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Non-Insulin-Dependent Diabetes Mellitus Among American Indians: A Problem in Human Ecology

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THE NATURE OF THE PROBLEM

Diabetes mellitus among American Indians is not only a major health problem and a challenge to physicians and epidemiologists but represents an opportunity for anthropologists and population geneticists to help in understanding why such a detrimental disease has persisted in human populations and increased its incidence dramatically during the past fifty years. For a variety of reasons, susceptibility appears to be uniquely high among selected North American Indian groups, despite the fact that early in this century diabetes was virtually unknown among these populations. At the same time, other Indians exhibit rates of diabetes that are lower than the average rates for Caucasians. These variations lead to questions concerning both the factors that contribute to the onset of diabetes as well as to more fundamental issues involving Indian origins and their adaptations to different environments. The purpose

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of this paper is to examine what is known about the problem and suggest general directions for further inquiry.

It should be stated at the outset that this article is in the limited nature of a review rather than a detailed epidemiological study. To the extent that there are broader, and arguably related, issues involving poverty, the exposure to environmental pollutants, and malnutrition among Indians, they are not addressed directly. This omission does not speak to their lack of relevance but is, on the contrary, in recognition of their significance. Each one of those issues is sufficiently complex to be the subject of additional studies that extend far beyond the bounded scope of the present effort. In addition, and despite the obvious needs, this paper is not intended to provide a blueprint for specific action. It is an oft repeated truism that diabetes is a multidimensional problem and there are a variety of preventive and palliative treatments available. By outlining what is known about this condition and why susceptibility appears much greater among Indians than among other groups, this article can contribute to the process of specifying the most effective approaches to predicting and ultimately eliminating the disease.

Diabetes mellitus is not a single disease but is more accurately described as encompassing a variety of syndromes in which the body's ability to metabolize food efficiently is disrupted. Over time, the disruptions cause problems within cardiovascular, neurological, and metabolic systems[1] and may involve eyes, kidneys, and feet as well as other organ systems.[2] There are two fundamental types of diabetes: Type I or insulin-dependent diabetes mellitus (IDDM) and Type II or non-insulin-dependent diabetes mellitus (NIDDM). Some commentators have noted limitations inherent in this simplified categorization,[3] but for the purposes of this review this classification scheme will be used. IDDM is an auto-immune disease which accounts for approximately 10 percent to 25 percent of all diabetes cases in the United States and generally appears by adolescence or early adulthood.[4] This condition is closely associated with genetic mutations in the human leukocyte blood group (HLA) system, which is also associated with a number of other diseases. Despite its seriousness, the scope and effects of IDDM will not be reviewed. The nature of that disease is such that prior to the development of insulin therapy, it constituted a reproductive handicap because many of those who developed IDDM never lived long enough to have children. In other

words, there is no selective advantage (i.e., anything that contributes to one's ability to successfully reproduce) in having one's insulin-producing cells in the pancreas destroyed by one's own immune system. In addition, IDDM occurs primarily as the result of an inherited genetic defect and does not appear to be environmentally induced.

Type II, or non-insulin-dependent diabetes mellitus (NIDDM), represents an entirely different disorder that is not characterized by the absence of insulin production per se, but by a failure of insulin to perform its metabolic functions properly. The pathophysiology of NIDDM is complicated, involving both genetic and environmental variables,[5] and while its biochemical elucidation is outside the confines of this article, some aspects of NIDDM etiology should be appreciated in order to postulate ideas about why Indians are so susceptible. McGarry[6] reviews several theories concerning NIDDM development and concludes that the disease arises from some type of abnormal fat metabolism rather than from abnormal sugar metabolism. The difference is important because the persistence of NIDDM within Indian populations suggests that at some point in the distant past, the presence of this particular genetic composition (genotype) may have conferred a selective advantage. If one approaches the problem from the perspective of how the human body breaks down and utilizes dietary fat (lipid metabolism), the ideas concerning the adaptation for which this genotype was initially selected will be very different from those which approach the problem from the perspective of the breakdown and utilization of carbohydrates (glucose metabolism). Stated in another way, it makes a difference whether the underlying genetic composition evolved in a lipid-rich, carbohydrate-poor environment, such as the Arctic or sub-Arctic regions where food energy is secured primarily through animal protein, as opposed to a carbohydrate-rich, lipid-poor environment, such as tropical or subtropical environments in which the consumption of plant materials predominates. A related concept is that of "insulin resistance," a condition that may be maintained in varying degrees by up to 25 percent of non-diabetic Americans. Insulin resistance refers to the overproduction of insulin by pancreatic cells in response to the consumption of carbohydrates (sugars and starches) which ultimately become converted to body fat.[7] Not everyone who exhibits insulin resistance develops NIDDM, but the fact that a significant number do strengthens the links between obesity and diabetes

that have been clinically observed and underlines the fact that insulin resistance characterizes many groups at risk for NIDDM.[8,9]

NIDDM occurs in epidemic proportions among some Native Americans and a plethora of studies have documented the increased susceptibility of Indians relative to Caucasians and admixed groups such as Mexicans and Caribbean Islanders.[10,11] When considering disease frequency in populations, a distinction is made between the measurement of *prevalence* and *incidence*.

> Prevalence, or the fraction of the population with a disease at a certain point in time, is computed by dividing the number of people with the disease by the total number of people in the population. Incidence, or the rate at which new cases of disease develop over time, is computed as the number of cases developing during a period of time divided by the person-years at risk of the disease (i.e., the sum of time at risk for all susceptible people in the population).[12]

Published data also reveal tremendous variations in NIDDM prevalence among Indian tribal groupings.[13,14,15] Weiss and others[16] compiled several studies comparing diabetes prevalence among Indians, Hispanics, and non-Hispanic Caucasians. The authors found that some Indians exhibit prevalence rates which exceed those of Caucasians by a factor of 10, but the difference between the highest Caucasian and lowest Indian rate (4.2 to 8.3 percent) is substantially less than the differences between the lowest and highest Indian rates (8.3 to 39 percent). These data suggest that either differentially selective forces have been operating upon a single Indian genotype for NIDDM susceptibility or that there are several different, albeit similar, genotypes that have become fixed within Indian populations. Another possible explanation for intertribal prevalence variabilities may be that some Indian groups, particularly eastern tribes, have received substantial infusions of non-Indian genes, thus reducing their susceptibility relative to other Indians through the process of admixture.

The Seminole represent an intriguing case, as that tribe did not exist until the eighteenth century when refugees from the dissolving Creek Confederacy, together with runaway slaves, convicts, and indentured servants, moved into south central Florida and possibly mixed with groups of indigenous inhabi-

tants. Following the Seminole Wars of the 1830s and 1850s, most Seminoles were forcibly relocated to Oklahoma, although a remnant population remained in the Everglades. Despite their common origins, the Florida group exhibits a prevalence rate for NIDDM that is approximately 30 percent less than that of the Oklahoma group.[17, 18] A conceivable explanation is that the original Seminoles constituted more of an admixture of genetic heritages, including both African and Caucasian genes, and have refrained from contact with other groups until recent times, while the Oklahoma Seminoles mixed with numerous other tribes and have actually become genotypically "more Indian" over the past 150 years. This possibility is strengthened by a recent study of the Eastern Band of Cherokee Indians.[19] Not only was the overall prevalence of diabetes within that group discovered to be four times greater than the average U.S. rate, but the highest rates were found among those individuals having the highest percentage of Indian inheritance. Similar conclusions have been reached in connection with studies of NIDDM among Mexican populations.[20] According to Schulz and Weidensee, a greater degree of Indian genetic admixture creates an increased risk for developing NIDDM which is then exacerbated by the effects of industrialization and economic development.[21] In any event, the present inability to resolve such questions does not preclude a consideration of how the expression of the underlying genetic heritage has been affected by selective forces operating within the social as well as physical environments during the thousands of years that Indians have been present in the Americas.

THEORETICAL EXPLANATIONS

The seminal work attempting to account for the persistence of diabetes among Indian populations, despite its selective disadvantage, is James Neel's paper describing a "thrifty" genotype.[22] Neel considers two of the more obvious characteristics associated with diabetes, namely heritability and obesity, and concludes that a "thrifty" genotype could metabolically adjust to the "feast or famine" conditions that characterized the hunter-gatherer existence of early humans. In other words, Neel surmises the existence of a metabolic adaptation to environments that are characterized by regular food shortages.[23] The idea is that under unpredictable and nutritionally stressful

conditions, a quick release of insulin is necessary in order for the body to derive the full benefit from glucose molecules (the simplest of several organic sugar compounds whose breakdown provides metabolic energy) from available food. During periods of high food availability, an overproduction of insulin stimulates the liver to convert sugar (glucose) into fat (lipids) that can be stored by the body for conversion into energy during periods of low food availability. Without this overproduction of insulin, glucose would be metabolized for immediate energy. [24]

Neel's "thrifty genotype" was initially a general concept, although in a more recent article,[25] he suggests three alternate mechanisms to explain why people develop NIDDM. One mechanism, based upon overresponsive insulin receptor cells (which produce insulin as part of the normal process of food metabolism) is essentially a restatement of Neel's original concept of a "quick insulin trigger." In this case, overstimulation of insulin receptor cells (from too much food containing too much glucose) causes these cells to malfunction. Susceptible persons are those who have inherited this quick trigger. Under conditions of regular, albeit unpredictable, food shortages this ostensible "defect" actually facilitates efficient food metabolism by overproducing insulin in response to the presence of glucose. Under contemporary, "food-available" conditions, the continuing operation of this trigger results in obesity and associated conditions such as NIDDM.[26] Neel's second hypothesis is similar to the first except that susceptible individuals simply develop fewer receptor cells.

The third mechanism that Neel considers involves the interaction of insulin formation and lipid metabolism. Unlike his first two hypotheses, this lipid-based model treats obesity as a result, rather than as a cause of NIDDM, so that individuals with a high degree of susceptibility to NIDDM become obese because of the antilipolitic effects (substances that inhibit the metabolic breakdown of fats) of increased insulin production. The lipid model is consistent with other findings[27, 28] and appears to be in concert with recent studies which indicate that obesity alone is not necessarily the preeminent predictive factor for NIDDM.[29, 30] In his most recent work it appears as if Neel has returned to his original idea of the overstimulated "quick insulin trigger" as the best explanation for NIDDM.[31] While it can be argued that Neel's original model is insufficiently comprehensive and does not synthesize the full range of data from

genetics, cultural anthropology, and archeology, recent studies have revived and expanded this model to the point where it is once more proposed as a basis for explaining the phenomenal rates of NIDDM among Indians.[32] Despite the absence of clear proof that a "thrifty genotype" actually exists, implicit support for its operation (and by inference its existence) has been obtained from studies that demonstrate how a sedentary lifestyle and a rich laboratory diet can result in obesity and metabolic diseases within rat species that do not exhibit such conditions in the wild.[33] As summarized by Zimmet and O'Dea, "The concept of selective insulin resistance with switch-on/switch-off features as part of the feast and famine scenario does provide a reasonable explanation of how the 'thrifty genotypes' might operate."[34]

Wendorf[35] uses the thrifty gene hypothesis as a takeoff point for an explanation of the Paleoindian settlement of North America. In order to construct his hypothesis, Wendorf concentrates upon the Paleoindian megafaunal hunters who lived prior to 12,000 B.C. in eastern Beringia, the land mass that connected Siberia and Alaska during a series of ice age events that occurred in cycles during the Pleistocene Epoch (70,000 to 12,000 years ago). Wendorf considers Beringia to have been a relatively resource-poor zone, and this lack of food resources resulted in the adoption of a mobile existence in which temporary camps were located at major kill sites. Paleoindians brought this subsistence strategy with them through an ice-free corridor that is assumed to have opened between the major glacial epochs in northern Canada between about 12,000 and 20,000 years ago, and which provided a passageway to the central plains of North America.

In Wendorf's view, even prior to the peopling of the Americas, a thrifty gene had already evolved as a physical adaptation to food unpredictability in eastern Beringia. This gene was maintained in populations that moved onto the plains, where large game animals were already becoming scarce so that numerous small episodes of food shortages between kills were common. According to Wendorf, "the relationship between food metabolism and female fertility may have selected for the thrifty genotype by allowing women with thrifty genes to be fertile, carry the child successfully to term and finally nurse the infant during frequent periods of big game kills."[36] Wendorf suggests that once these thrifty genes had been selected for their adaptive value, they continued to be

inherited until their human carriers were exposed to modern diets and subsequently experienced obesity, NIDDM, and other metabolic disorders in epidemic proportions. Indian groups that exhibit very low rates of NIDDM (i.e., the Na-dene or Athapascan speakers such as Navajo and Dogrib Indians) never faced the selective pressures to evolve a thrifty gene because of an assumption that they entered the ice-free corridor into North America thousands of years after the Paleoindians and were presented with a richer, more diverse environment that did not reward the selection of a thrifty gene. Although the early Athapascans were hunters and gatherers, they were not megafaunal specialists like the Paleoindians from eastern Beringia and did not face the same ecological stresses that selected for the thrifty gene.

Wendorf asserts that Athapascans developed a more diverse subsistence strategy than the earlier Paleoindians and never had to adapt to a "feast or famine" existence. The theory is intriguing and may be valid to the extent that he recognizes the possibility of two separate genotypes (Athapascan-based and Paleoindian-based) for NIDDM susceptibility, but the mechanisms that Wendorf hypothesizes for their genesis are the least persuasive part of his argument. While it is true that Athapascan groups exhibit much lower incidence rates of NIDDM than do other Indians, the environments in which Athapascans evolved and lived were not so very different from those of the Paleoindians. A number of anthropologists believe that ancestral Athapascans originated in northeastern Siberia and, after occupying portions of Beringia, moved into the Alaskan interior and along the south Alaskan coast.[37] With the exception of coastal groups that adopted a strategy of fishing and marine mammal exploitation, most Athapascans were big game hunters, with caribou as well as moose, deer, and bear constituting the most dependable prey following the extinction of most megafauna at the end of the Pleistocene Epoch. If Wendorf's logic is correct, a thrifty gene would have been as useful to Athapascans inhabiting cold boreal forests, where periods of abundant food (fall and spring caribou kills) alternated with periods of near starvation, as it was to hunters in eastern Beringia. If an environmentally induced mechanism for NIDDM susceptibility exists, it must account for all of these diverse elements. Recent evidence of increasing NIDDM prevalence among Navajo groups that previously exhibited

very low rates strongly suggests the presence of some environmental causative factors.[38]

One such theory has been proposed by Szathmary,[39] who rejects the thrifty gene model (primarily because of its insulin-glucose focus) and has concentrated upon the adaptation of early northern hunters to a high-protein, low-carbohydrate diet with seasonal nutrient variability. Szathmary asserts that this type of diet resulted in the selection of a glucose-sparing genotype largely because of the relative unavailability of glucose in that environment. In Szathmary's model, northern hunters secure fuel for their daily needs through the metabolism of fatty acids (gluconeogenesis), which are much more accessible than carbohydrates in the typical northern hunting subsistence system. In other words, this particular environment rewards efficient fat users by increasing their reproductive potential in a carbohydrate-poor environment. As a result of a selection process operating for thousands of years, a genotype was selected that could not metabolize efficiently in the presence of a large volume of carbohydrates. When populations that retain this genotype are exposed to modern high-carbohydrate, low-protein diets, they exhibit high NIDDM incidence rates because their bodies are physiologically unable to produce sufficient insulin to metabolize the large volume of available glucose.

A series of studies with the Dogrib Indians,[40] a hunting group living in Canada's Northwest Territories, provides some support for Szathmary's conclusions, but some questions remain unanswered. For example, Wendorf raises an issue concerning northern hunter adaptations to the nutritional opportunities provided by the tundra and steppe environments of Beringia and Northern Canada. He notes that a number of ancestral European and Asian groups inhabited the same types of environments and presumably relied upon the same types of food.[41] If Szathmary's northern hunter adaptation is valid, then at least some European and Asian groups should have the same elevated NIDDM rates as do Indians. One explanation for the absence of such elevated rates among Europeans is that their early adoption of agriculture has given them 10,000 years of exposure to high carbohydrate diets.[42] Unfortunately, this rationalization finesses and does not account for the enormous spatial and temporal variations that characterize the evolution of agriculture. In any event, in light of the discrepancies in NIDDM rates among diverse groups,[43] it appears as if several

NIDDM rates among diverse groups,[43] it appears as if several mechanisms are at work that are not explained by the northern hunter adaptation.

A different perspective has been developed by Weiss and others[44, 45, 46] that integrate concepts from population genetics, epidemiology, and human ecology into a unified hypothesis encompassing a number of interrelated metabolic conditions to which Indians appear particularly susceptible. Weiss' New World Syndrome (NWS) views NIDDM as only one of a number of component problems that include obesity, gallbladder disease, and certain digestive system cancers. The prevalence of all of these conditions among Indians has increased dramatically, arguably in response to the environmental changes experienced by these groups during the past fifty years. The strength of the NWS model is that it places a number of seemingly related diseases into a comprehensive model that systematically links both genetic and environmental components. The only problems with this theory are those common to all theories involving Indians and NIDDM, namely, what is the precise genetic defect which is involved (i.e., *why* are Indians more susceptible) and what mechanism in the modern environment (i.e., dietary changes, declining rates of physical activity, etc.) translates that susceptibility into astronomical NIDDM rates? Weiss' studies suggest that a problem with lipid metabolism is the culprit underlying all of the NWS components, a theory that, despite its widespread support, does not explain why different groups of Indians should experience different rates of NIDDM or other related diseases. One grim possibility is that as the time, depth, and intensity of acculturation increase, virtually all Indian groups will experience similar high levels of NIDDM, with the degree of admixture with non-Indian populations being an important variable (see, for instance, Szathmary[47]). As Weiss and others recognize, "Many of the same (NWS trait) patterns are found in non-Amerindian populations, and it may be that variables observed to date are secondary or tertiary manifestations of some more fundamental physiological variant as yet undiscovered."[48] Recent studies involving Australian Aborigines[49] and Melanesians from Papua, New Guinea[50] appear to support this conclusion.

MODERNIZATION AND ITS IMPACT

No investigator who has considered the relationship of NIDDM, obesity, and Indian ancestry can help but be struck by the unprecedented increases in the incidence and prevalence of both conditions during the past several decades. Anecdotal and ethnographic evidence suggest that prior to the twentieth century, Indians were neither obese nor did they suffer from NIDDM in substantial numbers. One should not assume any physiological uniformity prior to the twentieth century, however, as observers such as Lewis and Clark noted differences in the appearance of groups living along the Pacific drainages of the Rocky Mountains. For example, they described the Tushpaws (Salishan) and the Pierced Nose (Nez Perce) as "stout and portly" and the Solkulks as tending towards "corpulency,"[51] whereas most other groups, including the Chinooks, were variously described as "low in stature" or "diminutive."[52] It may be impossible to relate groups observed in 1805 accurately to contemporary populations, but at least one published study considers rates of NIDDM (but not of obesity) among groups who formerly inhabited the Columbia River drainages. In comparing prevalence rates among residents of the Warm Springs Indian Reservation measured twenty years apart (1965, 1985), the author states:

> All evidence gathered to date indicates that many residents of the Warm Springs Indian Reservation probably did not experience problems with control of their blood sugar metabolism until ten to twenty years prior to 1965, the first year in which the Warm Springs Reservation population was surveyed.[53]

More significantly, the author suggests that although the residents of Warm Springs exhibit lower prevalence rates than those found in other tribes (Zuni, Pima, Tohono O'odham, Maricopa), they nevertheless appear to be following a pattern of increasing prevalence similar to, albeit temporally behind, these other tribes.[54] This is the same conclusion that has been reached by several studies conducted among Indian tribes living in eastern Canada.[55, 56, 57] The Warm Springs study suggests that the observed increase in NIDDM appears to be genuine rather than statistical or the result of sampling bias, and sup-

ports those hypotheses that link NIDDM to various environmental risks.

While the problems associated with the economic changes and acculturation brought by western societies have been a part of Indian life for 500 years, the process has speeded up. Beginning with the Roosevelt administration in the 1930s, the "development" of western water resources became an indelible part of America's domestic policy. Government-subsidized development and industrialization achieved tremendous momentum during World War II with a proliferation of military bases, research facilities, and defense-related industries. This momentum continued unabated after the war when favorable economic and physical environments lured millions of people to the West. Economic change and acculturation are neither synonymous, nor do they necessarily correlate in a "cause-and-effect" relationship. Nevertheless, the cumulative effects of these processes resulted in a general shift from subsistence farming or hunting and gathering to wage labor and a cash economy, new types of living arrangements and dietary regimes, and some dissociation from traditional lifestyles. The process of acculturation did not affect all groups at the same time or at the same rate, but it is generally recognized that subsequent to the 1940s, Indians have been subjected to an increased rate of acculturation to urban industrial and post-industrial lifestyles.[58]

The process of how these changes translate into increased rates of NIDDM has been considered but has never really been explained. Modernization, after all, is not a uniquely American phenomena, nor is NIDDM. A number of studies have addressed this question,[59, 60, 61] but not even the concept of NWS can adequately account for what appears to be a pan-continental or world regional phenomena. In other words, an examination of NIDDM susceptibility (or lack thereof) among Indians cannot ignore the susceptibility of other indigenous groups exposed to rapid modernization. More than twenty-five years ago, Eaton concluded that the environmental factors of dietary change and acculturation stress were preeminent contributors to cross-culturally observed increases in diabetes incidence.[62] In studies involving non-Indians with Asian origins, investigators have noted the same correlations with obesity, NIDDM, and acculturation to modern lifestyles that have been observed among Indians. Hornick and Hanna studied groups of Samoans and found that groups of "modernized" Samoans,

including those living in Hawaii, as well as those living in Samoa, had substantially higher prevalence rates for both diabetes and obesity than did rural Samoans living a more traditional and active lifestyle.[63] Similar results have been obtained in a study comparing urban and rural Papuans.[64]

In neither of the aforementioned studies did the prevalence of NIDDM approach the measured rates among Indian populations, particularly the Pima and Tohono O'odham (formerly named the Papago) Indians. As an illustration, consider that urbanized Samoans exhibit prevalence rates of between 4.3 and 8.0 percent and urbanized Papuans exhibit rates of 15.8 percent. The highest recorded rates of NIDDM among non-Indians are found among inhabitants of Nauru, an island in the central Pacific Ocean, where approximately 25 percent of the population have the disease,[65] a striking example that approaches the rates observed among the Pima and Tohono O'odham where at least one-half of the population over age thirty-five has NIDDM.[66] Another study has found that the Waingela, a Papua, New Guinea group, also exhibit a rate of NIDDM that is almost as high as those of the Pima and Nauruans.[67] Zimmet, who directed the Waingela study, believes this rate is the result of a combination of genetic predisposition together with changes to a "modern lifestyle" that echo Weiss' New World syndrome.[68]

Aside from the Nauruans and Waingela, a broad, comparative study of Pacific populations reveals a range of NIDDM prevalence of between 1.3 percent and 14.8 percent, with Asian Indians living in Fiji and South Africa, and Australian Aborigines exhibiting the highest rates.[69] Beizer suggests that the notable differences in NIDDM prevalence between Austronesian and non-Austronesians, irrespective of the degree of acculturation, strongly support the existence of a fundamental genetic mechanism.[70] None of the Oceanic or Pacific groups have been identified as having adapted to a "northern hunter-type" of dietary regime with high volumes of protein and fat, and low volumes of carbohydrate, so that if there is some type of thrifty gene or other genetic mechanism at work, a more comprehensive model is needed. Such a model also must be able to account for chronological differences in the occupation of different areas. The conservative view holds that America was probably colonized sometime between 15,000 and 20,000 years ago by groups of Northern Asians. Australia, on the other hand, was probably colonized between 50,000 and

60,000 years ago by groups of Southern Asians, while Oceania was colonized much more recently by entirely separate groups of Southern Asians. Hawaii, as possibly the last point reached by the Polynesians, was colonized within the past 2,000 years. Despite the fact that the Pacific and Oceanic populations have not exhibited NIDDM rates as high as those of Indians, some of the Oceanic rates are still quite high relative to the rates for Caucasians. If there is a genetic explanation for the susceptibility of such diverse groups, its origin may be quite ancient.

One previously noted idea that may tie diverse groups together and serve as the focus for additional research involves problems associated with lipid metabolism.[71] Several theories have posited a relationship between lipid metabolism malfunctioning and the genesis of NIDDM, but what may be equally important is an ethnographically recognized desire for fatty foods among hunter-gatherers. One of the conclusions reached by Hayden in an exhaustive survey of contemporary hunters and gatherers is that the ethnographic record is so replete with evidence of preferences for fats that mere taste and palatability preferences are insufficient explanations and some deeper biological processes are probably at work.[72] Table 1, adapted from Hayden's article, offers several examples of the valuation of fat consumption among various groups of Africans, Asians, Australians, and North Americans. According to Hayden, fat consumption

> is a widespread phenomenon linked to specific nutritional requirements, especially in lean seasons or years. Such conditions probably prevailed during most of the Pleistocene, and the emic value attached to hunting game species among modern hunter/gatherers may constitute an adaptation to the need for lipids.[73]

Hayden includes agricultural societies by noting the value that these groups place on oil-bearing plants and seeds,[75] a view echoed in archeological theories that explain the origins of agriculture in eastern North America during the Early and Middle Woodland Periods (1,500 B.C. to A.D. 500). Two of the wild foods that were cultivated as part of the Eastern Agricultural Complex of early domesticates, namely sunflowers and marsh elder, have very high seed oil content, a characteristic that presumably contributed to their nutritive value.[76]

TABLE 1

Contemporary Hunters and Gatherers Emic Valuation Associated With Fat Consumption

Groups		*References*
Nootka	Parts with fat considered choice, delicious, and delicacies; heavy emphasis on fats	Drucker 1951:62
Tlingit	Fish oil consumed in large quantities at feasts; large gatherings to obtain oil-bearing fish	Oberg 1973;69
Hadza	Fat rare on game animals, thus fatty animals were precious and marrow was extracted	Tomita 1966:160
!Kung	Fats were scarce and sought	Lee 1972a:344 Yellen and Lee 1976:39
Aranda	Intestinal fat "esteemed a great delicacy"	Spencer and Gillen 1927:18
Western Desert Aborigines	Lean carcasses often abandoned	Tindale 1972:248
Murngin	Lean emus considered poor eating; melted intestinal fat considered a great delicacy	Warner 1958:130–31
Andamanese	Pigs often abandoned in hot season (because of lean condition?)	Radcliffe-Brown 1922:39
Kutchin	Fat very important; excess boiled, preserved, and traded	Osgood 1936:30, 37
Mistassini	Hare were "starvation food, since they possess very little fat"	E. Rogers 1972:111
Tasaday	All observed animals were lean, possibly explaining "delicacy" status of fatty, bad-tasting palm grubs	Yen personal communication

Speth and Spielmann use anecdotal and ethnographic observations regarding preferences for fat consumption as a starting point for an in-depth analysis of the nutritional role of fats.[77] Their review is replete with examples of situations in which groups of hunter-gatherers avoided lean meats as being nutritionally undesirable, even during periods when few alternative food sources were available. Researchers agree that fats are essential for hunter-gatherers living in areas without easy access to carbohydrates because of the nutritional roles that fats have in the maintenance of linoleic acid production (needed for growth, internal water balance, and to help fight off infections) as well as in facilitating calcium absorption.[78]

Nevertheless, it is the protein sparing effect of both fats and carbohydrates which is of particular interest for this review. Protein sparing is a process that reduces the loss of body protein (such as from muscle tissue) when there is insufficient caloric and protein intake to otherwise meet the body's energy

needs. In the absence of fats and carbohydrates, the body metabolizes amino acids that constitute proteins in order to provide operating energy, but then these proteins are no longer available for use by the body. When either fats or carbohydrates are present, the loss of body protein is reduced, but carbohydrates have a much greater protein-sparing effect than do fats.[79] Problems develop among people who are physiologically adapted to low carbohydrate regimes (i.e., the Arctic and sub-Arctic) and rely upon fats for food energy and their attendant, albeit limited protein-sparing effects, and who are then exposed to high carbohydrate diets. In any comparison between fats and carbohydrates, the latter are biochemically and nutritionally more efficient (and desirable) for both roles, but when carbohydrates become constantly available and there are no cyclical periods of famine to draw down the body's fat reserves, the increased efficiency and protein-sparing results in more fat storage. This process ultimately leads to obesity, one of the primary risk factors associated with NIDDM. In a sense, one is presented with another version of the thrifty gene hypothesis that is akin to Szathmary's ideas, except that the preferences for fats among hunter-gatherers are more likely to be biologically rather than culturally mediated.

A broad hypothesis that purports to explain the need for dietary fat suggests that although modern humans evolved in such a way so as to require lipids for optimum health, the process of migration resulted in the occupation of numerous environments in which lipid acquisition required different adaptations. Over tens of thousands of years, natural selection and genetic drift (the property of finitely-sized populations to exhibit genetic frequencies that deviate from mathematically derived predictions),[80] combined to create divergent populations that metabolize lipids in slightly different ways. Such differences, when combined with genetic divergence, may explain some of the observed variations in NIDDM susceptibility. Irrespective of the differing prevalence rates, the overall trend among Indians and other indigenous people appears to be one of increase over time. No one who has considered the published data can deny the correlations between the shift from traditional to post-industrial lifestyles with recorded increases in a variety of metabolic diseases, but a correlation is not a cause and the fundamental mechanisms behind these increases have continued to remain tantalizingly out of reach.

THE CASE OF THE PIMA AND TOHONO O'ODHAM INDIANS

In consideration of the broad problems involving genetic and environmental factors operating upon large Indian populations, a number of studies have concentrated upon smaller groups, especially those exhibiting particularly high rates of NIDDM. In all of the literature concerning Indians and NIDDM, two of the most examined groups are the Pima and Tohono O'Odham tribes who live in central and southern Arizona and portions of northern Mexico. Even among Indians, NIDDM rates in these groups stand out. Studies among the Pima reveal incidence rates that are routinely measured at between twenty-five and thirty cases per 1,000 person-years, with prevalence rates measured between 42 and 65 percent in adults at least thirty-five years old.[81, 82] That more than half of the adults have this disease at any one point in time is remarkable,[83] but what is more remarkable is that if a Pima or Tohono O'Odham lives long enough, he or she is virtually assured of developing this disease.

It is notable that NIDDM is not the only pressing health problem faced by these groups. Tohono O'Odham suffer from abnormally high rates of infant deaths, malnutrition, and mental impairment among school-age children. Insufficient food, alcoholism, poverty, and lack of education contribute to these problems, and the basic Tohono O'Odham diet has been found to be generally deficient in vitamins A, C, niacin, and riboflavin.[84] There are, in short, a myriad of adverse conditions whose synergistic effects may substantially exacerbate the impact from any single problem. One interesting observation from a somewhat limited study is that traditional foods (both wild or home-grown) eaten by many poorer Tohono O'Odham provide better sources for calcium, iron, and vitamins than the modern Western diets adopted by more well-off Tohono O'Odham.[85] Whether such isolated findings can be dovetailed into general theories regarding the overall impact of modernization and its relationship to NIDDM remains to be seen.

Although the Pima and Tohono O'Odham reside in the same general Sonoran Desert region, at least through the middle of the nineteenth century the Tohono O'Odham traditionally inhabited more desert areas and relied upon wild plant and animal resources for most of their diet, whereas the Pima lived closer to natural waterways and relied upon irrigation agricul-

ture for the majority of their diet.[86] With the arrival of the Spanish, both groups continued their fundamental strategies of resource diversification and accepted some of the European crops and stock animals. The Tohono O'Odham, consistent with their traditional animal product orientation, adopted cattle raising, whereas the more horticultural Pima stressed wheat farming. During the seventeenth and eighteenth centuries, largely as a result of their remoteness from the centers of Spanish and Mexican settlement, the Pima and Tohono O'Odham remained relatively free from intensive European influences.[87] A major divergence between subsistence orientations occurred during the mid-nineteenth century when Americans encouraged increased wheat production in order to satisfy demands caused by the California gold rush and the Civil War. The Pima intensified wheat production without regard to traditional crop diversification and became acculturated to a cash and consumer-goods economy. When the wheat boom ended in the late nineteenth century, traditional techniques that had been relied upon to ameliorate environmental perturbations were no longer in use, and consequently relatively little food was obtained through conventional subsistence activities.[88] Federally financed water development projects during the first half of the twentieth century were largely unsuccessful in reestablishing large-scale Pima agriculture, with the result that wage work and social welfare formed the basis of a new subsistence regime. As a result of these transformations, Pima diets changed over the course of approximately one hundred years from being based primarily upon complex carbohydrates and high fiber foods to the high fat and high sugar (simple carbohydrates) content of modern foods.[89]

Although the Tohono O'Odham have not fared much better than the Pima, they have retained cattle raising as a resource base and have also maintained a more traditional and decentralized form of social organization.[90] Whereas both groups have been sedentary agriculturists exposed to Euro-American foods for almost 450 years, the Pima have a somewhat earlier and more intense history of acculturation. In neither group was NIDDM a noticeable problem until the mid-twentieth century. If acculturation is a contributing factor for NIDDM, then one might expect both groups, or at least the Pima, to suffer from higher rates of NIDDM than Indians with different cultural histories.

In this vein, some comparisons may be made with the Navajo, whose reservation comprises an area almost as large as New England and is located in the arid Four Corners region, where the boundaries of Arizona, New Mexico, Colorado, and Utah all meet. The Navajos are an Athapascan-speaking group related to Na-dene speakers living in western Canada. While traditional Navajo beliefs hold that their people have always lived in the Dinetah area near the Four Corners region, most archeologists have concluded that the ancestors of the Navajos and Apaches (another Athapascan-speaking group) migrated into the Southwest from Canada sometime during the fourteenth century.[91] From the seventeenth through the nineteenth centuries, Navajo subsistence was primarily based on hunting, gathering, and raiding, and it was not until the mid- to late nineteenth century when American policies forced the Navajos to adopt a more sedentary existence based on agriculture and pastoralism.[92] Even that lifestyle could not be called sedentary by contemporary standards as the Navajo continued to reside in widely dispersed communities and maintained a lifestyle that necessitated substantial amounts of walking or horseback riding.[93] What is pertinent to this review is that Navajos have traditionally exhibited relatively low prevalence rates of NIDDM in comparison with other Indian and Caucasian groups. Prior to 1965, NIDDM prevalence rates among Navajos were less than 1 percent. Even though these rates have increased dramatically over the past three decades (to approximately 10 to 12 percent),[94] they remain substantially lower than the rates for groups such as the Pima (in excess of 50 percent)[95] and the Tohono O'Odham (in excess of 30 percent).[96] Whether the observed differences in NIDDM rates between Navajos, Pima, and Tohono O'Odham are the result of different ethnic origins or evolutionary histories is not clear. It is curious that groups living in the Southwest and exposed to many of the same external forces have, up to this point in time, exhibited noticeably different NIDDM rates.

A study by Saad and others reports that Pimas exhibiting high glucose intolerance have the highest probabilities of developing NIDDM.[97] It is noteworthy that despite more than 450 years of exposure to Euro-American foods, NIDDM rates among Tohono O'Odham did not begin to rise until after the 1930s. Whether Navajo rates will reveal a similar rise with continued exposure to "modern" diets and lifestyles is a question waiting to be answered, but at least one study reveals such a

rise.[98] Indeed, what Hall suggests is that there is a strong environmental component to NIDDM, and that the Navajo are merely at an earlier point of progression along a continuum of NIDDM prevalence than are the Tohono O'Odham. An underlying implication is that regardless of any unique susceptibility factors maintained by the Pima and Tohono O'Odham, these factors were not triggered merely because exotic foodstuffs, nutritionally different from traditional foods, were added to their diets. As one commentator notes, "It was in keeping with the security orientation of the [Tohono O'Odham] culture that its treatment of the introduced plants and animals was additive rather than substitutive."[99]

Another theory that deserves consideration concerning NIDDM among the Pima and Tohono O'Odham has been offered by Nabhan and focuses on things that have been eliminated from traditional Indian diets as well as items that have been added.[100] This view, consistent with some of Greene's findings[101] as well as those of Boyce and Swinburn,[102] is that a wide variety of traditional wild foods "are unusually rich in soluble fiber and complex carbohydrates [that] can prevent or control diabetes."[103] Nabhan concentrates on tepary beans because of their traditional role in supplying substantial amounts of protein, minerals, and fiber in Pima and Papago diets. He notes that tepary consumption has decreased precipitously over the past fifty years and implies that the transition from traditional foods to mass-marketed, store-bought foods is related to the epidemic of diabetes among these groups.

> Further, native desert foods such as beans, mesquite-seed gum, prickly-pear pods and plantago seed have all been proven effective enough in controlling blood sucrose levels to reduce or eliminate the need for insulin shots for diabetics. Ironically, these very foods are those which have fallen out of the desert peoples' diets at the same time that diabetes has become more prevalent among them.[104]

Unfortunately, some of the sources to which Nabhan refers do not clearly support his theory. In a comparison study of traditionally grown Hopi beans with commercially available beans, the authors found that whereas traditionally grown tepary beans are often nutritionally superior to commercially available beans, it is not an absolute rule.[105] While there may be some diminution in the percentages of vitamins, minerals, and

protein that can be obtained from commercially available beans relative to traditionally grown beans, this diminution can be made up through alternative food sources that were not available until recently. Similarly, a comparison of the nutritional value of teparies with a number of commercially available legumes reveals that while teparies are an excellent source of protein, iron, niacin, and several other vitamins, they are not overwhelmingly superior to other grain legumes.[106] Indeed, the report concludes that the true value of teparies may lie in their ability to adapt successfully to arid environments, thus offering a predictable food source, rather than in their superior nutritional quality. Nabhan's approach is intriguing but does not account for all of the observed differences in NIDDM prevalence rates among Indians living in the Southwest. Nevertheless, a nutrition-based approach may be consistent with both genetic and environmental theories, as it has been noted "that traditional Pima carbohydrate sources are more slowly digested and raise glucose and insulin levels less than do western cereal products. A traditional diet may have placed less stress on a system adapted to high protein intake."[107] Despite some empirical and anecdotal support[108] as well as a history of adopting Euro-American foods and lifeways, there is nothing uniquely within the cultural history of the Tohono O'Odham to explain the enormous incidence and prevalence of NIDDM, nor are there any "quick fixes" with which to alleviate it.

UNANSWERED QUESTIONS AND FUTURE RESEARCH DIRECTIONS

It is apparent that research programs must consider the interplay between genetic and environmental explanations for the NIDDM epidemic. Despite recent advances in molecular biology that strongly suggest a genetic component, scientists have yet to isolate a specific gene or series of genes that causes NIDDM.[109] Current models are based upon an assumption that multiple alleles (different forms of particular genes) located at certain loci on human chromosomes contribute to an individual's overall susceptibility to NIDDM, but the inability to correlate specific genotypes (an identifiable series of alleles) to a specific phenotype (the physical manifestation of a genotype—in this case, someone with NIDDM) continues to frustrate

researchers. A series of studies summarized by Ferrell and Iyengar implies that there are at least two general regions on the chromosomes where genetic markers suggest some involvement with NIDDM.[110] Most recently, researchers have identified and described a genetic mutation that appears to be associated with the onset of both NIDDM and obesity.[111] Cross-cultural data suggest a direct link between the mutation and some kind of lipid metabolism malfunction, but the research team was careful to emphasize the causative interplay of both genetic and environmental factors in the onset of NIDDM. It is important for this type of work to continue as the identification of one or more genes that correlate with NIDDM susceptibility could not only help to illuminate the causes for NIDDM, but could open up the potential for archeological investigation using DNA analysis of skeletal samples that could trace the spread of these alleles through prehistoric populations. This portion of the discussion is more speculative and assumes scientific breakthroughs that have only been hinted at but are certainly not beyond the pale of potential research. A consideration of the political implications attendant with such studies is beyond the scope of this paper, but one can be optimistic that the potential gains from such research in terms of Indians' health would be recognized and that this work would be encouraged rather than irrevocably foreclosed.

Many of the current theories regarding NIDDM susceptibility are based upon some variation of the theme of twentieth-century urban Western lifestyles colliding with ancient genotypes, little changed since the Pleistocene. Much of the research concerning Indians and NIDDM has avoided the period between the initial Paleoindian occupation of North America and the twentieth century, despite the occurrence of three significant events, namely the megafaunal extinction, the development and spread of agriculture, and European contact and colonization. Although agriculture evolved in different areas and at different rates, it constituted a fundamental change from the preceding hunter and gatherer subsistence systems. As a result of this change, settlement patterns gradually became more sedentary and, although traditional agricultural practices require a substantial degree of physical labor, a number of Indian societies (Mississippian chiefdoms,[112] Classic Hohokam[113] and Northwest Coastal tribes[114]) secured a sufficient level of surplus time and wealth to develop a greater degree of social and political complexity than most of their con-

temporaries. In a great many areas, dietary composition changed from a hunting diet of low carbohydrate, low fiber, moderate fat, and high protein to the farming diet of high carbohydrate, high fiber, moderate protein, and low fat. In some respects the change from hunting and gathering to agriculture represented as radical a change as the change to a modern diet, which is high in carbohydrates, moderate in fat, moderate in protein, and low in fiber. Unfortunately, there is a dearth of early ethnographic evidence concerning either NIDDM or other metabolic health problems. The reasons for the absence of such reports include an initial lack of interest among Euro-Americans for whom the study of chronic non-infectious diseases was not a priority, together with the fundamental ignorance that existed prior to the twentieth century regarding the etiology of most diseases.

Prospective studies of groups experiencing the inevitable and increasingly rapid process of acculturation is one avenue with which to approach the problem. For example, recent ethnographic studies of unacculturated South American hunters and gatherers practicing limited agriculture indicate that neither obesity nor NIDDM constitute significant health problems.[115] Similarly, while a formal research design is beyond the scope of this review, studies among the Rarámuri Indians (also known as the Tarahumara Indians) living in the Sierra Madre Occidental of northern Mexico may shed some light on both the prevalence and incidence of metabolic diseases such as NIDDM.[116] The Rarámuri consist of groups of relatively unacculturated agriculturists, more acculturated groups living in close proximity to Mexican towns, and some admixed groups of Rarámuri-Mexicans. The typical Rarámuri diet is high in protein and low in meat and is based primarily on corn with some beans, squash, and fruit but very little sugar. Nutritional studies have noted the endurance and lack of coronary disease among the Rarámuri,[117] but little work has been done with respect to the prevalence of NIDDM. When their demographic and physical attributes are considered in concert with the unavoidable stresses associated with the intrusion of large-scale agricultural development and tourism into their traditional mountain valleys, it is suggested that the Rarámuri represent a highly desirable population for future study.

Another area for investigation involves dietary preferences. Such preferences began to diverge hundreds, if not thousands, of years ago and could partially explain why traditional agri-

culturists such as the Mandan, Hidatsa, and Tohono O'Odham have higher rates of susceptibility to NIDDM than do traditional hunters and gatherers such as the Paiute, Dogrib, and Passamaquoddy. The arrival of Europeans brought immediate and deleterious nutritional changes, including the easy availability of refined flour, sugar, and alcohol, but it may not necessarily be the fact of contact alone that has caused metabolic problems. Over the course of 500 years Euro-American influence has become pervasive, but it is an arguable point whether the impact occasioned by this contact during its first 450 years was of a different kind or merely one of degree relative to what has occurred during the past fifty years.

What is not arguable is the seriousness of the NIDDM epidemic that has manifested itself throughout Indian communities. An honest evaluation would conclude that the mechanisms underlying this epidemic remain unknown, nor is it understood how to prevent it from continuing. The most promising directions for research involve testing models that interrelate genetic, metabolic, and environmental factors together with anthropological and archeological studies directed towards understanding subsistence practices and nutrition among historic and prehistoric groups. While conventional diabetes treatments involving dietary management and medication may be palliative in the short run, only long-term efforts directed towards understanding fundamental causes offer the possibility of effective NIDDM management.[118] Successful efforts will require cooperation between the scientific and Indian communities. It is reasoned common sense rather than knee-jerk political correctness to assert that even the best-designed diabetes control programs must be able to reconcile modern knowledge with traditional medical and dietary practices or risk being labeled as just another unwarranted imposition.[119] In a recent editorial, Zimmet and Lefebvre make the very strong point that NIDDM should be viewed less as a disease to be diagnosed and treated than as "a symptom of a much larger global problem" involving the disruptive impacts of modernization.[120] It is only though a truly integrated approach that is committed to improving the social, cultural, and economic status of the most highly impacted groups that any progress in the amelioration of the NIDDM epidemic will be achieved.

NOTES

1. J.D. McGarry, "What if Minowski Had Been Ageustic? An Alternative Angle on Diabetes." *Science*, 258 (1991), 766-770.

2. K.M. Weiss, J.S. Ubrecht, P.R. Cavanagh, A.V. Buchanan, "Diabetes Mellitus in American Indians: Characteristics, Origins and Preventive Health Care Implications." *Medical Anthropology*, 11 (1989), 283-304.

3. W.C. Knowler, D.R. McCance, D.K. Nagi, D.J. Pettitt, "Epidemiological Studies of the Causes of Non-insulin Dependent Diabetes Mellitus." In *Causes of Diabetes—Genetic and Environmental Factors*, ed. R.D.G. Leslie (Chichester, England: John Wiley & Sons, 1993), 187-218.

4. McGarry, "What if Minowski Had Been Ageustic? An Alternative Angle on Diabetes," 766.

5. M. McCarthy and G.A. Hitman, "The Genetic Aspects of Non-insulin-dependent Diabetes Mellitus." In *Causes of Diabetes—Genetic and Environmental Factors*, ed. R.D.G. Leslie (Chichester, England: John Wiley & Sons, 1993), 157-186.

6. McGarry, "What if Minowski Had Been Ageustic? An Alternative Angle on Diabetes," 769.

7. Molly O'Neil, "So It May Be True After All: Eating Pasta Makes You Fat." *New York Times* (February 8, 1995), C-6.

8. T. Kue Young, "Diabetes Mellitus Among Native Americans in Canada and the United States: An Epidemiological Review." *American Journal of Human Biology*, 5 (1993), 403-405.

9. S.M. Haffner, H. Miettinen, M.P. Stern, "Nondiabetic Mexican-Americans do not have reduced insulin responses relative to nondiabetic non-Hispanic whites." *Diabetes Care*, 19(1) (1996), 67-69.

10. B. Muneta, J. Newman, S. Wetterall, J. Stevenson, "Diabetes and Associated Risk Factors Among Native Americans." *Diabetes Care*, 16(12) (1993), 1619-1621.

11. Knowler, et al., "Epidemiological Studies of the Causes of Non-insulin Dependent Diabetes Mellitus."

12. W.C. Knowler, P.H. Bennett, and P.J. Savage, "Obesity and Diabetes in Pima Indians: The Effects of Parental Diabetes on the Relationship of Obesity and Diabetes." In *Genetic Environmental Interactions of Diabetes Mellitus*, ed. J.S. Melish, J. Hanna, and S. Baba (Amsterdam: Excerpta Medica, 1982), 95-100.

13. S. Valway, W. Freeman, S. Kaufman, T. Welty, S. Helgerson, D. Gohdes, "Prevalence of Diagnosed Diabetes Among American Indians and Alaska Natives, 1987." *Diabetes Care*, 16(1) (1993), 271-276.

14. H.F. Delisle, M. Rivard, J.M. Ekoe, "Prevalence estimates of diabetes and of other cardiovascular risk factors in the two largest Algonquin communities of Quebec." *Diabetes Care*, 18(9) (1995), 1255-9.

15. P. Brassard, E. Robinson, C. Lavallee, "Prevalence of diabetes mellitus among the James Bay Cree of northern Quebec." *Canadian Medical Association Journal*, 149(3) (1993), 303-307.

16. K.M. Weiss, R. Ferrell, and C. Hanis, "A New World Syndrome of Metabolic Diseases with a Genetic and Evolutionary Basis." *Yearbook of Physical Anthropology*, 27 (1984), 153-178.

17. Weiss, et al., "Diabetes Mellitus in American Indians: Characteristics, Origins and Preventive Health Care Implications."

18. McCarthy and Hitman, "The Genetic Aspects of Non-insulin-dependent Diabetes Mellitus."

19. M.A. Farrell, P.A. Quiggens, J.D. Eller, P.A. Owle, K.M. Miner, E.S. Walkingstick, "Prevalence of diabetes and its complications in the Eastern Band of Cherokee Indians." *Diabetes Care*, 16(1) (1993), 253-256.

20. L.O. Schulz and R.C. Weidensee, "Non-insulin dependent diabetes mellitus in Mexico." *Progress in Food and Nutritional Science*, 17(2) (1993) 99-117.

21. Ibid.

22. James V. Neel, "Diabetes Mellitus—A Thrifty Genotype Rendered Detrimental By 'Progress'." *American Journal of Human Genetics*, 14 (1962), 353-362.

23. Jonathan Marks, *Human Biodiversity—Genes, Race, and History*. (New York: Aldine De Gruyter, 1995), 195-196.

24. O'Neil, "So It May Be True After All," C-6.

25. James V. Neel, "The Thrifty Genotype Revisited." In *The Genetics of Diabetes Mellitus*, ed. J. Kobberling and R. Tattersall (New York: Academic Press, 1982), 283-293.

26. James V. Neel, *Physician to the Gene Pool* (New York: John Wiley & Sons, 1994), 353.

27. Weiss, et al., "Diabetes Mellitus in American Indians: Characteristics, Origins and Preventive Health Care Implications."

28. McGarry, "What if Minowski Had Been Ageustic? An Alternative Angle on Diabetes."

29. W.C. Knowler, P.J. Savage, M. Nagulesparan, B.V. Howar, D.J. Pettitt, J.R. Lisse, S.L. Aronoff, P.H. Bennett, "Obesity, Insulin Resistance and Diabetes Mellitus in the Pima Indians." In *The Genetics of Diabetes Mellitus*, ed. J. Kobberling and R. Tattersall (New York: Academic Press, 1982), 243-250.

30. R. Taylor, P. Zimmet, and S. Whitehorse, "Is the Role of Obesity as a Risk Factor for Diabetes Overstated? Studies in Rural and Urban Polynesians (Western Samoa)." In *Genetic Environmental Interactions of Diabetes Mellitus*, ed. J.S. Melish, J. Hanna, and S. Baba (Amsterdam: Excerpta Medica, 1982), 179-183.

31. Neel, *Physician to the Gene Pool*, 353-355.

32. P. Zimmet, and K. O'Dea, "Thrifty Genotypes." In *Causes of Diabetes—Genetic and Environmental Factors*, ed. R.D.G. Leslie (Chichester, England: John Wiley & Sons, 1993), 269-290.

33. Ibid., 270-271.

34. Ibid., 287.

35. Michael Wendorf, "Diabetes, the Ice-Free Corridor and the Paleoindian Settlement of North America." *American Journal of Physical Anthropology*, 70

(1989), 503-520.

36. Ibid., 517.

37. D.E. Dumont, "A Reexamination of Eskimo-Aleut Prehistory." *American Anthropologist*, 89 (1987), 32-55.

38. Teri R. Hall, Martha E. Hickey, and Terry B. Young, "Evidence for Recent Increases in Obesity and Non-Insulin-Dependent Diabetes Mellitus in a Navajo Community." *American Journal of Human Biology*, 4 (1992), 542-553.

39. Emöke J. E. Szathmary, "Application of Our Understanding of Genetic Variation in Native North America." In *Genetics of Individual Family and Population Variability*, ed. C.F. Sing and C. Hanis (Oxford: Oxford University Press, 1993), 212-238.

40. Emöke J. E. Szathmary and Nasha Holt, "Hyperglycemia in Dogrib Indians of the Northwest Territories, Canada: Association with Age and Centripetal Distribution of Body Fat." *Human Biology*, 55 (1993), 493-515.

41. Wendorf, "Diabetes, the Ice-Free Corridor and the Paleoindian Settlement of North America."

42. J.C. Miller, S. Caliguri, "The carnivore connection: dietary carbohydrate in the evolution of NIDDM." *Diebetologia*, 37(12) (1994), 1280-1286.

43. Sarah Valway, William Freeman, Stephen Kaufman, Thomas Welty, Steven Helgerson, Dorothy Gohdes, "Prevalence of Diagnosed Diabetes Among American Indians and Alaska Natives 1987." *Diabetes Care*, 16(1) (1993), 271-276.

44. Weiss, et al., "Diabetes Mellitus in American Indians: Characteristics, Origins and Preventive Health Care Implications."

45. Weiss, Ferrell, and Hanis, "A New World Syndrome of Metabolic Diseases with a Genetic and Evolutionary Basis."

46. Kenneth M. Weiss, Anne V. Buchanan, Rodolfo Valdez, John H. Moore, Janis Campbell, "Amerindians and the Price of Modernization." In *Urban Health and Ecology in the Third World*, ed. S.M. Bilsborough, A. Schell, L. Watts (Cambridge: Cambridge University Press, 1993), 221-243.

47. Szathmary, "Application of Our Understanding of Genetic Variation in Native North America."

48. Weiss, et al., "Amerindians and the Price of Modernization."

49. M. Gracey, "New World Syndrome in Western Australian Aborigines." *Clinical and Experimental Pharmacology and Physiology*, 22(3) (1995), 220-225.

50. G.K. Dowse, R.A. Spark, B. Mavo, A.M. Hodge, R.T. Erasmus, M. Gwalimu, L.T. Knight, G. Koki, P.Z. Zimmet, "Extraordinary prevalence of non-insulin-dependent diabetes mellitus and bimodal plasma glucose distribution in the Wanigela people of Papua, New Guinea." *Medical Journal of Australia*, 160 (12) (1994), 767-774.

51. Meriwether Lewis And William Clark, *The History of the Lewis and Clark Expedition*, Volume II, ed. Elliot Coues (New York: Dover Publications Inc., 1893), 583, 623, 638.

52. Ibid., 700, 773, 775.

53. James Justice, "Twenty Years of Diabetes on the Warm Springs Indian

Reservation." *American Indian Culture and Research Journal*, 13(3 & 4) (1989), 66-67.

54. Ibid., 68, 73.

55. Delisle, Rivard, Ekoe, "Prevalence estimates of diabetes and of other cardiovascular risk factors in the two largest Algonquin communities of Quebec."

56. Brassard, Robinson, Lavallee, "Prevalence of diabetes mellitus among the James Bay Cree of northern Quebec."

57. H.F. Delisle, J.M. Ekoe, "Prevalence of non-insulin-dependent diabetes mellitus and impaired glucose tolerance in two Algonquin communities in Quebec." *Canadian Medical Association Journal*, 148(1) (1993), 41-47.

58. Cynthia Eaton, "Diabetes, Culture Change, and Acculturation: A Biocultural Analysis." *Medical Anthropology*, 1(2) (1977), 41-63.

59. Wendorf, "Diabetes, the Ice-Free Corridor, and the Paleoindian Settlement of North America."

60. Weiss, et al., "Amerindians and the Price of Modernization."

61. K.M. Weiss, A.V. Buchanan, J.M. Moore, R. Valdez, Yi Ahn, M.E. Russell, J. Campbell, P. Kris-Etherton, E. Georges, "Gene Environment Interaction: Diabetes and Related Diseases in Amerindians." (Unpublished manuscript, Pennsylvania State University, University Park).

62. Eaton, "Diabetes, Culture Change, and Acculturation: A Biocultural Analysis."

63. C. A. Hornick, and J.M. Hanna, "Increasing Prevalence of Diabetes and Obesity With Migration and Modernization Among Samoans." In *Genetic Environmental Interactions in Diabetes Mellitus*, ed. J.S. Melish, J. Hanna, and S. Baba (Amsterdam: Excerpta Medica, 1982), 83-87.

64. F.I.R. Martin, G.B. Wyatt, A.R. Griew, M. Haurahelia, L. Hoffman, J. Mathews, "Diabetic Surveys in Papua New Guinea—A Comparison of Urban and Rural Populations." In *Genetic Environmental Interactions in Diabetes Mellitus*, ed. J.H. J.S. Melish, S. Baba (Amsterdam: Excerpta Medica, 1982), 57-63.

65. Ian Anderson, "Modern Life Is Killing Pacific Islanders." *New Scientist*, 119 (1988), 38.

66. Knowler, et al, "Obesity, Insulin Resistance and Diabetes Mellitus in the Pima Indians," 244.

67. Ian Anderson, "Diabetes Epidemic Strikes Pacific Islanders." *New Scientist*, 143 (1994), 14.

68. Zimmet and O'Dea, "Thrifty Genotypes."

69. P.Z. Zimmet, R.L. Kirk, and S.W. Serjeanston, "Diabetes in High Prevalence Pacific Populations." In *The Genetics of Diabetes Mellitus*, ed. J. Köbberling and R. Tattersall (New York: Academic Press, 1982), 211-224.

70. Ruth Beizer, "Prevalence of Abnormal Glucose Tolerance in Six Solomon Islands Populations." *American Journal of Physical Anthropology*, 81 (1990), 471-482.

71. Gunther Boden, "Role of Fatty Acids in the Pathogenesis of Insulin

Resistance and NIDDM." *Diabetes*, 46 (1997), 3-10.

72. Brian Hayden, "Subsistence and Ecological Adaptation of Modern Hunter/Gatherers." In *Omnivorous Primates*, ed. R.S.O. Harding and G. Taleki (New York: Columbia University Press, 1981), 344-421.

73. Ibid.

74. Ibid., 396.

75. Ibid.

76. Bruce D. Smith, "The Independent Domestication of Indigenous Seed-Bearing Plants in Eastern North America." In *Emergent Horticultural Economies of the Eastern Woodlands*, ed. W.F. Keegan (Carbondale: Southern Illinois University Center for Archaeological Investigations, 1987), 3-48.

77. John D. Speth and Katherine A. Spielmann, "Energy Source, Protein Metabolism, and Hunter-Gatherer Subsistence Strategies." *Journal of Anthropological Archaeology*, 2 (1983), 1-31.

78. Ibid.,15-16.

79. Ibid., 13-15.

80. Jonathan Marks, *Human Biodiversity: Genes, Race, and History* (Hawthorne, New York: Aldine De Gruyter, 1995), 36.

81. Knowler, et al., "Obesity, Insulin Resistance and Diabetes Mellitus."

82. W.C. Knowler, P.H. Bennett, D.J. Pettitt, and P.J. Savage, "Obesity and Diabetes in Pima Indians: The Effects of Parental Diabetes on the Relationship of Obesity and Diabetes." In *Genetic Environmental Interactions of Diabetes Mellitus*, ed. J.S. Melish, J. Hanna, and S. Baba (Amsterdam: Excerpta Medica, 1982), 95-100.

83. Sara Stinson, "Nutritional Adaptation." *Annual Review of Anthropology*, 21 (1992), 151.

84. M.P. Greene, *A Diet Survey of the Prenatal Papago*. (Unpublished Master's Thesis, University of Arizona, 1972).

85. Ibid.

86. R.A. Hackenberg, "Pima and Papago Ecological Adaptations." In *Handbook of North American Indians, The Southwest*, ed. A. Ortiz (Washington, D.C.: Smithsonian Institution Press, 1983), 161-177.

87. Donald Bahr, Juan Smith, William Allison Smith, Julian Hayden, *The Short Swift Time of Gods on Earth* (Berkeley: University of California Press, 1994), 4.

88. Vicky L. Boyce, Boyd Swinburn, "The Traditional Pima Diet." *Diabetes Care*, 16(1) (1993), 369-371.

89. Ibid., 370.

90. Hackenberg, "Pima and Papago Ecological Adaptations," 166-167.

91. Lori S. Reed and Paul Reed, "The Protohistoric Navajo: Implications of Interaction, Exchange, and Alliance Formation with the Eastern and Western Pueblos." In *Cultural Diversity and Adaptation—The Archaic, Anasazi and Navajo Occupation of the Upper San Juan Basin* (Santa Fe: Bureau of Land Management, New Mexico State Office, 1992), 91-104.

92. David Brugge, "Navajo Prehistory and History to 1850." In *Handbook of North American Indians, The Southwest*, ed. A. Ortiz (Washington, D.C.:

Smithsonian Institution Press, 1983), 489-501.

93. Hall, et al., "Evidence for Recent Increases in Obesity and Non-Insulin-Dependent Diabetes Mellitus in a Navajo Community," 552.

94. Ibid., 551.

95. Justice, "Twenty Years of Diabetes on the Warm Springs Indian Reservation, Oregon," 71.

96. Hackenberg, "Pima and Papago Ecological Adaptations."

97. M.F. Saad, W.C. Knowler, D.J. Pettitt, R.G. Nelson, D.M. Mott, P.H. Bennett, "The Natural History of Impaired Glucose Tolerance in the Pima Indians." *New England Journal of Medicine*, 319:23 (1988), 1500-1506.

98. Hall et al., 552.

99. Hackenberg, "Pima and Papago Ecological Adaptations," 168.

100. G.P. Nabhan, C.W. Weber, and J.W. Berry, "Variations in Compositions of Hopi Indian Beans." *Ecology of Food and Nutrition*, 16 (1985), 135-152.

101. Greene, *A Diet Survey of the Prenatal Papago.*

102. Boyce and Swinburn, "The Traditional Pima Diet."

103. Gary Nabhan, "Native American Cornucopia." *Native Peoples*, 5:3 (1992), 10, 14.

104. Gary Nabhan, *Gathering the Desert.* (Tucson: University of Arizona Press, 1992), 121.

105. Nabhan, Weber, and Berry, "Variations in Compositions of Hopi Indian Beans."

106. J. C. Scheerens, A.M. Tinsley, I.R. Abbas, C.W. Weber, and J.W. Berry, "The Nutritional Significance of Tepary Bean Consumption." *Desert Plants*, 5:1 (1983), 11-14, 50-56.

107. Stinson, "Nutritional Adaptation," 153.

108. Thomas E. Sheridan, "Diet and Diabetes Among the O'odham." In *Paths of Life*, ed. Thomas E. Sheridan and Nancy J. Parezo (Tucson: University of Arizona Press, 1996), 130-131.

109. Robert Ferrell and Sudha Iyengar, "Molecular Studies of the Genetics of Non-Insulin-Dependent Diabetes Mellitus." *American Journal of Human Biology*, 5 (1993), 415-424.

110. Ibid., 420-421.

111. J. Walston, K. Silver, C. Bogardus, W.C. Knowler, F.S. Celli, S. Austin, B. Manning, A.D. Strosberg, M.P. Stern, N. Raben, J.D. Sorkin, J. Roth, A.R. Shuldiner, "Time of Onset of Non-Insulin-Dependent Diabetes Mellitus and Genetic Variation in the ß3-Adrenergic-Receptor Gene." *The New England Journal of Medicine*, 333(6) (1995), 343-347.

112. Brian Fagan, *Ancient North America—The Archaeology of a Continent.* (New York: Thames and Hudson, 1991), 394-403.

113. David Wilcox, "Hohokam Social Complexity." In *Chaco and Hohokam*, ed. Patricia Crown and W. James Judge (Santa Fe, NM: School of American Research Press, 1991), 253-275.

114. Harold E. Driver, *Indians of North America*, (Chicago: University of Chicago Press, 1969), 330-334.

115. Neel, *Physician to the Gene Pool.*

116. Bernard L. Fontana, *Tarahumara—Where Night Is The Day Of The Moon.* (Flagstaff: Northland Press, 1979), 104.

117. William E. Connor, Maria T. Cerqueria, Rodney W. Connor, Robert B. Wallace, M. Rene Malinow, and H. Richard Casdorph, "The plasma lipids, lipoproteins, and diet of the Tarahumara Indians of Mexico." *The American Journal of Clinical Nutrition,* 31 (1978), 1131-1142.

118. B. Muneta, J. Newman, s. Wetterall, J. Stevenson, "Diabetes and assorted risk factors among Native Americans." *Diabetes Care,* 16(12) (1993), 1619-1620.

119. Gretchen Chesley Lang, "Diabetics and Health Care in a Sioux Community." *Human Organization,* 44 (1985), 251, 255-257.

120. Paul Zimmet and Pierre Lefebvre, "The Global NIDDM Epidemic: Treating the Disease and Ignoring the Symptoms."