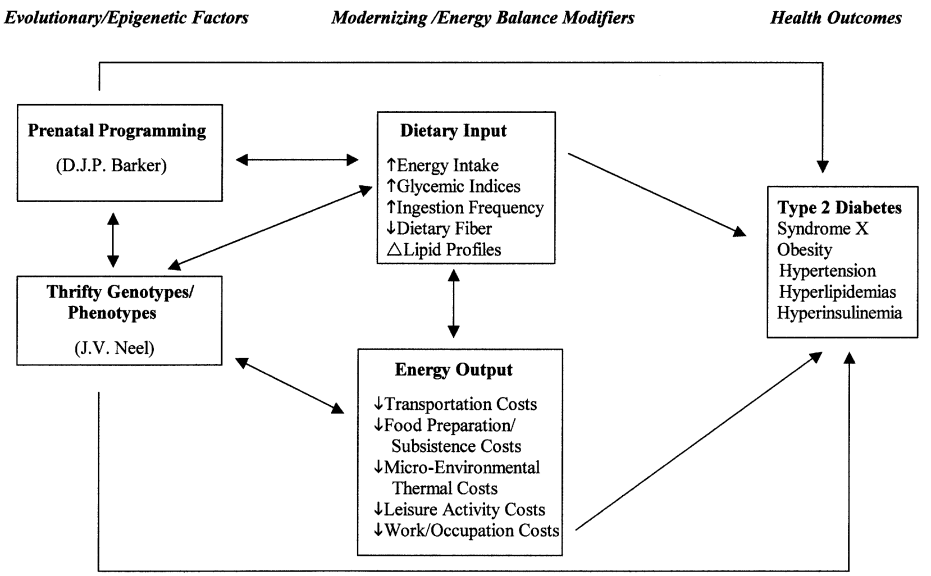

Figure 1 Evolutionary and modernizing influences on type 2 diabetes.

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for diabetes and its related disorders in the United States alone exceeded 100 billion dollars in 2002 (232). Among European Union countries diabetes and its comorbidities accounts for 5–10% of all health care costs (9).

The etiological classification of diabetes has three major subdivisions. Type 1 or juvenile diabetes is an autoimmune disease that destroys the beta cells of the pancreas and accounts for approximately 5% of diabetes worldwide. Type 2 or adult-onset diabetes is characterized by hyperinsulinemia in response to insulin resistance of the target tissues. It accounts for approximately 90% of diabetes worldwide and is often considered a "disease of modernization" since it occurs disproportionately among populations adopting a Westernized lifestyle (18, 21, 22, 30, 58, 77, 79, 98, 100, 128, 130, 131, 148, 170, 172, 190, 198, 235, 236). Obesity is the most significant risk factor for type 2 diabetes. Approximately 5–10% of diabetes is due to other causes that are often transient rather than chronic. These include gestational diabetes (2–5%), drug or chemically induced diabetes, genetic syndromes, infections, and other endocrine diseases. The current classification of diabetes lists more than 50 specific causes (7, 37, 38).

Worldwide Prevalence of Diabetes

DIABETES PREVALENCE AMONG ADULTS In 2000 the worldwide estimate was 151 million adults (4.6% of the 20–79 age group) with type 2 diabetes compared to 135 million in 1995 and 30 million in 1985. The projected global estimate is

for a doubling to 300 million by 2025 (90). Because higher energy intake and lower energy expenditures associated with modernization are having differential impacts on developed and developing countries, the 1995 to 2025 prevalence of type 2 diabetes in developing countries is expected to increase by 170% compared to 41% in developed countries (90). Approximately half of this increase will be Asian and Pacific Island populations. A prevalence increase of 68% is predicted for China, 59% for India, and 41% for other Asian and Pacific Island countries (100). The rise in prevalence of overweight and obesity parallels the diabetes trend (9, 10, 42, 45, 91, 107, 137, 138, 149, 201, 203, 212, 214, 217, 227–229). By comparison, the worldwide estimate for type 1 diabetes (4.9 million in 2000) is not expected to show a major increase.

The *Diabetes Atlas 2000* (90) contains estimates of diabetes prevalence for 5.5 billion people in 130 countries within the seven regions of the International Diabetes Federation. Paralleling rates of modernization, the lowest regional prevalence rates (1.2%) are in sub-Sahara Africa; the highest rates are in the Eastern Mediterranean, Middle East, and North America (7.8%). The United States has 16 million individuals with diabetes (38), with wide variation in prevalence among ethnic groups: 15.1% American Indian, 13% black, 10.2% Hispanic/Latino American, and 7.8% non-Hispanic white (86, 137, 138). The diabetes incidence rate in the United States increased by 30% from 1990 to 1998 (137, 138). The 16 countries with the highest prevalence rates are listed in Table 1. The countries with the largest numbers of adults with diabetes (in descending order) are India, China, United States, Pakistan, Japan, Indonesia, Mexico, Egypt, Brazil, and Italy (90). The first three countries account for nearly half of the world's population with diabetes, and the countries comprising the Western Pacific region account for another 44 million people with diabetes (90).

DIABETES PREVALENCE AMONG CHILDREN Modernization is driving the rising prevalence of obesity and type 2 diabetes among children and adolescents (48, 214, 215, 231). Studies among adults find a consistent relationship between obesity and economic development with a positive association in developing countries but a negative one in developed countries (193, 194, 197). The correlation is less consistent for children (214). Six million U.S. children (25%) are obese and one in four overweight children have impaired glucose tolerance (149). U.S. minority children from populations with high adult rates of type 2 diabetes (Native American, African American, Hispanic American, Pacific Islander) (6, 231, 236) are disproportionately affected. Type 2 diabetes was diagnosed in 4% of children in 1990 but 8–45% of children in ethnically diverse patient populations in 2001, of whom 85% were obese at the time of diagnosis (6, 231). This review argues that these trends are not surprising given the evolutionary selective factors that favor energy conservation in insecure dietary ecologies. Some of these once-favorable metabolic adaptations can be traced to our nonhuman primate and early hominid legacies.

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TABLE 1 Prevalence of diabetes (20–79 age group), top 10 countries

Country	Prevalence (%)
Papua, New Guinea	15.5
Mauritius	15.0
Bahrain	14.8
Mexico	14.2
Trinidad and Tobago	14.1
Barbados	13.2
Aruba	12.1
Bermuda	
British Virgin Islands	
Cayman Islands	
Grenada	
Hong Kong	
St. Kitts and Nevis	
Pakistan	11.8
Czech Republic	11.7
Tonga	11.5

Data from (90).

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EVOLUTIONARY TRENDS

Nonhuman Primates

Reconstruction of the diets of fossil primates and detailed analysis of contemporary nonhuman primate diets shed light on the primate dietary legacy that has shaped hominid evolution, including gut morphology, passage kinetics, dentition, body size, and physiology related to energy and nutrient utilization (134, 135, 179). Nonhuman primates primarily eat plants, with most fiber passing unchanged through the small intestine and some digested by cellulolytic bacteria in the hindgut. For example, a New World species—the Howler monkey (genus *Alouatta*)—has a diet of 50% leaves, 40% fruits, and 10% flowers. The diet averages about 88 gm/day fiber compared to most human consumption of 20–40 gm/day or less. These animals have a large colon with slow food passage. In contrast, the diet of the Spider monkey (genus *Ateles*) is three fourths fruit, and these animals have a small colon and short transit time. Higher energy intake allows for a day range approximately twice that of the Howler monkey. Although body weights are about the same (608 kg), the brain size of the Spider monkey is twice that of the Howler monkey (134).

Apes also eat a diversity of plants and plant parts: fruits, seeds, flowers, leaves, pith, bark, and roots. An exhaustive analysis of plant foods for gorillas, chimpanzees, and orangutans lists a mean of 94 (median 102, range 17–201) plant species per site (179). Some wild fruits and vegetables have higher micronutrient content than cultivated species (146). Diets of monkeys and apes are low in fat, comprising about 17% of the daily energy intake or about half that of contemporary human diets. Ratios of polyunsaturated (p) and saturated (s) fats vary from 1.0 p/s to 0.4 p/s. Protein is derived primarily from leaves, fruits, and flowers that are 6.5%–25% protein by crude dry weight (134).

The energy demands for chimpanzees are not as high as those estimated for early hominids or contemporary hunter-gatherers (Table 2). The relationship

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TABLE 2 Estimated physical activity levels of nonhuman primates, fossil hominids, and contemporary human populations

Population	Sex	Physical activity level
Chimpanzee	M	1.46
(*Pan troglodytes*)	F	1.36
Australopithecus (4–2.5 mya)	—	1.59
Homo habilis (2.5–1 mya)	—	1.70
Homo erectus (1.8–0.5 mya)	—	1.80
Early *Homo sapiens* (800,000–100,000)	—	1.80
!Kung (African)	M	1.7
hunter-gatherers	F	11.51
Ache (Paraguay)	M	2.08–2.15
hunter-gatherers	F	1.88
Igloolik (Canadian)	M	1.80–1.82
hunters	F	1.79–1.84
Asian Indians	M	1.56–1.96
rice cultivators	F	1.53–1.69
Filipinos	M	2.25
rice cultivators	F	—
Turkana (African)	M	1.29
pastoralists	F	1.37
Office workers	M	1.18
	F	1.16
Composite horticulturalist	M	1.87
	F	1.79
Composite agriculturalist	M	2.28
	F	2.31
Composite industrialist	M	2.38
	F	2.20

PAL = total daily energy expenditure/basal metabolic rate or total daily energy expenditure/resting metabolic rate. (Use of RMR gives slightly lower PALs than use of BMR). Mya = million years ago. Data from (44), (94), (119), and (184).

between body mass and basal energy requirements is well known and described by a power function between 0.67 and 0.75 [e.g., BMR = 70 $W^{0.75}$, where BMR = basal metabolic rate (kcal/d) and W = body mass (kg) (3, 105)]. Daily energy expenditures (DEE) are increased by moving, feeding, socializing, reproduction, growth, and other activities. There is a close relationship between body size and DEE (r = 0.995) for anthropoid apes and early hominids (3). These correlate well with reported calculations for the total energy expenditure (TEE) of early hominids in the work of Leonard & Robertson (r = 0.995) (119–121).

Milton (134, 135) concluded that nonhuman primate and early Plio-Pleistocene hominids are adapted to plant-based diets that show diversity, supply sufficient macro- and micronutrients and energy, are low in fat, and high in fiber.

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Paleonutrition: Early Hominid Diets and Lifeways

Nutritional anthropologists argue that reconstructing the evolution of human diet over the previous 4.5 million years since the origins of the earliest hominids is essential to understanding the current nutritional needs and adaptive and deleterious responses seen among contemporary human populations (59–63, 119). Paleocological and dietary reconstructions are based on findings of zooarchaeologists who study the remains of plants and animals and their archaeological context (175, 195, 196, 224), by bioarchaeologists who study bone mineral composition, density and stable isotopes related to diet (117, 187), and by paleoanthropologists who examine hominid and nonhominid primate dental and skeletal evidence of dietary choice, adequacy, and processing (8, 41, 112–114, 208). Furthermore, cultural and biological anthropologists contribute insights on the evolution of subsistence activities and dietary transitions by studying contemporary hunters and foragers (58–63, 94, 147). An omnivorous dietary niche involving hunting and foraging characterizes 90% of hominid evolution. Reconstructions of subsistence systems indicate a wide range of food resources, extensive seasonal variation, and high levels of energy expenditure (3, 43, 62, 147, 184, 196, 199, 207, 208).

Evolutionary trends of increased body and brain size, enhanced muscularity, and large fat depots influenced and were influenced by adaptations of ingestive, digestive, and assimilation processes. Food choices and attendant development of new subsistence strategies and technologies moved from monkey- and apelike diets of high-fiber/low-nutrient density to diets lower in dietary fiber, either through food selection or processing, and higher in nutrient density with greater bioavailability. More meat and animal products (e.g., bone marrow) were added to the diet of *Home habilis* and later hominids (61, 63, 94, 147).

Eaton et al. (61) have reconstructed Paleolithic diets. Fruits, roots, legumes, and other noncereals would have provided 65–70% of the subsistence base for preagricultural diets (34). O'Connell and colleagues (147) make a strong case for the importance of tubers, rhizomes, and bulbs. Both dietary reconstructions and contemporary ethnographies on hunting and foraging populations indicate a modal 65:35 plant-to-animal ratio (58–63, 94).

Estimated carbohydrate intake of ancestral humans and current populations in affluent nations is similar in magnitude, 45–50% of daily energy intake (12.58 MJ, 3000 kcal) (58–63). However, Paleolithic populations consumed vegetables and fruits whereas the major portion of carbohydrate starting in the early agricultural Neolithic was from cereal grains (8, 41, 63, 112–114).

Current recommendations are for 20–35% of total energy intake from dietary fat, with saturated fat accounting for 10% or less (70). Paleolithic diets contained an estimated 20–25% of energy from fat, and most of that was from unsaturated fats (63).

Paleolithic diets generally had a higher proportion of protein, with daily intakes ranging from 12% in more tropical areas to more than 30% of total caloric intake among northern latitude hunting and fishing groups (51, 69, 190, 207). With the exception of some northern latitude aquatic animals, wild animal meat generally has low fat content (2–4%). With a seasonal reliance on high-animal-protein/low-carbohydrate/moderate-fat diets (58–63, 195, 196), selection would favor efficient gluconeogenesis (44, 61, 156, 177).

Dietary fiber has long been viewed as a missing component in Westernized diets that leads to a range of recent pathologies (203). Studies of contemporary hunters-foragers and coprolites from prehistoric American archaeological sites indicate a fiber intake of as much as 100 grams/day (94, 115, 116, 199).

Because it is difficult to measure total daily energy expenditure under field conditions, much of the literature is based on extrapolations from resting metabolic rates, anthropometrics, time/task allocation data, and laboratory measurements (3, 94, 119–121, 205). Physical activity levels (PALs) are estimated for nonhuman primates, fossil hominids, and contemporary human populations with a range of subsistence systems (Table 2). Energy output for modern sedentary populations have been estimated to be 50–65% of estimated expenditures of a hunting-gathering lifestyle, although other estimates are not significantly different: 2,086 kcal/d for *Homo erectus* and *Homo sapiens* (3, 94). Trained individuals, as a model for ancestral humans, respond to a glucose load by secreting less insulin and have lower peak plasma glucose levels than do nonathletes (44). Acute exercise enhances glucose uptake by skeletal muscles and chronic training is associated with increased skeletal insulin sensitivity and reduced plasma insulin levels (44). Twentieth century hunter-gatherers, for example, the !Kung and Ache, have insulin sensitivity that is exceptional when compared to individuals living a Westernized lifestyle. When a group of urbanized Australian Aborigines temporarily converted to a foraging lifestyle, their serum insulin and glucose levels were reduced (148).

Neolithic Transitions in Diet and Lifeways

The adoption of agriculture and animal husbandry about 12,000 years ago in the Near East and North Africa and later in the New World (~4000 BC) created a dietary revolution with lasting effects on food consumption and disease ecology (60, 112–114). The major dietary changes were an increased reliance on high-carbohydrate cereal crops (i.e., rice, wheat, barley, maize) and tubers (i.e., potatoes,

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taro, cassava). A consequence was a reduction in the dietary breadth that had characterized both nonhuman and human foraging societies (57, 60, 112–114, 199). Grains contributed an estimated 40–90% of daily caloric intake. Dietary fat intake was low and contained a higher percentage of long chain polyunsaturated fats relative to contemporary diets. Pastoralists had higher intakes of animal protein and fat, but these populations were generally small and marginalized relative to agriculturalists (41, 87).

The advent of settled villages altered disease ecology, which created additional selective pressures, for example, malaria with selection for hemoglobin variants resistant to the *Plasmodia* pathogenic parasite. Diets with cyanide compounds proved to be helpful in moderating some of the deleterious effects of sickle-cell hemoglobin (92, 93). Analyses of skeletal materials document protein deficiencies and periodic food shortages that led to decreased infant growth, reduced adult stature and skeletal robusticity, increases in dental caries and enamel hypoplasia, nutritional anemias, and a host of other nutritionally related pathologies (8, 78, 112–114).

Modern diets have alleviated some of these conditions with increased dietary breadth, secure food supplies, and fortification of foods. However, modernization has created another set of deleterious conditions, whereby both dietary and exercise patterns play roles in the development of obesity and type 2 diabetes.

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Biological Legacy

NATURAL SELECTION FOR FATNESS AND FAT INFANTS The literature on genetic thriftiness has focused on selective pressures operating in adulthood. However, Kuzawa (110, 111) focuses on human infancy and early childhood supporting a strong selective advantage for a quick insulin trigger and enhanced fat storage with traditional morbidity and mortality patterns among infants. Epidemiological data indicate that individual differences in fatness contribute to differential survival during infancy through both the maintenance of fat stores and the ability to rapidly replenish lipid stores depleted through periodic, frequent bouts of infectious disease (153). Data from the World Bank (225) indicate that in many countries children are sick for approximately 60% of the first four years of life. Adipose tissue becomes an important energy resource during infection because disease disrupts appetite, digestion, absorption, and caretaker feeding behavior.

A relationship between initial weight-for-height and subsequent morbidity has been firmly established for most common childhood infectious diseases (110). Refeeding after starvation, respiratory illness, or diarrheal illness is accompanied by increases in insulin production. Furthermore, infants who are small for their gestational age demonstrate reduced glucose tolerance and are at risk for insulin resistance metabolic syndrome later in life (13–17, 24, 34, 39, 72, 82, 118, 129, 159, 171, 200, 230). Hediger and colleagues (88), using the National Health and Nutrition Examination Survey III data, show that infants in the lowest weight tercile relative to higher birth weight infants show catch-up weight gains favoring fat stores. These data suggest that nutritional insufficiency in utero forces the developing fetus into a "thrifty" mode of glucose sparing and efficient energy

storage. This version of the selection for fat-favoring thrifty genes is complemented by the Barker hypothesis of prenatal origins of later life diseases, including diabetes (110, 111).

TASTE AND FOOD PREFERENCES Psychophysiological and psychosocial factors influence dietary intake (12, 53, 126, 181, 183, 211). The preponderance of evidence indicates that taste is a main influence on food selection and has been influenced by evolutionary selective factors (20, 53, 99, 126). The hedonic or pleasurable component to taste with an innate liking for sweetness is demonstrated in utero and among neonates in their positive responses to lactose (56). Although there is a strong preference throughout life for sweetness, children have a preference for higher concentrations of sucrose in beverages and foods (44, 45, 110, 157–160, 184). Other components, such as aroma and textures, affect food choices and food habits (52, 176).

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Parent/offspring and twin studies suggest genetic components to food preferences and energy intake (23, 25, 157, 158). The Framingham Children's Study (150) demonstrated concordance between children and parents for saturated fatty acid and cholesterol intakes and there are greater similarities in food intake and preferences among monozygotic than dizygotic twins (25, 157, 158, 219). Perusse et al. (157, 158) suggest that about 20% of the variance in carbohydrate and fat intake is genetic, 10% is accounted for by shared culture, and 70% is nontransmissible as within individual variation.

Obese compared to lean individuals have shown few differences in preference, liking, and intake of sweets. Yet, some obese individuals have an elevated preference for foods high in fats, such as ice cream, chocolate, or pastries, in contrast to anorectic subjects who show a preference for sweet but not for fatty foods (53). Obese subjects with high compared to low weight fluctuations show an enhanced preference for sweet/fat mixtures (141). Evans & Foltin (65) report that obese women have a reduced sensory-specific satiety that leads to excessive consumption of sweet foods, possibly related to fewer brain dopamine receptors (186, 216). Furthermore, the thermic effect of food is blunted in some energetically efficient obese individuals (141, 189).

Preference for sugar increases with experimental acute hyperinsulinemia. However, the influence of chronic hyperglycemia on taste responses is not well documented (10, 165). Research is needed to elucidate the role of leptin and other newly discovered peptides in taste and consumption patterns among lean and obese people with diabetes (141).

Simply tasting (not swallowing) fat, either in cream cheese or peanut butter, increases insulin production and serum triglycerides. Such findings suggest that sensory receptors in the mouth initiate digestive responses not triggered directly by the nutrient and that the sensory qualities of fat may promote preference for fatty foods (148).

Anthropologist Abrams (1, 2) concludes that the hominid proclivity for sweetness conferred a selective advantage in nutritional quality and energy intake and

the avoidance of bitter foods containing toxic chemicals (176, 182, 183). Selection for sweet taste may be related to the ingestion of pharmacologically important micronutrients and nonnutritive compounds that influence metabolism (29, 99, 127). Jackson (92, 93) makes a strong case for the coevolution of domesticated plants, taste, and plant constituents related to disease. Only with the advent of processing foods such as sugar beets and sugar cane have sweet foods become abundant, inexpensive, and available year-round (136, 211).

The nutrition transition includes a preference for and increased consumption of dietary fats (54, 164–167, 169). The intakes of populations in both developed and developing countries converge on diets with 30–40% of calories derived from fat because of the global availability of inexpensive vegetable oils and fats (53, 54, 122, 123, 164–167). Preference for fat, in part, is the palatability it confers in foods, increasing creamy and smooth textures and adding juiciness to meats and moistness to baked goods (83, 84). Fat exposed to high temperatures creates desirable textures that are crispy and crunchy (53).

Harris (86) points out in *Good to Eat* that preferred foods tend to have higher concentrations of calories, fat, protein, vitamins, and minerals than nonpreferred foods. The preference for animal fat and protein has been well documented for traditional cuisines and for the addition of new foods to the diet (2). Baschetti (18, 19) hypothesizes that the increased prevalence of diabetes is due to the consumption of "genetically unknown foods." Western diets abound with evolutionarily recent high-fat and high-sucrose items that present a metabolic challenge to modernizing populations that retain genotypes and phenotypes adapted to low-fat/low-sucrose diets. The preference for high-protein/high-fat foods can be seen in the expansion of such franchises as McDonald's and Kentucky Fried Chicken. The expansion of ice cream, doughnut, and candy outlets provides foods to satisfy our evolutionary-based sweet/fat preferences (1, 2).

EVOLUTIONARY THEORIES AND DIABETES

Thrifty Genotypes

Forty years ago, geneticist J.V. Neel proposed a thrifty genotype for glucose utilization among Native American populations as an evolutionary explanation for their high prevalence of type 2 diabetes (143–145). He hypothesized that a feast-and-famine existence conferred a selective advantage and increased reproductive fitness for those individuals who had the ability to release insulin quickly, to thriftily store energy during times of food abundance, and to efficiently utilize energy depots during dietary deprivation (143–145). Shifts to modern lifestyles with increased food abundance, a lack of periodic food shortages, and a reduction in energy expenditure rendered a once adaptive genotype detrimental, leading to obesity and type 2 diabetes (130, 143–145, 151). Many authors have expanded on this hypothesis in other populations, adding other selective pressures: cold stress from water and long oceangoing voyages for Pacific Islanders (21, 22, 130, 131, 235, 236); extreme cold stress for Eskimo and Aleut populations (69, 190); reduced hunting

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success with unfamiliar animals for Paleoindians (221); and high seasonal energy demands during slavery for African Americans (76, 125). Recently Campbell & Cajigal (34) postulated selection for physiological mechanisms enhancing energetic efficiency of skeletal muscle, citing evidence for genes governing glucose transporters, mitochondria, leptin receptors, and uncoupling proteins.

Szathmary (198) and Ritenbaugh & Goodby (177) questioned the utility of the thrifty gene model for explaining high rates of diabetes in indigenous North American populations because diets of founding New World populations were high in protein and fat and low in carbohydrate. They hypothesize intense selection pressure for enhanced gluconeogenesis, not glucose uptake. This thriftiness for metabolic conversion is rendered disadvantageous by high-carbohydrate diets. Allen & Cheer (5) write of a nonthrifty genotype for a slow insulin trigger that would have conferred protection against diabetes and obesity in dietary environments with abundant carbohydrate and fat intakes. They suggest this was the case 10,000–12,000 years ago for some European and Near East populations, who transitioned from hunting/foraging to farming/dairying (56, 192). These populations also have a high rate of adult lactase sufficiency.

In conclusion, the thrifty genotype hypothesis does not fit all cases well, but it does raise the possibility of a strong genetic explanation for the high prevalence of type 2 diabetes for many populations in conjunction with other microevolutionary processes (e.g., founder effects for island populations) and recent dietary change.

In addition to carbohydrate utilization, there is evidence for thriftiness in the metabolism of other previously limited dietary constituents that have now become abundant (e.g., salt, cholesterol) and conversely, dietary constituents that were once abundant and now limited (e.g. dietary fiber) (29). Broadhurst (29) makes a case for the diabetogenic effects of reduced intakes of omega-3-polyunsaturated fatty acid (PUFA), chromium, plant phytochemicals, and fiber and increased intakes of omega-6-PUFA and saturated fatty acids in contemporary Western diets relative to Paleolithic and traditional diets.

NEW WORLD SYNDROME New World Syndrome (NWS), a collection of metabolic disorders with a higher prevalence rate among females compared to males, is characterized by type 2 diabetes, young adult obesity, high blood lipids, gallstones, and gallbladder cancer. Weiss and colleagues (219, 220) have hypothesized that NWS resulted from a combination of founder effect and selective pressures encountered in harsh arctic environments by the first New World immigrant populations. The epidemic of NWS has increased dramatically since World War II in populations with a high Native American genetic admixture. It shows familial aggregation. In some tribes, more than 20% of Native Americans have type 2 diabetes and more than 50% are obese (77, 86). The unique aspect of NWS is early-onset gallbladder disease with the formation of cholesterol gallstones. Bile salts are mutagenic but other mechanisms are also proposed for gallbladder cancer (219, 220). Both gallbladder disease and diabetes are indicative of inabilities to metabolize dietary energy sources, fats and carbohydrates, respectively.

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Syndrome X: Insulin Resistance Metabolic Syndrome

Gerald Reaven (173, 174) coined the term Syndrome X in an article on diabetes in 1988. Obesity, centripetal fat distribution, hypertension, dyslipidemia and glucose intolerance, insulin resistance, hyperinsulinemia, and other cardiovascular risk factors characterize Syndrome X. Many of these factors have high heritability (23, 25). Reaven argues that physical inactivity is also important in the decomposition of glucose tolerance (173, 174). Exercise reduces abdominal fat and improves insulin sensitivity by increased oxidative enzymes, glucose transporters (GLUT4), and capillarity in muscles (34, 39).

There is a fourfold variation in insulin-stimulated glucose uptake in individuals who are euglycemic, with approximately 25%–30% showing insulin resistance and hyperinsulinemia (71, 133, 173, 174). First-degree relatives of diabetics who remain euglycemic show impaired glucose tolerance and insulin resistance.

High-carbohydrate diets lead to increases in ambient plasma insulin and triglyceride concentrations and are significantly correlated with the development of hyperinsulinemia. Dietary fats also modify insulin release and insulin action in skeletal muscle (34). Modernization of diets includes both increases in fat intake and novel fatty acid profiles of foods that alter membrane sensitivity to insulin, postreceptor metabolism of glucose and may have a pacemaker role in the overall metabolic activity of the body (34).

Epidemiological studies indicate that individuals with the highest risk for Syndrome X have low birth weight, high adult weight, and large fat mass (13–17, 82). Individuals with low birth weight who maintain low adult weights are at low risk for the development of Syndrome X. In contrast, high birth weight infants who maintain a low adult weight are also at low risk while those who have high BMIs in adulthood are at moderate risk for the development of Syndrome X (Table 3).

Prenatal Phenotypic Programming

David Barker, a British epidemiologist, has worked with collaborators since the early 1980s to develop the theory of fetal origins or prenatal programming of later life diseases based on in utero nutritional deficiencies. His initial observation was that low birth weight (LBW) infants had an increased risk for coronary heart disease, stroke, type 2 diabetes, insulin resistance, increased blood pressure,

TABLE 3 Relative risk of Syndrome X

Birth weight	Adult weight	Risk
Low birth weight	Low adult weight	Low risk
Low birth weight	High adult weight	Very high risk
High birth weight	Low adult weight	Low risk
High birth weight	High adult weight	Moderate risk

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hyperlipidemias, increased fibrinogens, or Syndrome X (13–17). He hypothesized that Syndrome X originates through fetal adaptations to undernutrition. These adaptations alter growth trajectories or programming at the expense of tissue development and physiological processes. Nutrient demand and supply vary depending on a number of factors, including maternal body composition, maternal dietary intake, placental blood flow, and the fetal genome. The fetus mediates hypoxic, metabolic, and endocrine changes (7, 67, 82, 86, 97). Some changes lead to glucose intolerance, insulin resistance, and an abnormal partitioning of energy substrates (72, 118). As adults, thin babies have a high prevalence of insulin resistance and type 2 diabetes; short babies, especially in relation to head circumference, have a higher prevalence of low density lipoprotein and plasma fibrinogen concentrations. Short and fat babies have a high prevalence of insulin deficiency and type 2 diabetes (13–17, 24, 72, 174, 230). Barker postulates that LBW babies have metabolically thrifty mechanisms for fat storage and glucose sparing with reduced rates of glucose oxidation in insulin-sensitive target tissues (110, 111). In addition, catabolic steroids rise with undernutrition, limiting lean body mass. For high birth weight infants, exposure in utero to excess glucose levels may down regulate receptors producing thriftiness for lipid utilization (210).

There is now extensive epidemiological support for Barker's hypothesis (13, 14), showing a robust correlation for LBW and for small body size with deleterious health outcomes later in life for such diverse groups as British men (82), American men (46), Mexican Americans in Texas (209), Asian Indian immigrants to England (170), and Pima Indians in Arizona (85, 172). However, the hypothesis has been challenged because mechanisms other than maternal nutritional status could account for LBW and other early life events confer risk for Syndrome X (72, 85, 162, 171). For example, the major increase in pancreas size occurs in the twelfth fetal week through the fifth postnatal month and LBW is associated with fewer islet cells (162).

Recent studies have identified two different candidate genes related to infant growth and insulin. The insulin gene VNTR3/3 genotype promotes fetal growth and could enhance infant survival. In contrast, a maternally inherited 16189-mitochondrial DNA variant is associated with restrained fetal growth and may enhance the likelihood of maternal survival. Both genotypes are associated with increased risk of adult type 2 diabetes (151). The glucokinase knock out mutation in mice leads to significantly smaller birth weights and impaired insulin response to glucose altering fetal growth and postnatal glucose metabolism (200).

In summary, associations between LBW, small body size, thinness, and type 2 diabetes have been repeatedly demonstrated. Size relationships are particularly strong because insulin resistance is programmed in late gestation, when disproportionate fetal growth is manifest. Consequently, those populations with a high prevalence of LBW infants are most at risk for the development of diabesity when they adopt Westernized diets and lifestyles. Additionally, glucose metabolism may be programmed by nutritional influences that do not alter birth weight. Barker calls for early life interventions to limit later life chronic disease (14).

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MODERNIZATION OF DIETS AND NEW FOOD SYSTEMS

Modernization Defined

Barry Popkin (164–167) has developed a comprehensive model of the nutritional transition. Modern societies across the globe are converging on a dietary pattern that is high in saturated fat, sugar, and refined foods and low in dietary fiber. Initiated earlier was the demographic transition from high fertility/high mortality to low fertility/low mortality and increased longevity that is typical of modern and industrialized nations. Modernizing populations also exhibit epidemiological transitions with infectious disease, famine, and poor sanitation replaced by a secure food supply, better sanitation, and an increasing prevalence of chronic and degenerative diseases.

The nutrition transition has been defined in five broad patterns. The first pattern is that of food collection that characterized 98% of hominid existence with hunting and foraging. In the second pattern diets became less varied and there were episodic periods in which there was extreme food shortage. This pattern of famine accompanied the advent of agriculture. These patterns are described above. Popkin suggests that in this phase social stratification began to appear and some segments of the population were more favored nutritionally than others.

In pattern three the famine began to recede and there was a resumption of the consumption of more fruits, vegetables, and animal protein as starches became less important in early civilizations. Dietary problems continued with undernutrition of children. Pattern three is characterized by increased agricultural productivity and the advent of the industrial revolution. Technological advances were labor saving and cooking technologies broadened the dietary breath.

Pattern four involves a major dietary shift to increased animal fat, sugar, and processed foods. Pattern four is most commonly seen among contemporary, Westernized societies, where few jobs involve physical activity and there is mechanized transportation and labor-saving household technologies. Pattern four is characterized by problems of overweight or obesity and degenerative diseases. Life expectancy is high, fertility low, population density high, and chronic diseases are related to diet and inactivity.

Pattern five focuses on behavioral changes, a reduction in dietary fat and processed foods, and an increased intake of complex carbohydrates, fruits, and vegetables. Individuals focus on a reduction of body fat and improve overall health. Leisure exercise grows to offset sedentary jobs. Life expectancy continues to rise and there is a decline in coronary heart disease and improvement in age-specific chronic disease profiles. In pattern five there is a return to lower density population concentrations.

Popkin has provided numerous examples of these transitions with regard to economic shifts in China, Thailand, India, Latin America, and the Caribbean (164). He observed that developing nations are now faced with problems of both under- and overnutrition, yet lack the public health capabilities of addressing these issues

(188, 204). For example, supplemental feeding programs in Chile have led to stunted children who are overweight (11).

In light of Popkin's historical and cultural transitions, the epidemic of obesity and type 2 diabetes can best be understood using an evolutionary focus with genetic and epigenetic factors selected for once-adaptive genetic complexes and phenotypes related to energy metabolism (Figure 1). These traits become disadvantaged with modernization and the adoption of Western economic systems and cultural traits leading to a surfeit of energy intake and a deficit of energy expenditure.

Energetics—Output

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MOVEMENT TRANSPORTATION AND ENERGY COSTS Human energy capture, conversion, and utilization are fundamental to human existence, show individual and population variability, and are amenable to a wide range of adjustments (64, 152, 205). As noted above, humans have an array of adaptive metabolic, morphological, and behavioral strategies to conserve energy expenditure. Thermogenic mechanisms are particularly important in cold climates (101, 178). For example, with undernutrition in childhood there is evidence of an increase in mechanical efficiency of muscle (191) related to the development of relatively more slow-twitch muscle fibers with increased contraction-coupling efficiency. This occurs under conditions of hypothyroidism (218). Behaviorally, humans adjust their walking and running gates to minimize the metabolic costs of locomotion and prefer speeds that minimize energy cost per unit distance (4). At speeds of up to two miles per hour, walking requires less energy than running. At higher speeds running is more economical. Energy costs are also increased by carrying heavy loads and modified by how the load is carried (e.g., on the back, head, or shoulders) (4). Classic work by Passmore & Durnin (152) calculated that walking accounted for 20% of the weekly energy expenditure for a clerk but 27% for a miner (9 hours versus 21 hours). Traditional Kung! San foragers of Botswana also walk about 9 hours a week (115, 116). Estimates are that increasing physical activity by walking an additional mile each day, and thereby expending an additional 100 kcal, theoretically would make a significant contribution to weight control for Americans.

By contrast, the increase in the number of motor vehicles worldwide is rapidly accelerating from 580 million in 1990 to a projected 816 million in 2010. There is increased availability of public forms of transportation (i.e., trains, buses, taxis) that service both urban areas and wider metropolitan and rural areas (66, 213). The modernizing forces that influence changes in transportation are: increasing population size and density, increasing incomes, decreasing car prices, increasing leisure time, prestige of vehicle ownership, and political and marketing factors (66).

FOOD PRODUCTION AND SUBSISTENCE ENERGY COSTS Subsistence activities are costly in terms of energy expenditure. Anthropologists have produced accurate time-task energy budgets for a number of different subsistence activities for populations around the world. Table 2 indicates the physical activity level (PAL) for human and nonhuman primates, fossil hominids, and contemporary human populations. Contemporary populations engaged in traditional maize, rice, and wheat

cultivation as well as those still engaged in hunting/gathering exceed energy expenditures relative to fossil hominids, contemporary nonhominids, and Westernized populations. In contrast, some populations using the same cultivars (e.g., rice) have significantly lower PALs, for example Filipino rice cultivators (PAL = 225) versus Indian rice cultivators (PAL = 156). Ulijaszek & Strickland (206, 207) note that small seasonal imbalances between intakes and expenditure are important. For example, Gambian traditional farmers average a seasonal loss of 2.4 kg in body weight with a negative energy balance of approximately 100 kcal/day.

Modernization has led to a rapid shift in occupation structure, reductions in energy expenditures, and the elimination of seasonal weight fluctuations in populations in developing countries with a marked decline in the percentage engaged in agricultural labor and a concomitant increase in the numbers in manufacturing and service sectors of the economy. This shift is facilitated by population migration to urban areas and the mechanization of agriculture (164–167, 222).

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Foods—Input

DIVERSITY AND GLOBALIZATION World food systems are being transformed by delocalization and dissemination of domesticated plant and animal varieties, international food distribution networks, the growth of food processing industries, and the migration of people who exchange foods, recipes, and cooking techniques (54, 124, 154, 167). The result is an increase in the diversity and quantity of food made available through governmental and commercial channels. Dietary acculturation alters ethnic food items to improve palatability and incorporate them into an increasingly diverse cuisine. Diets in transition involve substitution and supplementation as well as modification of existing dietary items and processing techniques (109, 124).

These processes may lead to losses in micronutrients and nonnutritive substances that affect energy metabolism and disease risk (109). The added costs of processing, packaging, advertising, and shipping may limit access to new foods for low-income segments of populations.

However, rapid globalization of fast food franchises is increasing both availability and affordability of energy-dense, high-fat foods. For example, the Coca Cola 2000 annual report (40) indicated that the worldwide unit case (24 8-oz. servings) volume was 17.1 billion, accounting for nonalcoholic drink market sales of 30% for North American, 26% Latin American, 21% European and Eurasian, 16% Asian Pacific, and 7% African and the Middle Eastern. Growth in sales in China and the Philippines outstripped other nations.

In 2001 Haagen Dazs ice cream franchises were in more than 55 countries, with more than 800 outlets (81). Kentucky Fried Chicken had 5231 outlets in the United States and 5595 outlets outside the United States, with 290,000 employees and worldwide sales of $8.9 billion and in 2001 (102). Pizza Hut is the world's largest pizza chain, with nearly 12,000 units and kiosks in more than 88 countries serving more than 1.7 million pizzas a day to four million customers. Highest volume Pizza Hut restaurants are in Paris, Moscow, and Hong Kong. Pizza Hut is part of the world's largest restaurant group, Tricon Food Service, which includes Taco

Bell and Kentucky Fried Chicken (140, 161). Dunkin Donuts, with 52 varieties of doughnuts, has 5000 locations in the United States and 40 other countries and daily sells 6.4 million doughnuts and 1.5 million cups of coffee to two million customers. On an annual basis, Dunkin Donuts sells 2.3 billion doughnuts and 650 million cups of coffee. In 2000, it opened its five-thousandth shop in Bali, Indonesia. From 1998 through 2000 Dunkin Donuts experienced a 25% sales growth (55).

Capitalizing on increasing world affluence, these corporations pursue global strategies introducing desirable Western dietary icons appealing to innate likings for sweetness and fat. For example, Japan has been an extraordinary market for U.S. fast food franchises: Haagen Dazs ice cream, Famous Amos cookies, Denny's, Mr. Donuts, Dunkin' Donuts, Wendy's, Kentucky Fried Chicken, and Domino's Pizza. Japan imports California wines and Coca-Cola is Japan's best-selling soft drink. Japanese children report that their favorite foods are hamburgers, spaghetti, French fries, and ice cream (140).

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SUPERSIZING FOODS Americans who value getting more for less and convenience are experiencing another diabesity trend. Since the 1990s fast food franchises have been supersizing drinks, French fries, and hamburgers. Advertising promotes these larger sizes and low per-unit costs make them highly desirable. The traditional McDonald's meal containing a hamburger, small French fries, and 16-ounce soft drink has 627 calories and 19 grams of fat. The McDonald's Big Extra with cheese, supersized soft drink, and French fries has 1805 calories and 84 grams of fat. One fast-food chain now dispenses a 64-ounce serving of soda containing 768 calories, which represents a 45% size increase. Candy bars have tripled in size since the 1970s, and in movie theaters, an extra-large popcorn with butter-flavored topping contains 1600 calories (122, 123). These foods tend to be eaten quickly and consumed completely so purchasing larger sizes increases consumption (180, 181).

PATTERNS OF FOOD INGESTION The confluence of many Westernizing factors has led to worldwide increases in both fat and sugar consumption (54, 136, 164, 167). For example, U.S. trends dating from the 1970s through 1990s show sweetener consumption—including sugar, corn syrup, and dextrose—has increased from 120 to more than 160 pounds/person/year (122). Driving the increase has been sweetened beverage consumption (35 gallons/person in 1980 to 53 gallons/person in 1997) and increased sizes of restaurant portions of ice cream and desserts. Increases in fat intake are attributable, in part, to increased consumption of fast foods. In addition, cheese intake has increased from 18 to 28 pounds/person from 1980 to 1997 and rivals ground beef as the largest contributor of saturated fat in the U.S. diet. Per capita chicken consumption was 50 pounds in 1998, primarily due to the popularity of fast-food fried chicken. Total added fat intake increased from 57 to 66 pounds/person from 1980 to 1997.

Furthermore, consumption of high-glycemic foods has also increased. Americans were consuming 110 pounds of white and whole wheat flour per person in

1980, 138 pounds in 1997, and more than 200 pounds/person of total flour and grains for the same year. Much of the increase is attributed to the consumption of prepared and prepackaged pastries, pizza, and other bakery products (36).

Overall these dietary trends indicate an increase in the total per pound consumption of foods and in the caloric density of foods. At the same time, the energy costs of obtaining food have decreased because of the availability of drive-in and pick-up restaurants, home delivery services, and the minimal preparation time required for meals prepared at home.

Popkin (164–167) and others (21, 22, 98, 131, 148, 155, 233, 234) have detailed recent dietary trends in increases in consumption of meat, milk, fish, oil, and sugar in developed and developing countries. The onset and rapidity of these obesiogenic and diabetogenic trends vary and generally have a greater impact on urban populations (9, 10, 33, 36).

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GLYCEMIC INDEX In addition to increased intakes, the metabolic impact of modern diets has changed and now favors an increased consumption of high glycemic index (GI) foods that demand enhanced insulin responses (73, 95, 96). Traditional low GI foods include peanuts, lentils, legumes, and dairy products. Traditional preparation techniques also lower the GIs of foods. High GI foods include refined cereals, breads, and starchy root vegetables. Dietary fat decreases the GI and acts as a countervailing trend in Western diets.

The glycemic index is defined as the incremental area under the two-hour blood glucose curve produced by a standard amount of carbohydrate in a food (usually 50 g) relative to the incremental area produced by a standard of either glucose or white bread (223). Because the amount of carbohydrate in a food or diet will vary, the concept of a glycemic load (GL), or the amount of carbohydrate multiplied by its GI, is used to describe diets and risks for chronic conditions and diseases (26, 76, 95, 160, 223). Numerous factors affect the amount and bioavailability of carbohydrate in food, and hence, the GI. These include fiber, fat, and protein content, heating and cooling, cooking techniques, fermentation, altering particle size, and the ripeness of fruit. GI and GL are affected by the rate of food ingestion, the mix of foods with varying GIs in test meals, and the GL of prior meals. In addition, characteristics of the individual affecting GIs include insulin resistance, prior plasma glucose levels, adiposity, fat distribution, physical activity, sex, and age (160). High GIs and GLs of diets and specific foods (e.g., white bread, soft drinks, French fries) have been linked to diabetes (223), cardiovascular disease (96), and obesity (26). Jenkins et al. (96) suggest that low GI foods result in slower absorption of glucose from the small intestine, thereby reducing acute insulin demands, avoiding wide excursion in plasma glucose levels, altering the partitioning of energy utilization favoring greater use of fat stores, and possibly prolonging satiety. Experimentally, weight loss is favorably affected by low GI diets as compared to isoenergetic high GI diets (26).

However, Pi-Sunyer (160) has noted that GI-related variables in foods are often not controlled for in clinical, experimental, or epidemiological studies and that

many studies have small or biased samples and research design flaws. He has called into question the research results and interpretations linking high GIs and GLs to enhanced risk for type 2 diabetes, obesity, and cardiovascular disease. Because no long-term results are available, Pi-Sunyer (160) has questioned the utility of focusing on the GI as a strategy to curb worldwide obesity and diabetes (232–234).

CONSEQUENCES OF POSITIVE ENERGY BALANCE

Adipose Tissue, Obesity, and Type 2 Diabetes in Adults

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The regulation of energy stores is acutely sensitive and has been selected for under very different conditions than those of our contemporary dietary ecology. Bray (27, 28) calculated that the "average" nonobese American male consumes approximately one million kcal a year. Yet a small 10% alteration in either intake or output can lead to a (13.6 kg, or 30 pound) change in body weight in a single year. If an individual gains 11 kg (24 pounds) of weight during a 40-year time span, the mean daily discrepancy between intake and expenditure is only 5 kcal/day. The National Health and Nutrition Examination Survey (NHANES) suggests a higher weight gain among young adults of nearly one kg per year (107). Individual differences in energy intake, utilization, and output are not well understood. Cross-sectional studies have found that obese individuals have high, normal, or even low energy intakes relative to normal weight subjects and that there is a poor correlation between daily energy intakes and expenditures (64, 142). Bouchard and colleagues in the 1980s and 1990s demonstrated a wide variation among twin pairs in energy expended as heat when they were overfed (23–25). Approximately one third of the variance was genetic. In the last decade it has been demonstrated that energy balance involves the complex interaction of several regulatory enzymes, neurotransmitters (e.g., neuropeptide Y), and hormones (e.g., leptin, ghrelin) acting on central nervous system mechanisms of hunger, satiety, and metabolism. Fat stores turn over slowly and a high-fat diet increases fat oxidation and preservation of carbohydrates stores to promote the stabilization of hunger and increase satiety signals. These mechanisms should limit fat and energy intake but overconsumption of high-fat diets increases fat stores, in part because of low energy expenditure (28, 89).

More than 80% of new cases of type 2 diabetes are associated with obesity. This association has been demonstrated in many populations and in many age groups worldwide. Women with a BMI $\geq$ 33 kg/m^2 have a risk that is 60 times greater than lean subjects of developing type 2 diabetes. Men with a BMI $\geq$ 35 kg/m^2 have a risk that is 40 times great than lean subjects of developing diabetes. Type 2 diabetes risk correlates with the degree of adiposity, duration of obesity, and distribution of body fat. The anatomical location of adipose depots shows differences in metabolic activity as measured by change in size of the depot, rate of the lipid turnover, and

glycolytic enzyme activity (163). A centripetal distribution of body fat is associated with a high intra-abdominal fat depot and is an independent and significant risk factor for the development of type 2 diabetes and other features of Syndrome X (173, 174). Furthermore, stunting and low birth weight leads to the selective accumulation of abdominal fat (188).

The adaptive role of adipose tissue in reproduction has been explored by a number of authors attributing sex differences in the distribution and abundance of adipose tissue to energy needs during pregnancy and breast-feeding (74, 75). A number of studies indicate a preference for females who have abundant adipose stores (31, 32, 35). In Helsinki, children with mothers who had a high body mass index in pregnancy had more rapid postnatal growth and an increased incidence of type 2 diabetes (72). Obese, diabetic mothers confer an increased risk for their offspring of early onset insulin resistance and type 2 diabetes (68, 172). In contrast, in rapidly modernizing China with populations more recently subjected to dietary privation, low maternal body mass in early and late pregnancy were associated with elevated levels of plasma glucose, insulin, and triglycerides in infants (97). Diet, body composition, and weight affect other areas of reproductive success, including age of onset of menarche, birth intervals, seasonality of birth, and birth weight. These variables directly impact the evolution of populations and selection for thrifty genes.

Worldwide the estimated number of individuals who are obese exceeds 1 billion (32) and an estimated 300,000 Americans die prematurely each year as a result of being overweight. Adult overweight and obesity has increased 50% between 1980 and 1994 among Americans, with 61% classified as overweight. The World Health Organization (WHO) (227–229) regional estimates for the percent of adults 45–59 years of age who are overweight are (for females and males, respectively): Europe 70%, 60%; North American 62%, 62%; Western Pacific 32%, 32%; South and East Africa 50%, 18%; Latin America 58%, 50%. The estimate for China is 15%. Diabesity is the usual phenomena but among some Asian populations increasing body weights within normal ranges are associated with type 2 diabetes. The WHO has suggested lower BMI risk levels for these populations (227–229).

Obesity underlies the rapidly increasing prevalence of type 2 diabetes among children. Obesity in children and adolescence is reaching epidemic proportions (108, 149, 168, 217, 231). Data for children 6–18 years of age from national surveys in the United States, China, and Russia were completed in the late 1980s to early 1990s. The reference BMIs of the U.S. National Center for Health Statistics defined obesity as $\geq$95th percentile and overweight as $\geq$85th percentile (227–229). The prevalence of obesity and overweight was 11.1% and 14.3% in the United States, 6.0% and 10.0% in Russia and 3.6% and 3.4% in China. Childhood obesity was more prevalent among higher socioeconomic level subpopulations in China and Russia but among lower socioeconomic strata in the United States. Obesity is concentrated in the cities as urbanized people adopt Western diets and sedentary lifestyles. For example, in the Congo, obesity is six times higher in the cities.

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Adipose Tissue, Obesity, and Type 2 Diabetes in Children

Based on cross-sectional data from 94 countries, the prevalence for overweight among preschool age children was 3.3%, with highest prevalences in the Middle East, North Africa, and Latin America (48). The WHO estimate is 22 million children under age five who are overweight. The prevalence of child obesity and overweight has doubled in North America over the past two decades. Nearly one fourth of the children in the United States are obese or overweight (176), and a disproportionate number of minority children are affected (202). In many transitional populations there is a more rapid rise in childhood obesity. In Thailand the prevalence of obesity in schoolchildren increased from 12% in 1991 to 16% in 1993 (139).

The probability that children with high BMIs will still be overweight and obese in adulthood increases markedly throughout childhood (50, 80). Although the etiology is complex, television watching time and the use of computer games has significantly reduced energy expenditure and is positively related to weight gain (48, 49, 132, 204). However, at least one study among Pima children suggests that a decrease in PAL follows the development of obesity (172, 185). U.S. adults who maintain a significant weight loss (13.6 kg for at least five years) do so with extraordinary effort and a mean energy expenditure of 11,830 kcal/week (106). In sum, the obesity epidemic is the precursor of the type 2 diabetes epidemic, with both stemming from evolutionary roots favoring metabolic mechanisms for energy conservation. These mechanisms are deleterious when lifestyles and diets promote chronic energy surfeits (33, 232, 234).

SUMMARY

This article has presented a case for an evolutionary perspective on the development of the current epidemic of type 2 diabetes and comorbidities associated with Syndrome X. Incidence and prevalence data indicate an acceleration of type 2 diabetes in both developed and especially developing countries as they adopt Popkin's pattern four demographic, epidemiological, and nutritional transition characteristics. Selection for metabolically thrifty genotypes and phenotypes starting prenatally and continuing throughout life presented an advantageous pattern for nonhuman primates, our fossil ancestors, and humans for 98% of our existence. Both genetic energetic thriftiness and prenatal programming, an adaptive response of the fetus to reduced nutrient availability, were efficacious in a postnatal environment with chronic or periodically limited dietary energy sources or high-energy demands. Both conditions changed with modernization and the advent of calorically dense/low fiber/high glycemic abundant diets and sedentary lifestyles. Culture-specific public health programs that target both decreases in energy intake and increases in energy expenditure as well as the elimination of low birth weight infants are needed to alter the modern obesiogenic and diabetogenic environments of globalized economies.

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