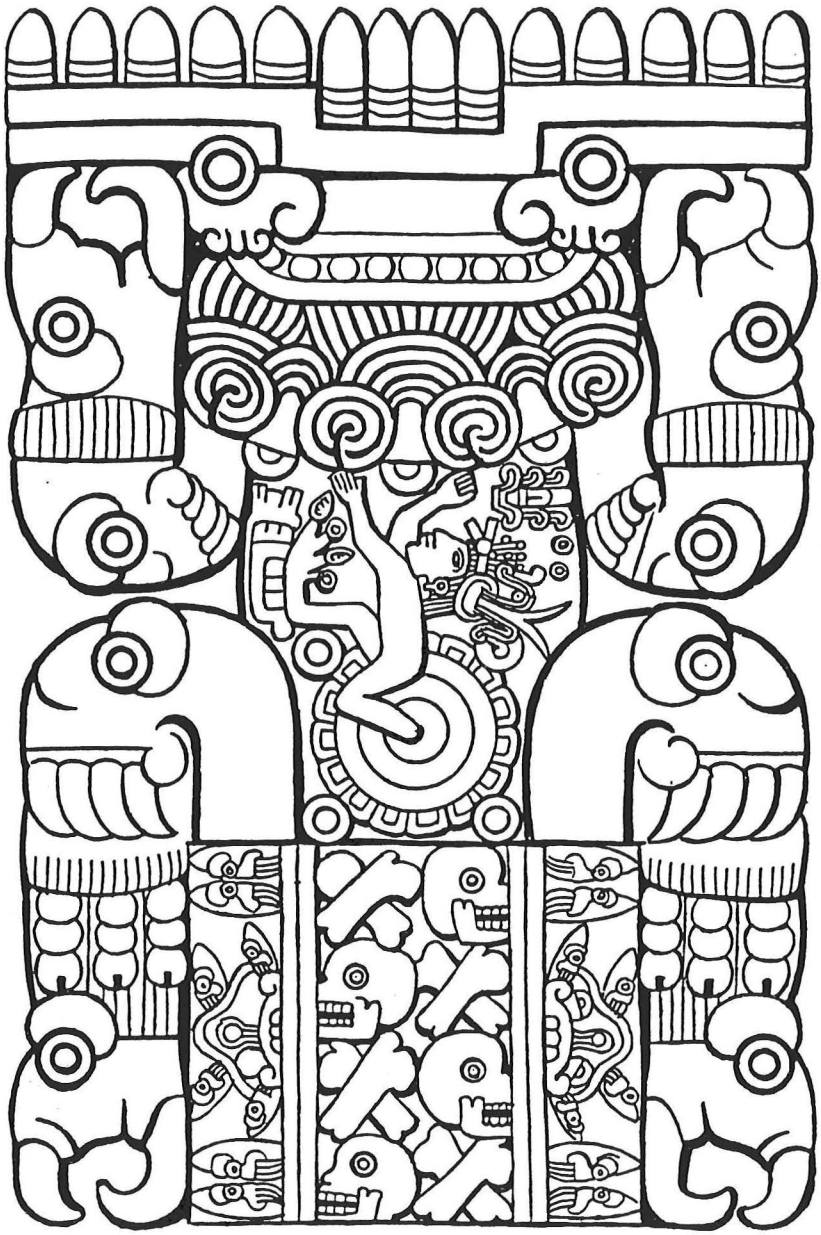
Medical Grand Rounds
John M. Dietschy

UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER



THE ORIGINS, GENETICS AND DISEASES OF

MEXICAN-AMERICANS

ACKNOWLEDGEMENTS

The author wishes to extend special thanks to a number of individuals who provided data and assistance in the preparation of this protocol. These individuals include the following:

Dr. Emöke J. E. Szathmary, Professor and Dean, The University of Western Ontario, for providing both published and unpublished data on the genetic characteristics of major groups of Amerindian, Athapascan-speaking peoples and Eskimo-Aleuts.

Dr. Craig L. Hanis, Center for Demographic and Population Genetics, Houston, for providing both published and unpublished data on the genetic characteristics of Mexican-American populations in Texas.

Dr. Andrew K. Diehl, Department of Medicine, San Antonio, for both published and unpublished data on disease prevalence in Mexican-Americans.

The author also wishes to express his appreciation to a number of anthropologists at the University of California, Berkeley, the Smithsonian Institute, Washington, D.C., and the British Museum, London, for providing advice and opinions concerning a number of controversial issues.

NEW WORLD SYNDROME

Central Obesity

Diabetes Mellitus

Disordered Bile Acid Metabolism

Cholesterol Gall Stones

Carcinoma of the Gall Bladder

In 1984, Dr. Craig Hanis and his colleagues at the Center for Demographic and Population Genetics in Houston defined a constellation of metabolic disorders in Mexican-Americans that they described as the "NEW WORLD SYNDROME". They defined this syndrome as "a cascading sequence of increasingly severe and diverse pathological conditions which begins at a clinically silent level as altered physiology. The sequence is manifest by a tendency, at or shortly after puberty, to become obese and/or to produce lithogenic bile leading to the formation of cholesterol gallstones, and later to develop adult-onset diabetes mellitus. The tendencies to obesity and gallstone formation are especially marked in woman and may be exacerbated by pregnancy. The syndrome is further manifest by the sequelae of obesity and diabetes, and possibly also includes an elevated risk of cancer in some middle digestive system organs apparently due to a variety of physical and metabolic mechanisms."

Earlier in this century a severe form of anemia was identified in American subpopulations of African origin. While it was subsequently determined that this anemia, sickle cell disease, was of genetic origin, it was puzzling how a genetic disorder that produced such severe disease could have become so frequent in the population at risk. Subsequent research demonstrated that the heterozygote for this disorder was resistant to the development of malaria. Thus, in Africa, this hemoglobin trait represented a distinct advantage and was selected for throughout the agricultural population of West Africa. However, when the environment was abruptly changed, i.e., when the West Africans were transported to the New World, this genetic alteration became manifest as a serious disease. Thus, sickle cell disease is taken as a major example of how environment and genetic alteration can interact in powerful ways to alter the well-being of a susceptible population.

Dr. Hanis has postulated that a similar environment-genetic interaction may account for the New World syndrome. In this case it is assumed that one or more genetic alterations occurred shortly after the entrance of man into the New World. Under the environmental conditions that existed for these hunter-gatherer groups, this genetic change was presumably advantageous for survival. However, with the coming of very significant alterations in environmental conditions brought about by social and economic forces after approximately 1940, this same genetic background suddenly became disadvantageous and has lead to the development of obesity, diabetes, gallstones and cancer.

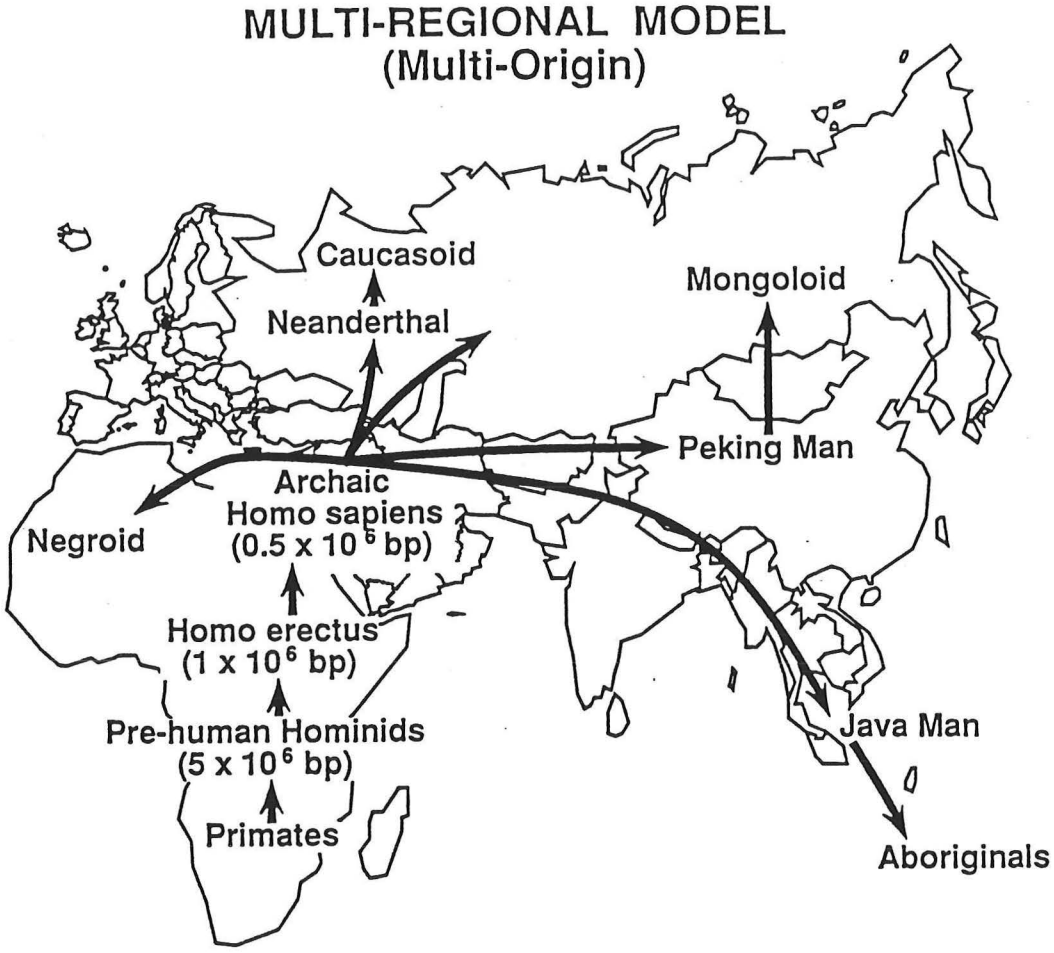


Figure 1

In Texas, the most rapidly increasing minority group is Mexican-Americans. Genetically, these peoples are largely derived from Amerindian and European gene pools. In any given individual, the risk for developing the New World syndrome appears to be directly related to the percentage of Amerindian genes carried by that individual. Since the incidence of these diseases is so common in the Mexican-American population, it is of considerable importance that physicians in this area be cognizant of the genetic background of these people and of the high incidence of these diseases and their effect on the health and welfare of the Mexican-American population.

The purpose of this review, therefore, is two-fold: 1) The most recent archaeological, linguistic and genetic data that describe the origins of the Mexican-American peoples will be presented and 2) The metabolic abnormalities, insofar as they are known, that lead to these specific diseases will be reviewed.

A. ORIGINS OF THE MODERN RACIAL GROUPS

There have been a number of developments within the last few years which have considerably altered our concept of the evolution of the major racial groups of man. The older, conventional view, as illustrated in Fig. 1, suggested that pre-human hominids evolved from lower primates in Africa approximately 5 million years before the present (BP). Homo erectus evolved

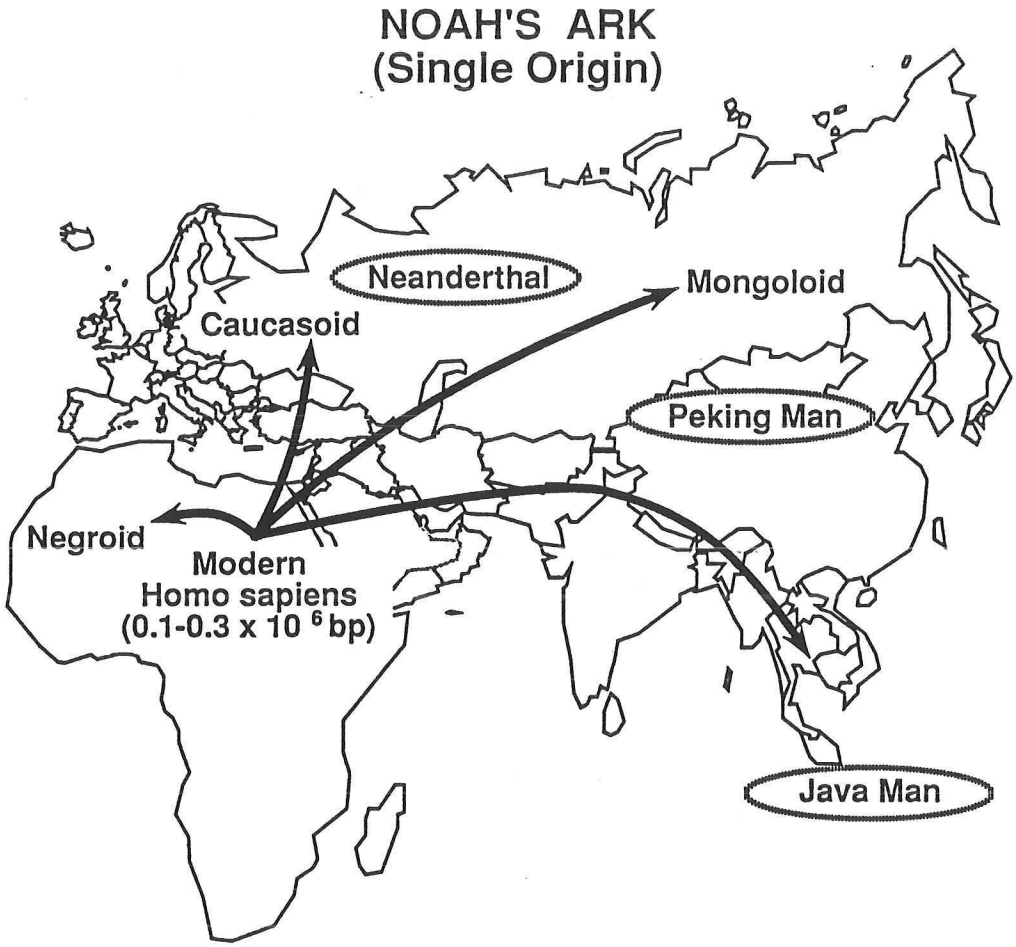


Figure 2

---

from these pre-human hominids approximately 1 million BP and these, in turn, evolved into the earliest forms of modern man, archaic homo sapiens, approximately 0.5 million years BP. These archaic homo sapiens migrated to all regions of the African and Eurasian continents and probably gave rise to the distinct forms of archaic man known as Neanderthal, Peking man and Java man. Each of these archaic homo sapien groups then underwent independent, regional evolution that gave rise to the races of modern homo sapiens classified as negroid, caucasoid and mongoloid, and the aboriginals of Australia. It should be noted that this multi-regional model would require independent evolution towards a common form of homo sapiens since recent data have shown that > 98 percent of the gene pool is the same in all modern humans, regardless of racial derivation.

A series of recent findings has challenged the multi-regional model and suggests that modern homo sapiens evolved in a single location and then spread throughout the African and Eurasian continent. Recent finds in North Africa, for example, have unequivocally established that modern homo sapiens occupied certain sites prior to the time they were occupied by archaic homo sapiens like Neanderthal. Many Neanderthal sites in Europe have now been dated to periods clearly later than the first appearance of modern homo sapiens in North Africa. It now seems established that modern homo sapiens coexisted with archaic homo sapiens like Neanderthal and Peking man for at least 60,000 years. Furthermore, an analysis of mitochondrial DNA suggests that all modern humans were derived from a single source approximately 100,000-300,000 years BP. Thus, the more recent view of human evolution, illustrated in Fig. 2, accepts that archaic homo

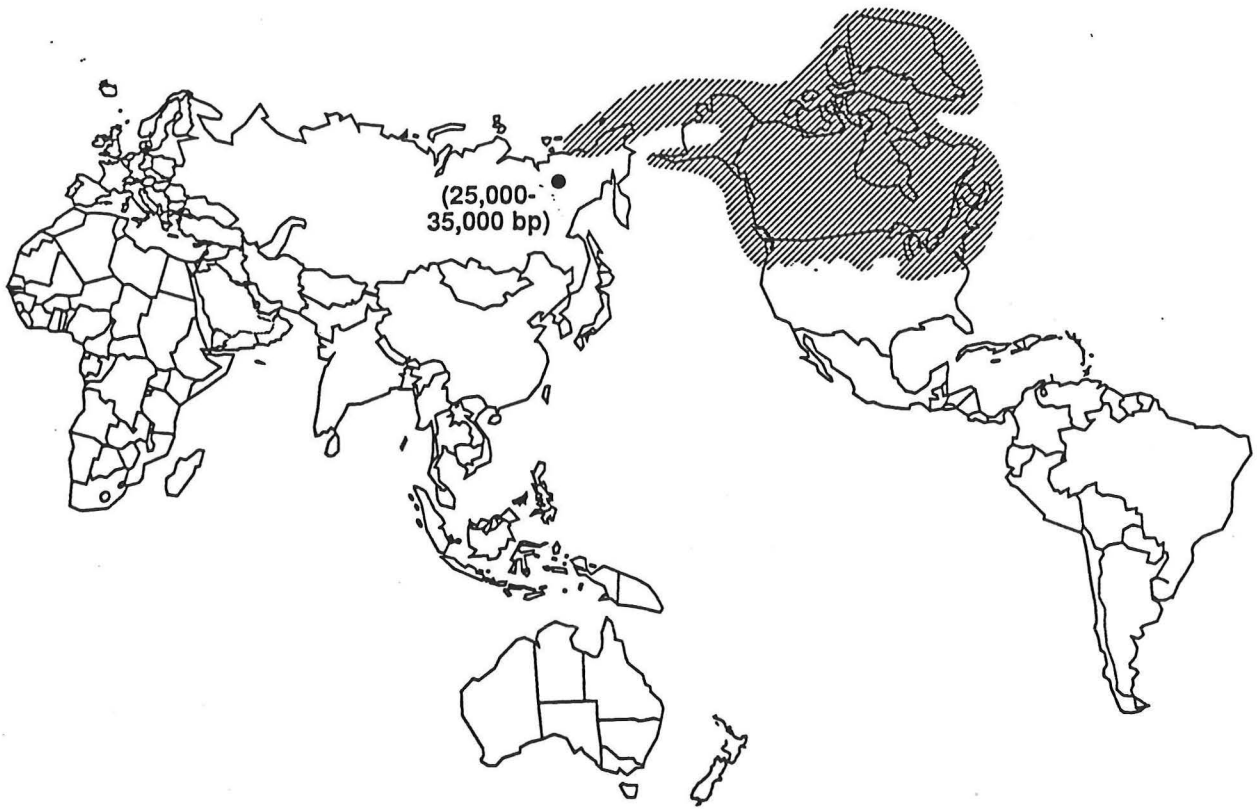


Figure 3

sapiens did evolve in Africa and migrated to various parts of the Eurasian continent. According to this thesis, however, these archaic humans all became extinct and did not evolve into modern man. Rather, modern homo sapiens evolved in Africa (or perhaps further east) only about 100,000-300,000 BP and rapidly spread throughout the African and Eurasian continents. There were then minor regional evolutionary changes resulting in the distinctive racial differences that exist in modern man but, fundamentally, all modern homo sapiens are the direct descendants of a common precursor group. While there is still considerable controversy about the details of this "single origin" model, it now seems likely that it is more consistent with the archaeological and genetic data than the multi-origin model.

Thus, while modern homo sapiens presumably rapidly migrated to thinly occupy the African, Eurasian and Australian continents over the last 100,000-300,000 years there is no evidence that archaic homo sapiens or even the early modern homo sapiens occupied the North and South American continents. While there were reports suggesting human occupation on the west coast of the United States during the last several hundred-thousand years BP, these reports have now been totally discredited. Rather, all modern data suggest that man entered the New World by migrating from far eastern Siberia, across the Bering Straits into what is now Canada (Fig. 3). Since the oldest archaeological dates for human habitation in northeast Siberia are approximately 25,000-35,000 years BP, it seems unlikely that this migration could have taken place prior to this time. Furthermore, during this period of the late Pleistocene a vast ice cap covered North America and acted as a potential barrier to any migration into the New World.

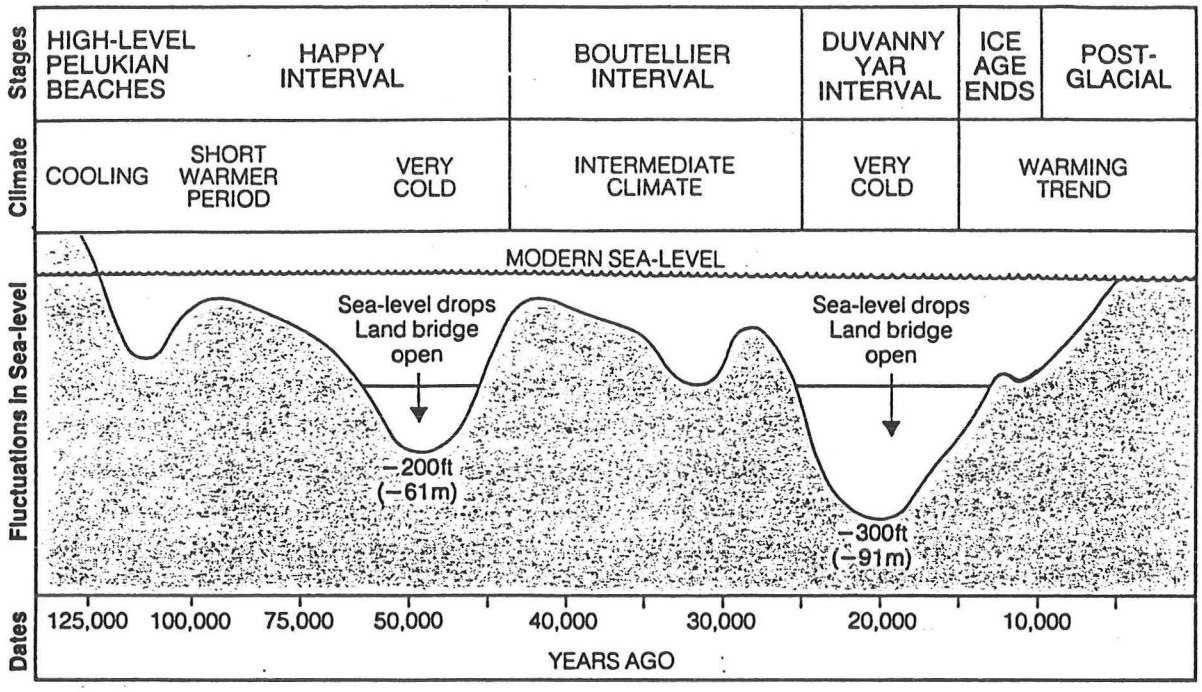


Figure 4

B. MOVEMENT OF MODERN MAN INTO THE NEW WORLD

During the past two years there has also been considerable progress in our understanding of the events that lead to the occupation of the North and South American continents by modern homo sapiens. As modern man migrated northeast across the Asian continent they probably reached far eastern Siberia approximately 25,000-30,000 years BP. Because of the severity of the climate, most ethnohistorians feel there was little likelihood that early man crossed the Bering Straits by sea. Rather, most investigators are convinced that such a migration occurred only during those times when sea levels dropped and a continuous land bridge (Beringia) connected eastern Siberia with what is now Alaska. Fig. 4 shows the periods of time during the late Pleistocene when such a land bridge could have existed. During two periods, 50,000 years and 20,000 years BP, the climate became so cold that large volumes of water were captured in large ice sheets and sea levels dropped 60-90 meters below modern levels. As a consequence, there was a continuous land bridge extending from Siberia to Alaska. Given the fact that archaeological evidence suggests that modern homo sapiens arrived in eastern Siberia only 25,000-35,000 years BP, it seems likely that human migrations into the New World took place only during the more recent ice age. Furthermore, during the coldest part of this ice age, there is geological evidence that the Laurentide and Cordilleran ice sheets fused and totally blocked the potential migratory route south through the MacKenzie Valley. This fusion occurred between approximately 18,000 and 15,000 years BP.

Early in this century, Clovis spear points were found imbedded in the bones of extinct large mammals in New Mexico and provided the first unequivocal evidence for the presence of early man in the New World. Subsequently, many Clovis (and Folsom) sites were found throughout the New World and these were carbon-dated to a very narrow period of time around 11,000-9,000 years BP. Other sites have yielded carbon dates as early as 20,000-34,000 years BP. However, several of these dates have been shown to be artifactual and, in general,

only those radiocarbon dates associated with the Clovis culture are uniformly accepted by archaeologists. Recent linguistic analysis has suggested that all of the indigenous languages in North and South America can be traced to a single precursor language. Furthermore, early studies using mitochondrial DNA suggested that all Indian groups in the New World had been derived from a single genetic population. This conclusion was also supported by a study of dental characteristics. Thus, as of 2-3 years ago all of these lines of evidence gave rise to the concept (Fig. 5) that the Amerindians of North and South America were derived from a single founding group. Presumably these individuals were sophisticated hunters, capable of killing large mammals, who migrated through Beringia some time after the MacKenzie corridor opened about 15,000 years BP. Mathematical modelling suggests that such primitive hunter groups could have thinly populated both North and South America within one millennium. There was also general agreement that two other groups of peoples had migrated into North America much later. These included the Athapascan-speaking peoples who now occupy western Canada and southern Alaska and the Eskimo-Aleut peoples. These latter two groups of immigrates were believed to be linguistically and genetically distinct from the Amerindian populations further south.

Figure 5

Within the past two years, however, a variety of new data have appeared in the literature that have seriously questioned the validity of this model. First, several new archaeological sites have been reported that unequivocally provided radiocarbon dates much earlier than 11,000 BP. At the Meadowcroft Rock Shelter in Pennsylvania, firm dates for human habitation of 16,000 BP have been established and more equivocal dates of 25,000 BP have been suggested. Similarly, in caves at Monte Verde in South America dates of 13,000 BP and earlier have been established. Assuming that primitive peoples would move at an average rate of 10-100 kilometers per generation, these new dates suggest that the major migration must have taken place around 20,000 years BP. Second, the concept that all of the indigenous language groups can be traced to a single precursor language has been severely criticized by a variety of other linguists. Third, mitochondrial DNA studies carried out on a much larger sampling now suggests that the Amerindian population of North America was derived from > 10 maternal lineages. Either the original migratory group contained > 10 unrelated females or, alternatively, there were multiple migrations of unrelated groups into North America. Other findings have even questioned the concept that the

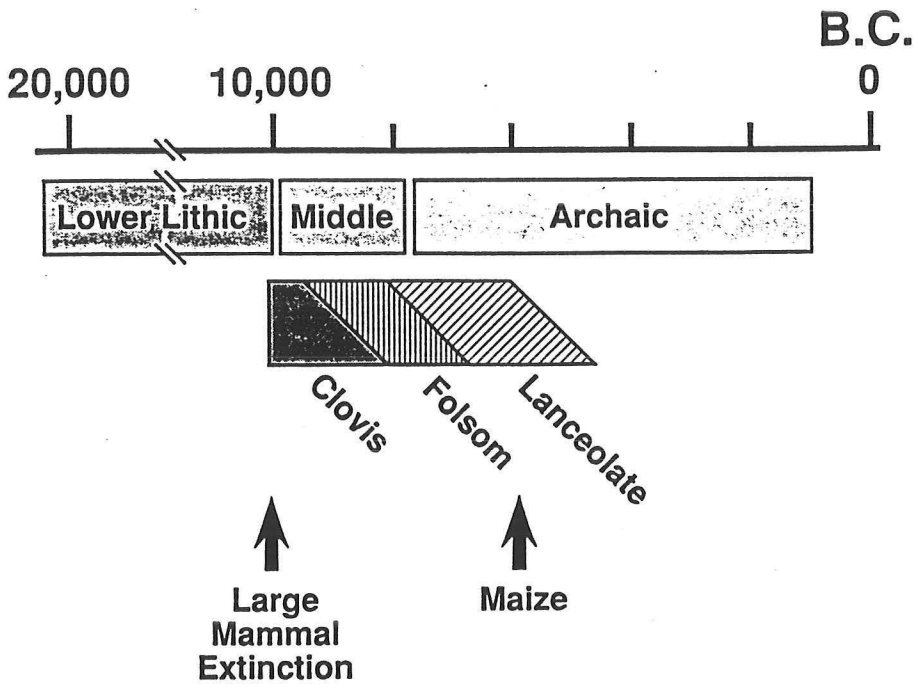


Figure 6

Athapascan-speaking people and Eskimo-Aleuts migrated into the area more recently and are genetically unique. Recent extensive genetic characterization by investigators such as Szathmary have shown that the Eskimo-Aleut are closely related to the Athapascan-speaking people and raises the possibility that the Eskimo-Aleut actually evolved in situ in Northern Canada.

Thus, in the last two years concepts concerning the migration of man into North and South America have changed considerably and were recently reviewed at a consensus conference of anthropologists in Colorado this year. It is now accepted that a major pre-Clovis culture existed in the New World. It now seems likely that multiple-founding bands of hunter-gatherers crossed Beringia just after the beginning of the recent ice age (20,000-25,000 years BP) before the MacKenzie migration corridor was closed by fusion of the Laurentide and Cordilleran ice sheets (18,000 BP). These hunter-gatherers very thinly populated the North and South American continents below the ice sheets. As the ice age ended (15,000-12,000 BP) and the ice sheets receded to the north, there was a dramatic improvement in the climate of North America and an explosion of the hunter-gatherer groups into what has become known as the Clovis and, later, the Folsom cultures. At this same time 31 genera of large herbivores also became extinct. These included such creatures as forest elephants, mammoths, horses and camels. In this scenario it is also postulated that other founding groups migrated from Siberia into Alaska at a later date. Their migration further south was blocked by the coalescence of the ice sheets (18,000-15,000 BP). Thus, these people evolved genetic and linguistic characteristics that were uniquely different from those Amerindians below the ice sheets. Furthermore, elements of this founding group presumably evolved separately into the Athapascan-speaking (Na-Dené) and Eskimo-Aleut peoples.

C. CULTURAL DEVELOPMENT IN MESOAMERICA, THE SOUTHWEST AND THE EASTERN CARIBBEAN

As summarized in Fig. 6, as the glaciers retreated, there was proliferation of the stone age cultures throughout Middle and North American. Because of very favorable climatic conditions, it is likely that the population of these hunter

groups became particularly dense in middle America. About 6,000 BC (8,000 BP) the first archaeological evidence for the domestication of corn (maize) appeared. The ability to cultivate maize, pumpkins, peppers and a variety of other foods set the stage for the development of the first civilizations within this area of the world. The ability of only a portion of the population working only a part of the year to produce large quantities of storable foods made it possible, for the first time, to have massive population growth with the development of administrative, religious and artistic hierarchies. The magnitude of this cultural development, however, varied dramatically in different regions, and, as shown in Fig. 7, these cultural areas are usually divided into the Mesoamerican culture area (the lower half of Mexico and extending into Guatemala), the Southwest cultural area (including northern Mexico and much of present-day New Mexico and Arizona) and the eastern Caribbean.

Figure 7

1) Mesoamerican Cultural Area

By far the most advanced and sophisticated cultural groups in this region of the world developed in Mesoamerica. Geographically, this cultural area included the lower two-thirds of present-day Mexico and extended south into Guatemala. All of the major cultures that developed within this region generally used the ritual 260-day calendar and evolved over a period of nearly 3,000 years, from approximately 1500 BC until the arrival of the Spanish in 1500 AD. While the various Amerindian groups in the southwest cultural zone and in the eastern Caribbean probably had contact with the cultures of Mesoamerican, their respective cultural evolutions remained distinct. By approximately 1500 BC there was probably sufficient development of high-yield agriculture to provide the support for an expanding population base and cultural development.

a) The Olmecs. Once radiocarbon dating became available, it was established that the "mother" culture for many of the subsequent societies was the Olmec culture of the southeast coast of Mexico. This culture arose along the rivers of the rich lowlands in the present states of Veracruz and Tabasco. Little is known about the day-to-day life of these people since nearly all of the artifacts have been destroyed by the hot and humid climate. Nevertheless, these people raised major ceremonial centers at locations such as San Lorenzo, La Venta and Tres Zapotes. These were almost certainly ceremonial centers devoted to religious practices and not "cities." It is now recognized that this society was probably the first to construct pyramids, create portraits, make

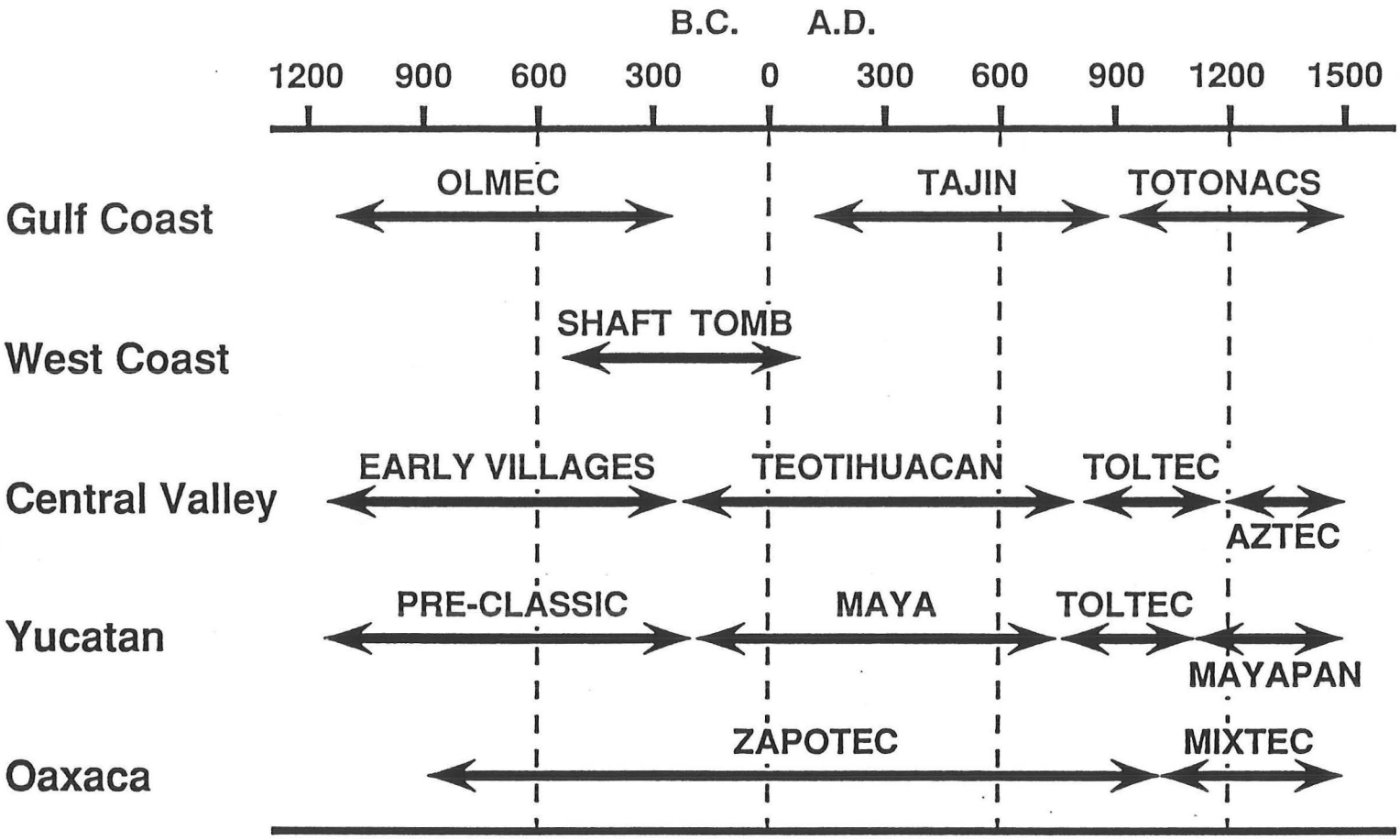


Figure 8

---

mirrors and bring into use a calendrical system. They produced several types of very sophisticated artwork including elegant jade effigy figures, monumental stone portraits and very sophisticated, three-dimensional stone figures. The figures often represented deities and, indeed, many of these gods were carried forward into other cultures. It is also now clear that the Olmec culture probably profoundly influenced the subsequent development of high cultures in other regions of Mexico. By 600 BC, for example, there is evidence of Olmec influence on the west coast of Mexico in the state of Guerrero and extending southward towards Costa Rica. Clear Olmec influence is also found in many of the figures produced during this era in the central valley of Mexico at villages such as Tlatilco. There is also evidence that the Olmecs had extensive interactions with the peoples of the Yucatan and in the Guatemalan highlands where artifacts have been found in graves that clearly contain Olmec symbols. While this society declined and essentially disappeared about 100 BC, this culture clearly played a critical role in the development of other Amerindian groups throughout lower Mexico and Guatemala.

b) Shaft Tomb Cultures of West Mexico. One of the regions of Mesoamerica that apparently did not come under Olmec influence in the first millennium BC was the Shaft Tomb cultures of the central western Mexican coast. These cultures were presumably built around farming and fishing communities and never developed monumental architecture of any note. Their culture is primarily known for the elegant terra-cotta figures that were made throughout the region and left as offerings to the dead in complex Shaft-Tomb structures. This cultural area is generally divided into several areas having distinctly different types of pottery and these areas include Colima, Jalisco and Nayarit. In addition,

many excellent stone pieces have also been recovered from the Mezcala River region. Most of these pieces are now thought to have been made between approximately 500 BC and 100 AD.

c) Classical Period. As the Olmec culture began to decline around 200-100 BC there is archaeological evidence that dense populations were developing throughout the Mesoamerican region. These various populations developed major religious and administrative centers with high levels of architectural and artistic achievement. This era, which is generally dated between approximately 100 AD and 800-900 AD, is referred to as the Classical Period. In the valley of Oaxaca the Zapotec people developed major ceremonial centers at locations such as Monte Alban. To the south major cities and ceremonial centers were being developed by the Maya both in the Yucatan and in the highlands of Guatemala. Along the Caribbean coast major, separate cultures developed in the region of Veracruz and Remojadas. In the central valley of Mexico many major cities evolved but the dominant society came to reside in Teotihuacan. There is abundant archaeological evidence to suggest that these different "power-centers" behaved much as the city-states of northern Italy during the Renaissance. There must have been abundant commercial trade, artistic exchanges, governmental interactions and occasional wars. For reasons that are not at all clear, these great city-states went into decline, essentially at the same time, towards the end of the first millennium AD. Teotihuacan went into decline probably from over-population of the valley with deforestation, soil erosion and drought. It was ravaged and burned about 650 AD, probably by surrounding tribes that had been subjugated. The other major ceremonial centers persisted for another century or so and then also went into decline. Nevertheless, very dense populations of Amerindians remained throughout these regions even though the centers of art, religion, architecture and government were disappearing.

d) Post-classical period. Following the decline of the major city-states of the classical period, new peoples moved into the various valleys from the north and established new cultures. In the valley of Oaxaca the Mixtec superceded the Zapotec culture and took over many of their ceremonial centers. In the valley of Mexico the Toltecs migrated down from the north in the tenth century to establish a capitol at Tula and to occupy several old Mayan cities in the Yucatan such as Chichen Itza. In the mid-1300s another northern tribe moved into the central valley of Mexico and eventually established a major city at Tenochtitlan. For the next 150 years these Aztec peoples were more-or-less constantly at war expanding the size of the empire eastward to the Veracruz coast and southward towards Guerrero. However, on November 8, 1519, the Spanish entered Tenochtitlan and independent development of the Mesoamerican culture essentially ceased.

2) Southwest Cultural Area

Cultural development north of the Mesoamerican area was far less sophisticated. Archaeological evidence suggests that the practice of cultivating maize reached this region approximately 3000 BC. Undoubtedly, this practice arose through contact with the more advanced civilizations to the south. Unlike Mesoamerica, the high deserts of northern Mexico and the southwestern United States were less able to support luxuriant agricultural development. Consequently, population density was considerably lower, as was cultural development. Nevertheless, significant cultural development with distinctive

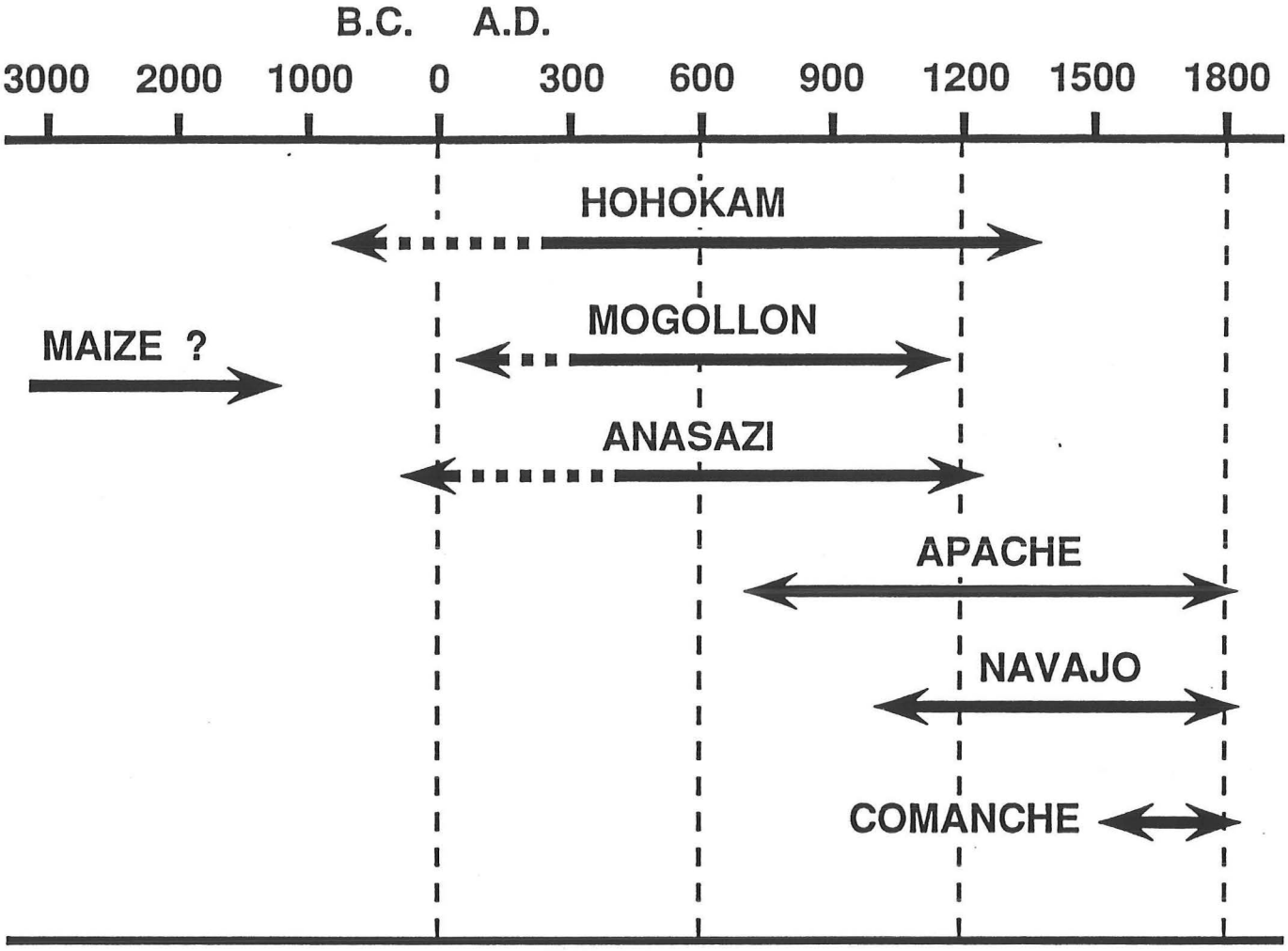


Figure 9

artistic and religious characteristics did evolve in this region of the continent.

a) The Hohokam Culture. It is likely that paleo-indians migrated into the region of the Gila River basin, perhaps from Mexico, around 300 BC. Despite the very severe climate of this region of Arizona, these peoples became fairly successful desert farmers and craftsman. They established several communities consisting of shelters with upright wooden walls and thatched roofs. Primitive irrigation systems were developed to draw water from the Gila River onto the surrounding plains where agriculture was carried out. Apparently these Hohokam peoples maintained cultural contacts with the Mexican cultures and so gained access to the technology of weaving and pottery construction. By approximately 1450 AD, the culture was in decline and many of the communities were abandoned. Nevertheless, it is possible that this ancient culture gave rise to some of the present day southwestern tribes including the Papago and Pima Indians.

b) The Mogollon Culture. The Mogollon culture arose in a similarly arid region of the southwest, eastern Arizona and southwestern New Mexico and extending down into the dry deserts of Chihuahua. These people probably were derived from an ancient group of hunter-gatherers called the Cochise culture. These people also acquired the agricultural knowledge to cultivate corn and also there is archaeological evidence that they collected a variety of wild grasses, nuts and plant bulbs. They lived in relatively primitive communities in pit

houses. While there were several periods of decline (500 AD and 1100 AD) the culture persisted until approximately 1250 AD. This demise may have been brought about by progressive drought and other climatic changes or by increasing pressures from the adjacent Hohokam and Anasazi cultures. Archaeological evidence suggests that these ancient peoples may have given rise, at least in part, to the contemporary Zuni, a unique group of Pueblo Indians who belong to the Penutian language family.

c) The Anasazi Culture. A third group of paleo-indians settled in the high desert of the Colorado plateau in northern Arizona and New Mexico and southern Utah and Colorado. This was a land of deep canyons and a hot and arid climate. By 700 AD the Anasazi communities had developed dry-land farming techniques and built rather elaborate dwellings in sheltered areas of the steep canyons. They also developed unique weaving and pottery styles that set them apart from the other southwestern cultural groups. In some regions they developed complex, multi-roomed pueblos such as found at Chaco Canyon. About 1200 AD there is evidence for progressive climatic change that may have forced the abandonment of many Anasazi communities. In addition, it is also possible that both the Mogollon and Anasazi peoples came under increasing pressure from the Apache, who migrated into this region at about this time. Nevertheless, it is likely that the modern Keresan-speaking Indians who occupy seven of the pueblos (including the one at Acoma) near the Rio Grande River in New Mexico are derived from the ancient Anasazi. Further to the west, it is also apparent that many of the weaving traditions of the Anasazi were passed to the modern people occupying the Hopi and Zuni pueblos. It should be noted that the Hopi and Zuni may well have been derived jointly from both the Anasazi and Mogollon traditions.

d) The Apache. The Apache clearly arose outside of the southwest cultural region and, indeed, are Athapascan-speaking peoples. It is now believed that a band of these people from western Canada began migrating southward along the eastern slope of the Rocky Mountains as early as 800 AD. These were a nomadic people who hunted and gathered food from the countryside. They raided the farming villages of the early pueblo people and very likely brought considerable pressure upon the peoples of the late Mogollon and Anasazi cultures. As the Apache spread throughout the southwest region from southern Texas through New Mexico and into Arizona, they developed significant genetic heterogeneity and often acquired the cultural characteristics of other societies that they came into contact with. Thus, the Lipan Apaches raised dogs to eat as did their southern neighbors. In the Oklahoma region, Apache bands came to live close to the Kiowa as the Kiowa-Apache. In the west, some bands of Apaches learned farming techniques from the pueblo peoples. Once they acquired the horse from the Spanish in the late 1600s, they became much more efficient raiders and continued to harass the surrounding tribes as well as Spanish settlers to the south (Western, Chiricahua and Mescalero Apaches).

e) The Navajo. Like the Apache, the Navajo are derived from the Athapascan-speaking peoples of western Canada. They are believed to have migrated southward into the Four-Corners region, however, much later than the Apache. This migration may have taken place some time between 1000 and 1200 AD. Like the Apaches, the Navajos survived in the dry environment as nomadic bands of hunter-gatherers. They also launched raids on the agricultural pueblos for food, property, women and slaves. Through prolonged contact with the Pueblo peoples, however, they gradually acquired new cultural traits including skills

in agriculture, pottery making and weaving. When the Spanish introduced sheep and goats, they became skilled herdsmen. Once they acquired the horse, they, like the Apaches, were able to extend their raiding activities to a far greater area.

f) The Comanche. The Comanches were very late arrivals in the southwest cultural zone. They speak a dialect of the Uto-Aztecan language group. It is believed that they were a band of, or at least closely related to, the Shoshone but broke away and began to migrate south along the eastern slope of the Rocky Mountains in the early 1600s. By the late 1600s they had gained use of the horse and developed into perhaps the most skilled horsemen of any Native American group. The horse became the measure of wealth of a given band and both young boys and young girls were taught riding skills. It is likely that the Comanche migrated south in order to be nearer the source of additional horses in the Spanish ranches of north Mexico. In 1719 the Comanches passed through what is now Kansas. Over the next century they moved into Texas, eastern New Mexico, western Oklahoma and as far south as northern Mexico. They were efficient and skillful raiders and attacked any settlement (Indian, Mexican or Texan) from which they could acquired horses, slaves and other useful booty. They were so fierce that even the Apache were forced out of these areas.

3) Caribbean Cultural Area

The islands of the eastern Caribbean were apparently originally inhibited by a group of people known as the Arawak Indians. Several thousand years ago these people migrated from Venezuela through Trinidad northward using seagoing canoes and rafts. Over many hundreds of years they gradually worked their way north, and occupied the Windward Islands, the Leeward Islands, Puerto Rico and, finally, Hispaniola and Cuba. These people lived by exploiting sea and shore resources and their major artifacts were large ocean going canoes. Approximately 1000 AD a second group of Indians began to migrate into the lesser Antilles from Venezuela. These were a more aggressive group of people known as the Carib Indians. For these people warfare was apparently a basic principle of social organization. Over hundreds of years they slowly moved north through the Windward Islands subduing the indigenous Arawak: they would generally kill and eat the men but would keep the women as wives. In this manner much of the ancient culture of the Arawak has been preserved. With the coming of the Spanish, the Indian populations of the Caribbean Islands were decimated, either through direct conflict with the Spanish (the Carib Indians) or through the spread of European diseases. As a consequence, when the Spanish began to establish large plantations on these islands it was necessary to import large numbers of West African slaves.

4) Summary of the Genetic Background of the Amerindian Populations

From these very brief descriptions of the major cultural developments in the southwestern United States and in Mesoamerica, it is apparent that there are very complex relationships between the various immigrant groups. This can be seen, for example, by looking at the distribution of the major modern Indian languages (Fig. 10). Mesoamerica contains a number of different language groups that generally follow the geography of the development of the regional empires. The Uto-Aztecan language family includes many of the tribes in western Mexico and the western United States and emphasizes the close relationship between such diverse tribes as the Shoshone, Panamint, Pima and Papago and the Aztecs and

Figure 10

PARTIAL LIST OF NORTH AND SOUTH AMERICAN INDIAN LANGUAGES

PHYLUM I: AMERICAN ARCTIC-PALEO-SIBERIAN
A. Eskimo-Aleut Family

PHYLUM II: NA-DENE
A. ATHAPASCAN FAMILY
1. Dogrib, Saschutkenne, Hare
2. Chipewyan, Slave, Yellowknife
3. Hupa
4. Navajo
5. San Carlos Apache
6. Chiricahua Apache, Mescalero Apache
7. Jicarilla Apache
8. Lipan Apache
9. Kiowa-Apache

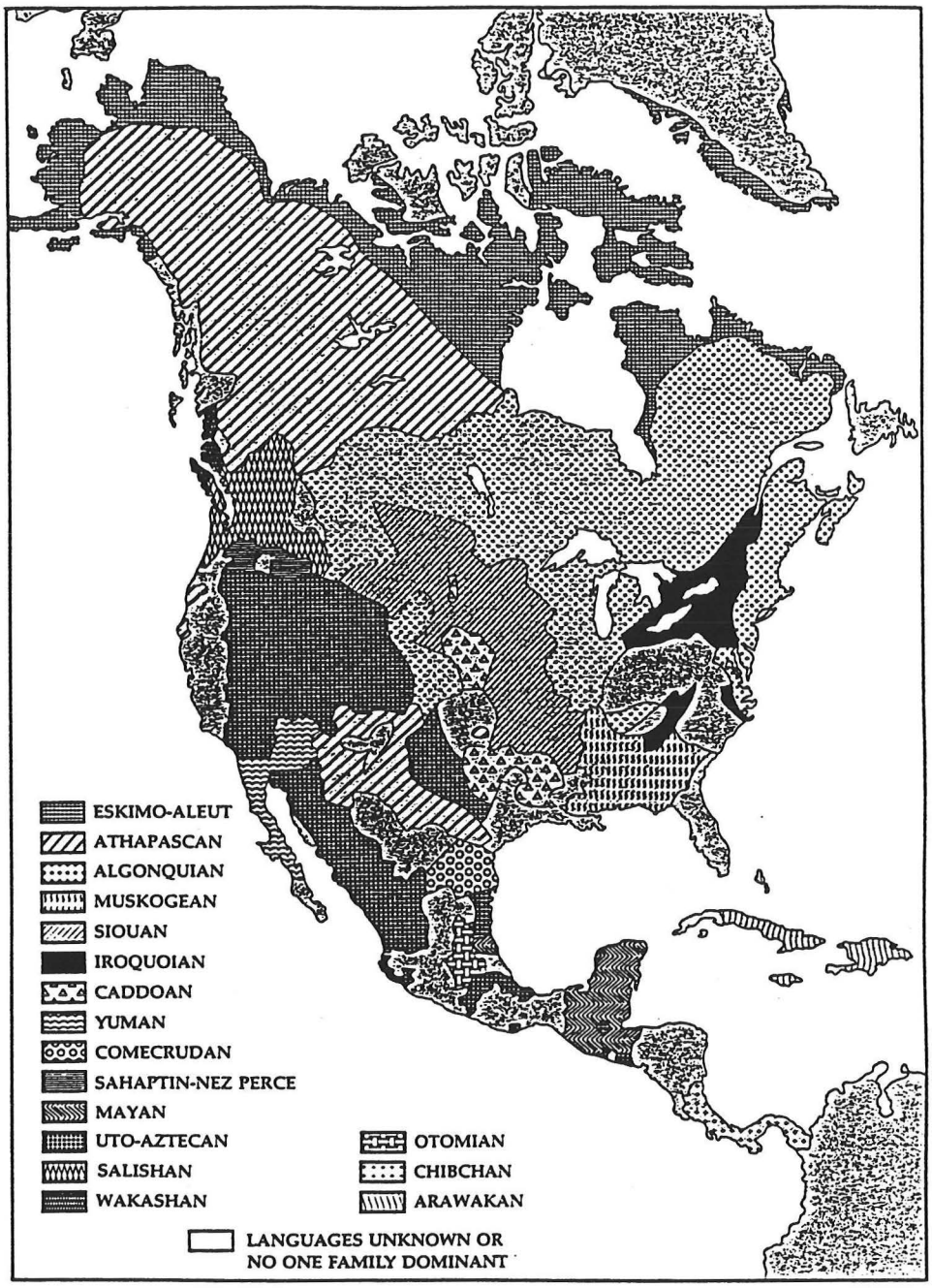
PHYLUM III: MACRO-ALGONQUIAN
A. ALGONQUIAN FAMILY
1. Blackfoot, Piegan, Blood
2. Cheyenne
3. Arapaho, Nawunena, Atsina

PHYLUM IV: MACRO-SIOUAN
A. SIOUAN FAMILY
1. Mandan
2. Omaha, Osage, Ponca, Quapaw, Kansa
3. Sioux (Dakota)

PHYLUM V: HOKAN
A. YUMAN FAMILY
1. Upland Yuman (Hualapai, Havasupai, Yavapai)

PHYLUM VI: PENUTIAN
A. MAYAN FAMILY

PHYLUM VII: AZTEC-TANOAN
A. KIOWA-TANOAN FAMILY
B. UTO-AZTECAN FAMILY
1. Shoshoni, Gosiute, Wind River, Panamint, Comanche
2. Hopi
3. Pima, Papago
4. Tarahumara
5. Nahuatl



3.34 DOMINANT LANGUAGE FAMILIES. *After Driver and Massey.*

GROUP VIII: UNDETERMINED PHYLA AFFILIATIONS

PHYLUM IX: OTO-MANGUEAN

PHYLUM X: MACRO-CHIBCHAN

PHYLUM XI: GE-PANO-CARIB

PHYLUM XII: ANDEAN-EQUATORIAL

Toltecs. As is also apparent in this figure, however, there is a large island of Athapascan-speaking Indians (the Apache and Navajo) widely separated from their parent tribes in western Canada and Alaska.

Nevertheless, there are several generalities that can be made concerning the genetic homogeneity (or lack thereof) in the Amerindian population of North and Central America in general, and in the southwestern United States and Mexico, in particular. First, while archaeological evidence now supports the thesis that there were multiple waves of immigration into the New World, all of these immigrant groups came from a fairly localized area (eastern Siberia). Thus, it would be reasonable to assume that all peoples derived from these original immigrant groups are of similar genetic background. There are at least two sources for potential variation, however, that are apparent from these archaeological considerations. First, there must have been significant gene drift as the Eskimos-Aleut and Athapascan-speaking peoples underwent independent evolution north of the Laurentide and Cordilleran ice sheets. These particular genetic variations were then reintroduced into the Amerindians of the southwest through migration of the Navajo and Apache peoples. Secondly, at a more local level it is clear that additional gene drift took place when segments of a population became isolated by geography or outside pressure and so underwent independent evolution. Such subtle genetic variation can now be detected in the different bands of Apaches, that were widely separated across the southwestern United States, and the Papago, that were separated because of constant pressure from the Apaches. Countering this type of genetic drift, however, was the constant flow of genes between the different cultures through constant warfare and the taking of hostages and slaves.

D. THE INTRODUCTION OF CAUCASOID AND NEGROID GENES INTO THE AMERINDIAN AND NA-DENE GENE POOLS

While there is considerable controversy as to the size of the Amerindian populations in the New World at the time of first contact with Europeans, estimates as high as 90-112 million have been made (Henry Dobyns). Various anthropologists have estimated that the pre-contact population of the Inca empire alone was of the order of 14-30 million and the number of individuals living in the densely populated Mesoamerican cultural area may have far exceeded this figure. Since the number of Spanish and other European groups that eventually settled in this region was small relative to these numbers of Amerindians one might anticipate that modern Mexican populations were derived primarily from Amerindian genes. This turns out not to be the case, however, since there is now abundant data that the population of Amerindians was drastically reduced in the New World shortly after contact with the Europeans. Furthermore, modern scholarship now indicates that this reduction was not brought about by the hostile activities that took place during the subjugation of the Indian populations by the Spanish, but rather it occurred because of the introduction of Western diseases into these immunologically naive New World inhibitants. These diseases included typhus, influenza, measles and, above all, smallpox. There are many historical recordings of the disastrous effects of these diseases on Amerindian populations throughout North and South America. In 1493 and 1495, only a few years after the initial contact with Europeans, the Arawaks of the eastern Caribbean was essentially exterminated by an epidemic that sweep from island-to-island. Early settlers in New England described epidemics of smallpox that essentially destroyed whole communities of Algonquians. Later, in the 1630s and 1640s this epidemic killed essentially 50

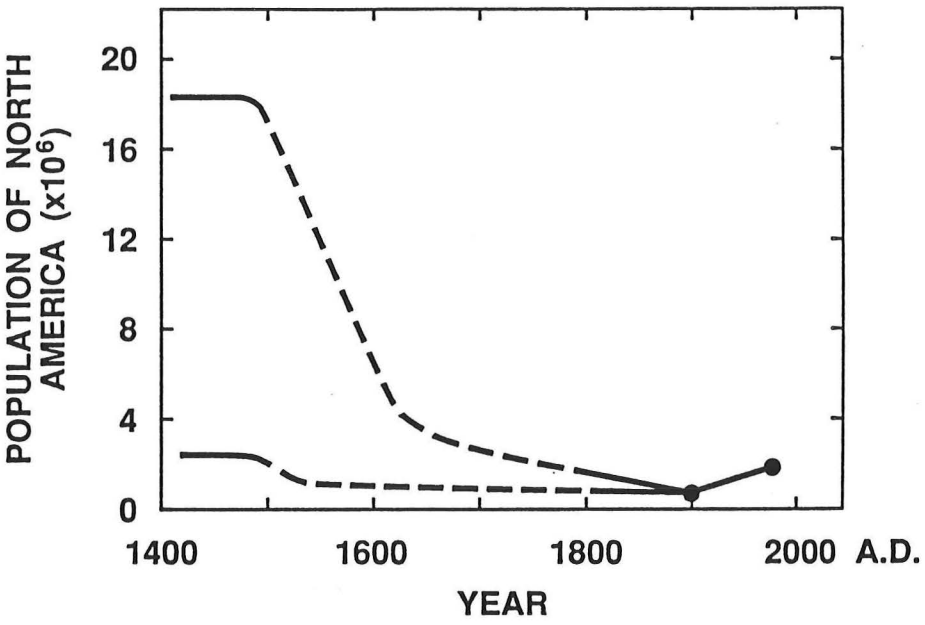


Figure 11

percent of the Huron and Iroquois confederations. In the early 1700s Jesuit and Mennonite missionaries recorded the widespread destruction of Cherokees and Catawbas by smallpox and, later, nearly two-thirds of the Omahas. It must be recognized that at the time of the first European contact with the Amerindians diseases like smallpox were endemic in the major cities of Europe. In London, for example, 80 percent of the cases of smallpox were said to occur in children under the age of two years. Thus, those children that survived these endemic diseases acquired life-long immunity. The Amerindians, in contrast, had had no prior experience with these Old World viruses and so attack raids as high as 50-90 percent were recorded in communities in the New World once a particular virus was introduced.

Over the past ten years, a new theory has been evolved by anthropologists suggesting that a massive epidemic of disease was touched off in the New World shortly after the first contact with the early European explorers. According to this thesis, these diseases spread inland along natural trade routes and essentially depopulated the entire North, Central and South America continents. Thus, when European explorers began to penetrate the interior of the continents they found an essentially empty countryside with only small, scattered tribes of indigenous peoples. There is now considerable evidence that this theory is correct. For example, smallpox was introduced into the Caribbean in 1518. Apparently this disease rapidly spread throughout middle America ahead of the Spanish invasion. A smallpox epidemic raged for 70 days in Tenochtitlan one year before Cortez entered the capitol of the Aztecs. Similarly, a major smallpox epidemic apparently killed nearly half of the Inca two years before Pizarro arrived. When DeSoto traveled through the southeastern United States, he described dense populations of Indians with major ceremonial centers (the Mississippian culture). Archaelogical evidence now indicates that these cultures abruptly came to an end in the 1500s and when Europeans began to immigrate into this region 200 years later they found an essentially empty land. When George Vancouver explored the far northwestern coast of the United States in the late 1700s, he found the beaches covered with human bones as if most of the population had died suddenly. The few remaining Amerindians had pockmarked faces. Thus, there is no longer any controversy among anthropologists that this massive post-contact kill-off of the Amerindian population of the Americas took place. The only controversy that is now going on concerns the magnitude of this kill-off. As summarized in Fig. 11, the Amerindian population of North America reached a low of approximately 500,000 in the year 1900. Estimates of the pre-contact populations vary from approximately 2.5 to 18 million. Thus, depending upon which figure one selects, from 80 percent to 97 percent of the Amerindian population in North America was probably killed by disease in the 100-200 years after initial contact with the Spanish and before major migration

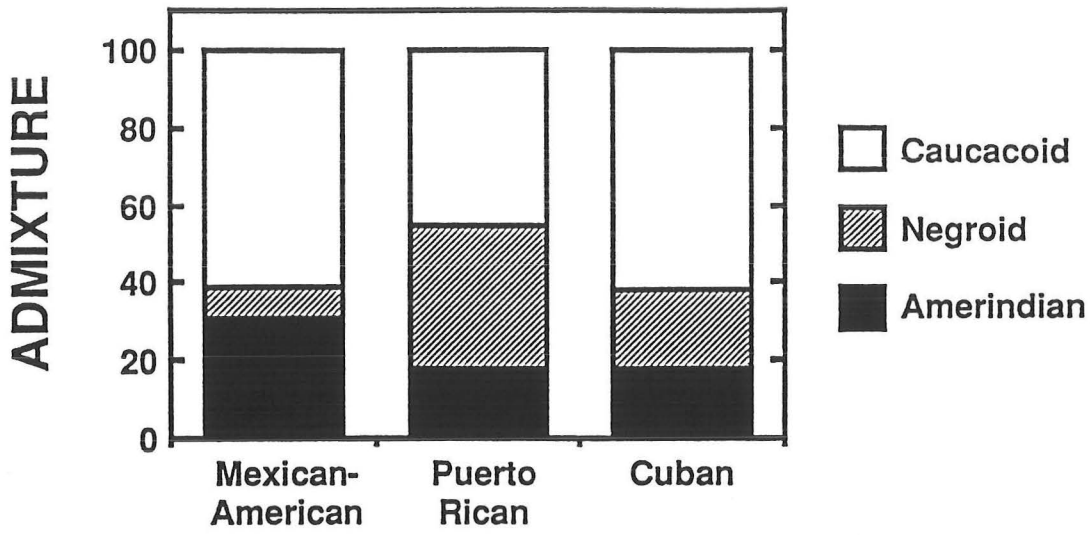


Figure 12

---

of Europeans into the central and western United States occurred. Similarly, massive kill-offs undoubtedly occurred in Mesoamerica and in South America where, for example, it has been estimated that 90-95 percent of the Inca population had died by the year 1600. Thus, with this massive kill-off of the indigenous population, the migration of Spanish and other European groups into Mexico during the Spanish-Colonial period would make it likely that Caucasoid genes would make up a major portion of the current gene pool in Mexico. Similarly, because of the nearly complete extermination of the Amerindian populations in the eastern Caribbean and the importation of large numbers of West Africans it is to be anticipated that the modern peoples of Puerto Rico, Cuba and the other Caribbean islands would be primarily derived from Caucasoid and Negroid gene pools.

Using modern genetic markers it is now possible to characterize a given population of people with respect to their ancestral origins. Essentially, these methods involve characterizing the gene frequencies in a large population sample for a variety of proteins including various red cell antigens, tissue enzymes or plasma carrier proteins. If the gene frequencies for these various polymorphic proteins are known, it is then possible to determine what percentage of genes in the population of interest was derived from the ancestral populations. Furthermore, when a whole battery of such determinations is made in each individual (up to twenty different measurements) it is also possible to calculate the probability that a particular allele selected at random in an individual is derived from a particular ancestral population.

As illustrated in Fig. 12, when such measurements are applied to the three major Hispanic groups in the United States, very different admixture profiles are seen. In Mexican-Americans, approximately 61 percent of the gene pool is Caucasoid, 31 percent is Amerindian and 8 percent is Negroid. It should be emphasized that this distribution of genes reflects that found in Mexican-Americans who have immigrated to southern Texas. Very limited data available from Mexico indicates, as expected, that very isolated areas have much higher Amerindian admixtures while higher socio-economic groups in the cities have less. Nevertheless, this admixture data is appropriate for those Mexican-Americans seen in the Texas health-care systems. In both Puerto Ricans and Cubans, the admixture of Amerindian genes is significantly less while the proportion of genes derived from West Africans is very much higher. Again, it

TABLE I

DIABETES IN AMERICAN INDIANS AND OTHER NATIVE POPULATIONS OF THE NEW WORLD

HIGH RATES

Cherokees (North Carolina)
Alabama-Coushattas (Texas)
Choctaws (Mississippi)
Choctaws (Oklahoma)
Kiowas (Oklahoma)
Comanches (Oklahoma)
Pimas (Arizona)
Papagos (Arizona)
Yumas (Arizona)
Hualapis (Arizona)
Havasupis (Arizona)
Cocopahs (Arizona)
Chemehuevis (California)
Pawnees (Oklahoma)
Seminoles (Oklahoma)
Seminoles (Florida)
Washoes (Nevada and California)
Paiutes (Nevada and California)
Caddo (Oklahoma)
Senecas (New York)
Winnebagos (Nebraska)
Maricopas (Arizona
Omahas (nebraska)
Mojaves (California)
Sioux (Montana and Dakotas)
Assiniboines (Montana)
Passamaquoddy (Maine)
Cherokees (Oklahoma)
Creeks (Oklahoma)
Chickasaws (Oklahoma)
Cheyenne-Arapahos (Oklahoma)
Osages (Oklahoma)
Sauk-Foxes (Oklahoma)
Kickapoos (Oklahoma)
Shawnees (Oklahoma)

LOW RATES

Eskimos
    Eastern and Western Greeland
    Eastern, Central and Western Canada
    Alaska
Navajos (Arizona)
Hopis (Arizona)
Apaches (Arizona)
Western Shoshones of Nevada
    (1954 report only)
Chippewas (North Dakota)
Athapascan Indians
Canada
Alaska

should be emphasized that these proportions reflect those individuals who have immigrated to the United States. Within the different regions of the Caribbean it is possible to find sub-populations that vary from almost 100 percent Negroid to 100 percent Caucasian. Individuals who have a high proportion of Amerindian genes, however, are very uncommon in this region.

The importance of these admixture data is that the incidence of the various clinical diseases associated with the NEW WORLD SYNDROME is directly related to the proportion of Amerindian genes carried by a particular population. For example, the prevalence of Type II diabetes in Pima Indians (> 90 percent Amerindian genes) is 50 percent, in Cherokees (65 percent Amerindian genes) is 30 percent and in Mexican-Americans (30-35 percent Amerindian genes) is 10-15 percent. Thus, in general, the incidence of the various diseases in the NEW WORLD SYNDROME in any particular sub-population seems to be related directly to the prevalence of Amerindian genes in that particular population. There is also

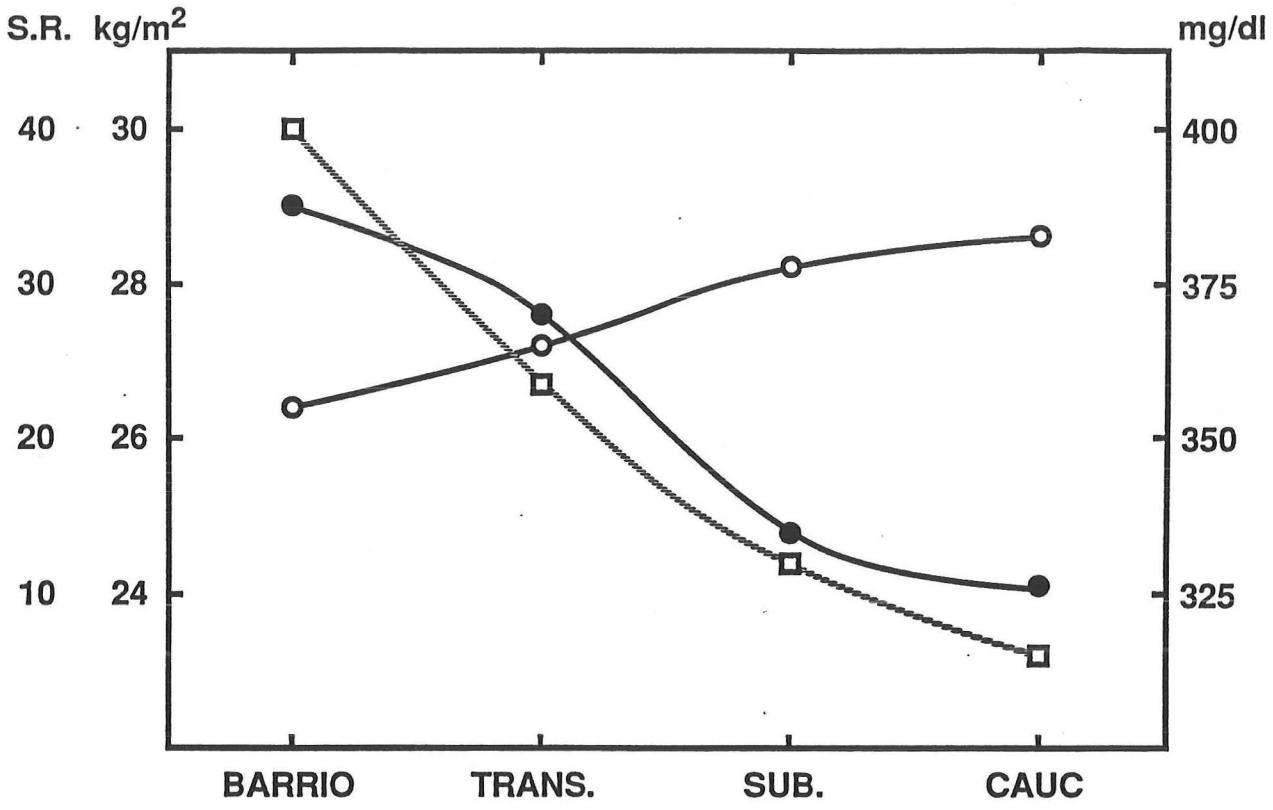


Figure 13

data suggesting that the paleo-Indian groups that entered North America later (or evolved separately) do not carry the genes that make them susceptible to this particular set of diseases. As shown in Table I, for example, the incidence of Type II diabetes appears to be very high in many American-Indians groups who carry a very high percentage of Amerindian genes. This includes tribes that are widely distributed in the country but that were all derived from Amerindians. In contrast, much lower rates of diabetes have been reported in contemporary population groups that ultimately evolved from either the Eskimos-Aleuts or the Athapascan-speaking peoples of Western Canada.

Not only does disease incidence in a whole population reflect the abundance of the Amerindian gene pool, but a similar relationship exists for sub-groups within the parent population. For example, as illustrated in Fig. 13, in studies from San Antonio it has been shown in Mexican-Americans that disease incidence directly reflects Amerindian gene content. Furthermore, these studies also demonstrate that skin reflectance can be used as a indirect measure of Amerindian gene prevalence. Thus, as illustrated in this figure, the poorest people living in the barrios had, on average, darker skin and a high percentage of Amerindian genes (about 46 percent) and a high incidence of obesity and glucose intolerance. In contrast, Mexican-Americans living in the suburbs had a greater skin reflectance, a lower complement of Amerindian genes (18 percent) and a lower incidence of obesity and glucose intolerance. Thus, not only does the percentage of genes derived from the ancestral Amerindian group determine the incidence of disease in a whole population but apparently this same relationship exists with respect to sub-groups (or even the individual) within that whole population. While the genetics of skin color are probably complex, the relationship between skin color and Amerindian genes in the Mexican-American population should be emphasized: darker skin implies a higher incidence of those diseases associated with the NEW WORLD SYNDROME.

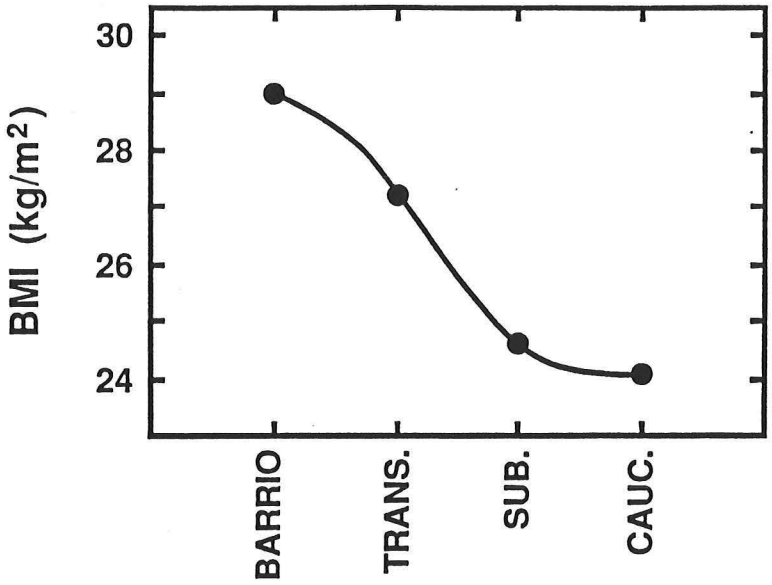


Figure 14

E. THE MAJOR SPECIFIC DISEASES OF THE NEW WORLD SYNDROME

Thus, from these various studies it is apparent that Texans of Mexican-American ancestry have approximately 30-35 percent of their genes derived from the Amerindian ancestoral group. It is also apparent that within this population there is significant variation in these admixture figures. It is now possible to relate the incidence of specific diseases to these percentage figures for Amerindian admixture.

1) Central Obesity

One of the very common associations with Amerindian gene content is centralized obesity. One common parameter of body size that is utilized in population studies is the body-mass index (BMI) which expresses body weight (in kg) as a function of height (m^2). In virtually all studies, in all regions of the country, Mexican-American populations have a higher BMI than Caucasian populations even when matched for socio-economic status. Isotope studies have unequivocally demonstrated that this increase in the BMI is due to an increase in adipose tissue, not muscle mass. In general, in both men and women adipose tissue makes up 4-5 percent more of total body weight in Mexican-Americans than in Caucasians. In population studies, the distribution of this excess fat can be measured in two ways: 1) the ratio of skin-flap thickness beneath the scapula to that over the triceps (centrality index) and 2) the ratio of the circumference around the waist to that around the hips. In Mexican-Americans both of these indexes are significantly elevated above those seen in Caucasians indicating that this excess adiposity is central or "upper body" in these populations. Thus, in general, Mexican-Americans have a high incidence of "central obesity" which in many different ethnic groups is associated with various systemic metabolic diseases. Within the Mexican-American population it is also apparent that the risk for this disorder is directly related to the percentage of Amerindian genes carried by a particular sub-population. As shown in Fig. 14, for example, the body-mass index correlates well with the level of Amerindian admixture. The highest body weights are seen in those individuals with the highest Amerindian gene admixture (barrio).

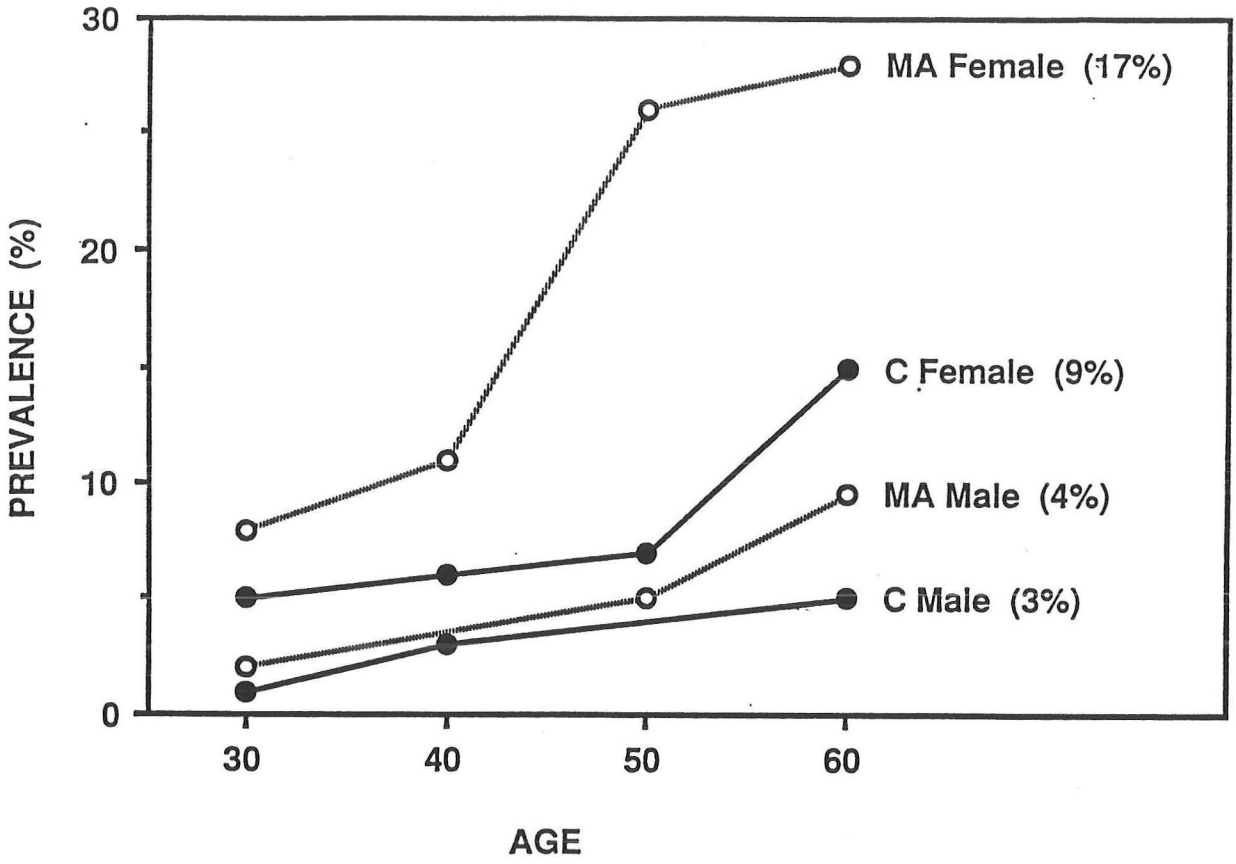


Figure 15

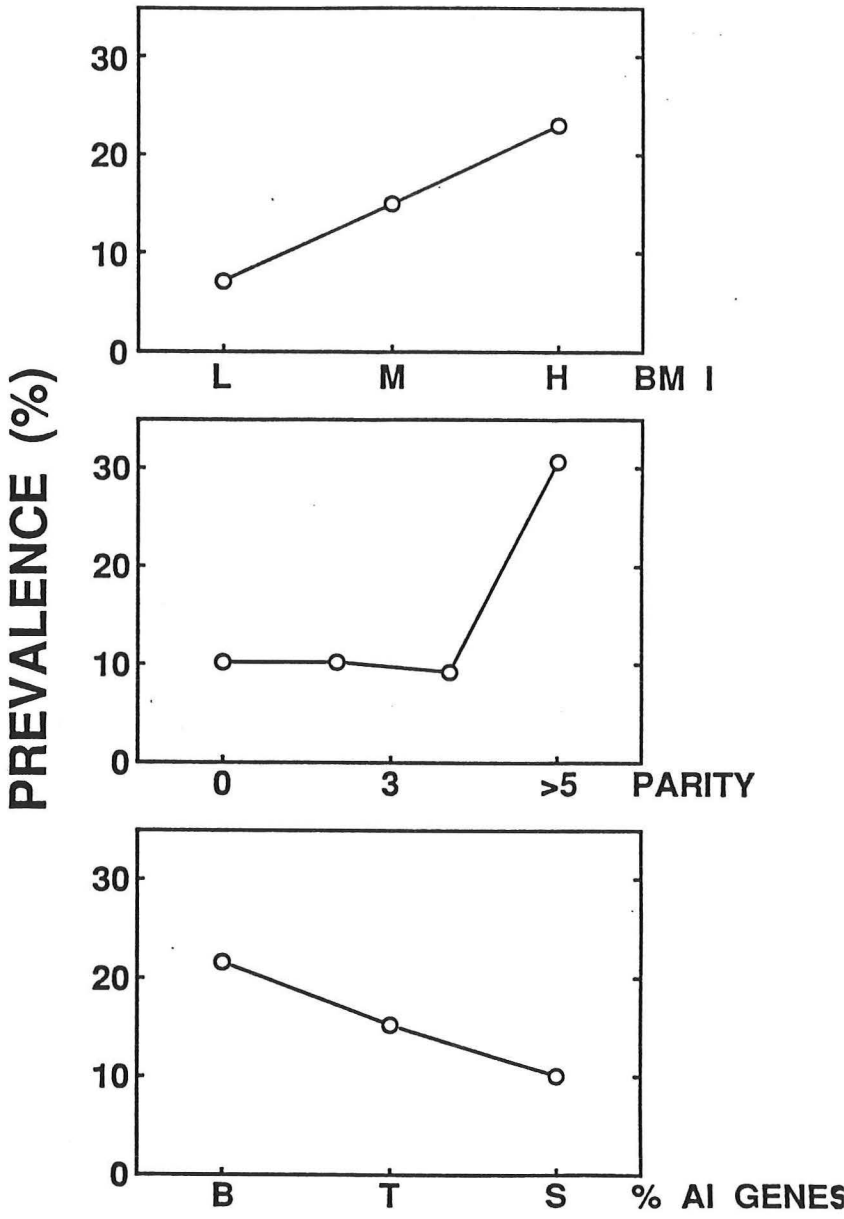
---

2) Gallbladder Disease and Cholesterol Gallstones

Non-cancerous, gallbladder disease is common in many ethnic groups and the prevalence seems to be related to the degree of obesity, gender and parity. In Caucasians about 80 percent of gallstones are made up principally of cholesterol while the remaining contain principally bilirubin. Bilirubin stones are more prevalent, however, in those ethnic groups having a high incidence of hemoglobinopthies. In those populations of Amerindian descent the incidence of gallstones is much higher than in any other racial group and they are predominantly cholesterol gallstones.

The prevalence of gallstone disease in Mexican-American populations is shown in Fig. 15. As is apparent the incidence in women is much higher than in men, both in Mexican-American and Caucasians populations. The prevalence increases with age in all ethnic groups. It should be emphasized that these data underestimate significantly the true incidence of cholesterol gallstone disease in these populations since these data were derived using a history of cholestectomy or the finding of gallstones after a period of symptoms. In other studies in which groups of individuals were sytematically surveyed using specific diagnostic tests, such as sonography, the prevalence of gallstones in these populations may be twice as great as indicated in this figure.

Fig. 16 shows the relationship between the prevalence of gallstones and several other patient characteristics. The upper panel illustrates that the prevalence of gallstones (corrected for age) increases directly with an increase in the body mass index: thus, while the Mexican-American population has an elevated average BMI, within this population the greater the body weight, the



greater the incidence of cholesterol gallstones. The second panel shows the relationship to parity and illustrates the marked increase that is seen with multiple pregnancies. Finally, the lower panel again illustrates the relationship between the prevalence of gallstones and the percentage of Amerindian genes carried in a particular sub-group. Those Mexican-Americans living in the barrio with nearly 50 percent of their genes of Amerindian origin have the highest incidence of cholesterol gallstones. In some American Indian tribes where the percentage of Amerindian genes exceeds 80 percent, the incidence of cholesterol gallstones is exceeding high and may approach 100 percent in older women. In all of these groups (Mexican-Americans, American Indians and Caucasians) there seems to be a relationship between obesity, parity and cholesterol gallstone formation. However, in several recent population studies in Mexican-Americans mathematical corrections have been made for the effects of parity and obesity and there still seems to be a very elevated prevalence of cholesterol gallstone disease in Mexican-Americans. Such data suggest that these individuals may have a genetically determined, underlying defect that is not necessarily related to the other factors of obesity, gender and parity. Furthermore, the additional fact that cholesterol gallstone disease is prevalence throughout the North and South American continents in any population carrying Amerindian genes suggests a genetic, rather than an environmental reason for this increased prevalence.

There are relatively few data concerning the metabolic defects that result in cholesterol gallstone formation in these populations. However, it has been shown that obese people, in general, and individuals carrying Amerindian genes, in particular, have increased rates of whole-body cholesterol synthesis and secrete excessive amounts of cholesterol into the bile. In addition, some of these groups have bile salt pools that are somewhat reduced in size. As a consequence of both of these metabolic abnormalities, the bile of these individuals at risk for gallstone disease is super-saturated with respect to cholesterol and this leads to cholesterol crystallization and cholesterol gallstone formation. It should be noted that in animal models in which there is

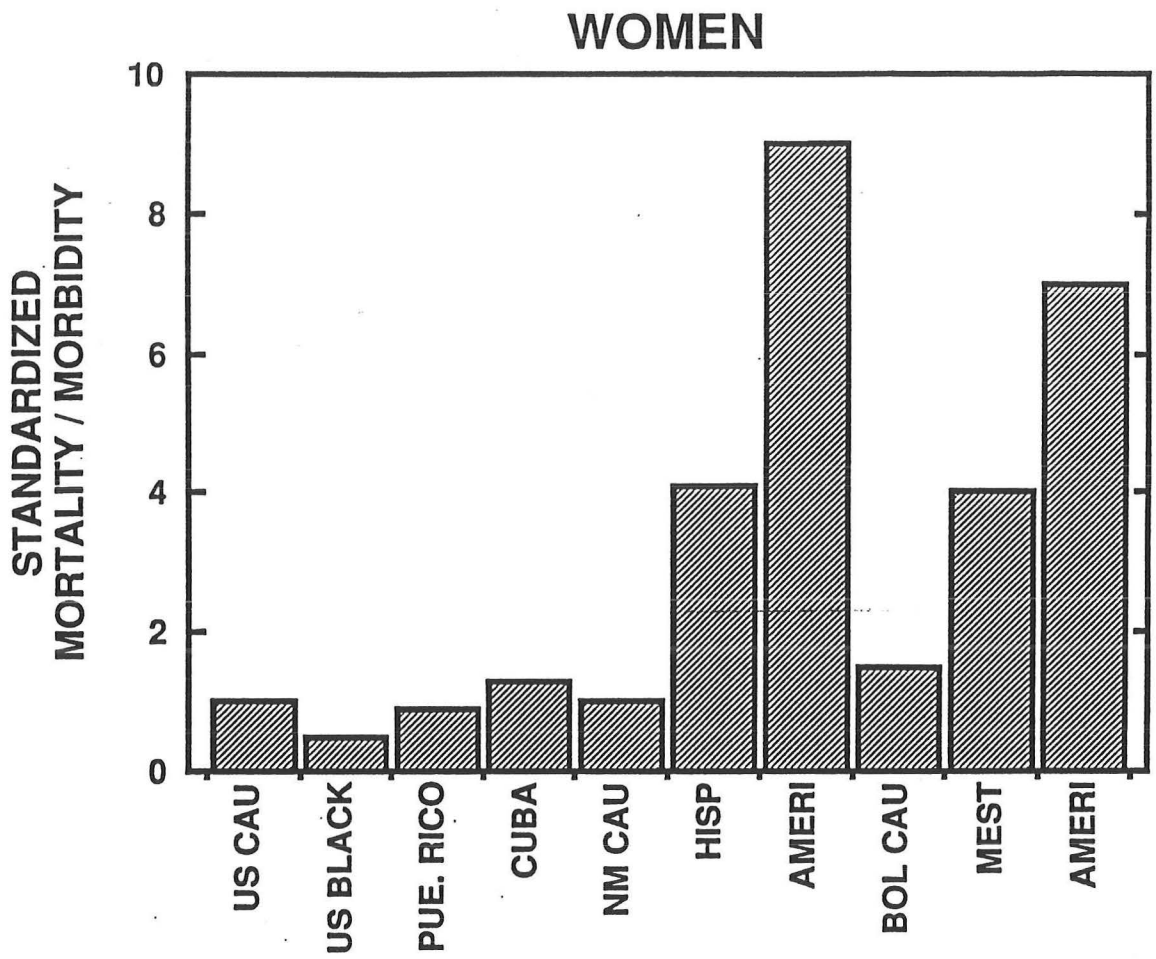


Figure 17

---

also excessive cholesterol secretion, there is usually a markedly increased rate of hepatic cholesterol synthesis while cholesterol synthesis in the peripheral organs is essentially normal.

3) Cancer of the Gallbladder

In Caucasian patients, cancer of the gallbladder is a relatively rare tumor that occurs in elderly females. The disease has a very poor prognosis since the vast majority of these tumors are already inoperable before the diagnosis is made. In those subjects of Amerindian derivation, however, this is a common tumor. In the past, there have been numerous reports of the high incidence of gallbladder cancer in Mexican-Americans from Texas, New Mexico and Los Angeles. In Mexico City various autopsy series also show a very high incidence of this malignant tumor.

Recent data concerning the incidence of gallbladder cancer in various ethnic groups is shown in Fig. 17. These data represent standarized mortality/morbitity data for the incidence of carcinoma of the gallbladder where the prevalence in U.S. Caucasians is taken as 1.0. Several series have shown that the incidence of gallbladder cancer is U.S. blacks is only about half that of Caucasians. It is of interest, therefore, that both Puerto Ricans and Cubans, who carry significant percentages of Negroid genes (and lesser amounts of Amerindian genes) have an incidence of gallbladder cancer that is not significantly different from U.S. Caucasians. In New Mexico the incidence of

this disease is 4.1 and 9 times more frequent in Hispanics and in American Indians, respectively. Similarly, in Bolivia, the relative incidence of cancer in Caucasians, Mestizos and Indians is 1.5, 4.0 and 7.0, respectively. Thus, as is true for obesity and cholesterol gallstone disease, the incidence of carcinoma of the gallbladder closely reflects the relative admixture of Amerindian genes in a given population. This is true even under conditions where these populations exist under very different geographical, cultural and environmental conditions.

Mexican-American populations may also have a slightly increased incidence of carcinoma of the biliary ducts and liver. However, the incidence of carcinoma of the stomach, pancreas, lung and breast is not significantly different from U.S. Caucasians. Rather consistently, the incidence of carcinoma of the colon is reported in several series to be significantly lower than the U.S. Caucasian population. Thus, the very high incidence of carcinoma of the gallbladder is unique and is probably associated with the high incidence of underlying cholesterol gallstones.

4) Type II Diabetes

There is now abundant evidence that individuals carrying significant proportions of Amerindian genes also have a very high rate of Type II diabetes. In contrast, Type I diabetes in these ethnic groups is very uncommon. While the data are incomplete, they do suggest that this high incidence of diabetes in Amerindian peoples is of relatively recent onset. During the early part of this century the incidence of overt diabetes on many Indian reservations appeared to be quite low. In the Indian Health Service Clinic at Lawton, not a single case of diabetes was found prior to 1940 even though urine sugar tests were commonly done. By 1978 the same clinic was caring for over 1,000 cases and, of these, the earliest year of discovery was 1939. Extensive interviews were carried out by Dr. Kelly West of older members of the 20 Oklahoma tribes, and only two cases of diabetes were detected prior to 1936. There are reports of the health problems of other Indian groups in 1928 and in 1933. Notably, obesity and diabetes were not mentioned in these reports. In 1937, Salsbury reported only one case of diabetes in 5,000 Navajos admitted to the Arizona Indian Hospital. In 1947, this same author reported his 25 year experience at Gage Memorial Hospital in Arizona: among 25,000 Navajo admissions there were only five cases of diabetes. After 1940-50, however, diabetes was reported to be very common in many Indian groups. In the Pima the incidence increased to ten times that found in the Navajos. In 1965 more than 25 percent of Cherokees over the age of 30 had diabetes. In a survey of the Indian Health Service in 1967, it became apparent that in several tribes the majority of individuals would eventually develop diabetes: this included several of the Oklahoma tribes as well as the Kiowas and Comanches. In 1972 diabetes was assigned as the cause of death in 1.7 percent of Oklahoma whites whereas 6.9 percent of deaths were attributed to diabetes in the Indian populations. (For a detailed discussion of the history of the development of obesity and diabetes in American Indian groups, see K. West, Advances in Metabolic Diseases 9:29-48, 1978).

While there are few data on the incidence of diabetes in Mexico during the early part of this century, between 1959-1961 the diabetes mortality rate for Mexicans was reported to be (45-64 years of age) 30.8 per 100,000. This was a rate that was four times higher than that reported for this age group in England. It should be noted that these data all suggest 1) that diabetes has

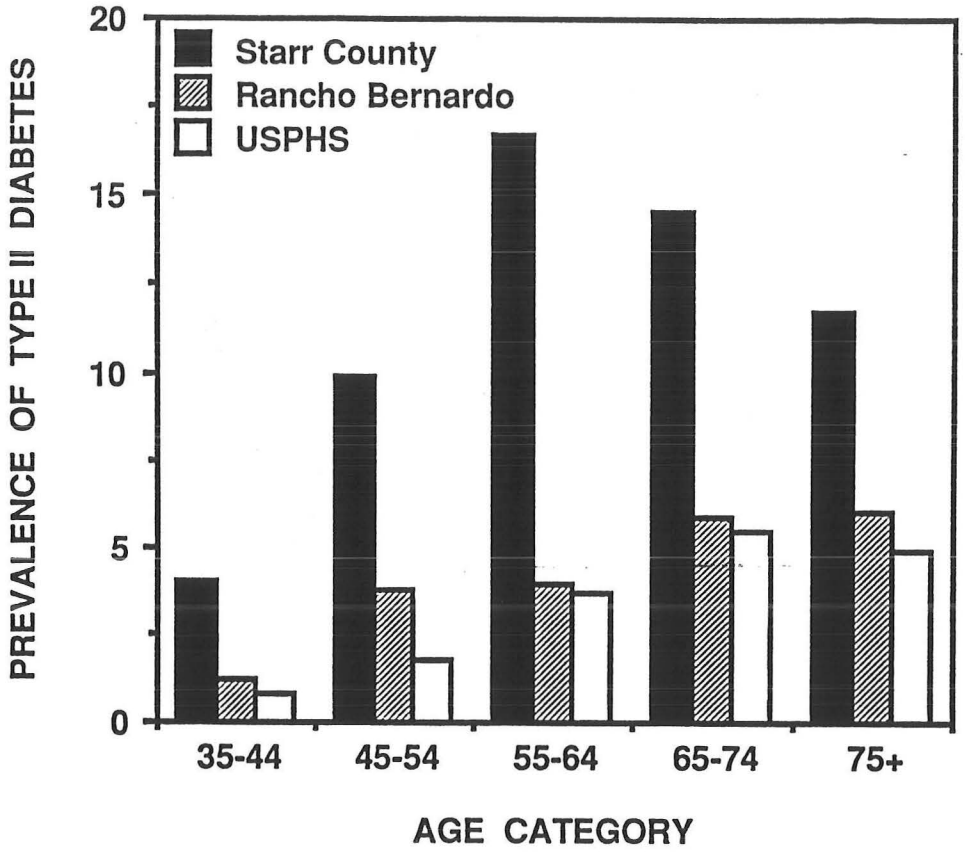


Figure 18

become extremely common in most Indian populations in Mexico and the Southwest United States and 2) this increase in prevalence is seen primarily in those peoples derived from the Amerindian stock and, apparently, not in those peoples derived from the Athapascan or Eskimo-Aleut groups. Thus, for example, the death rate per 100,000 from diabetes in Native Americans was 23 times greater in Oklahoma (primarily Amerindian-derived peoples) than in Alaska (primarily Athapascan and Eskimo-Aleuts).

Because of the high content of Amerindian genes in the major Hispanic groups, it would be anticipated that these people would also have a very high incidence of diabetes. This has proved to be the case in Mexico as well as in Mexican-Americans living in Texas. For example, in Texas, in the age range of 25-44 years old, Mexican-Americans account for 46 percent of the diabetic caseload even though this particular age group accounts for only 19 percent of the state's population. It is of interest that Type II diabetes is also very prevalence in Puerto Ricans. Thus, while the prevalence of gallstones and carcinoma of the gallbladder is not unusually high in Puerto Ricans, that of Type II diabetes apparently is increased.

As summarized in Fig. 18, there is a very high prevalence of diabetes in Mexican-Americans living in Texas. As illustrated in this diagram, the prevalence of Type II diabetes increases in Caucasian populations from about 2 to approximately 6 percent in older individuals. In any age group, the prevalence of Type II diabetes in Mexican-Americans is increased by 3-4 fold. There are also data to suggest that diabetes in Mexican-Americans is more severe than in Caucasians. In some surveys, at least, the mean fasting blood glucose

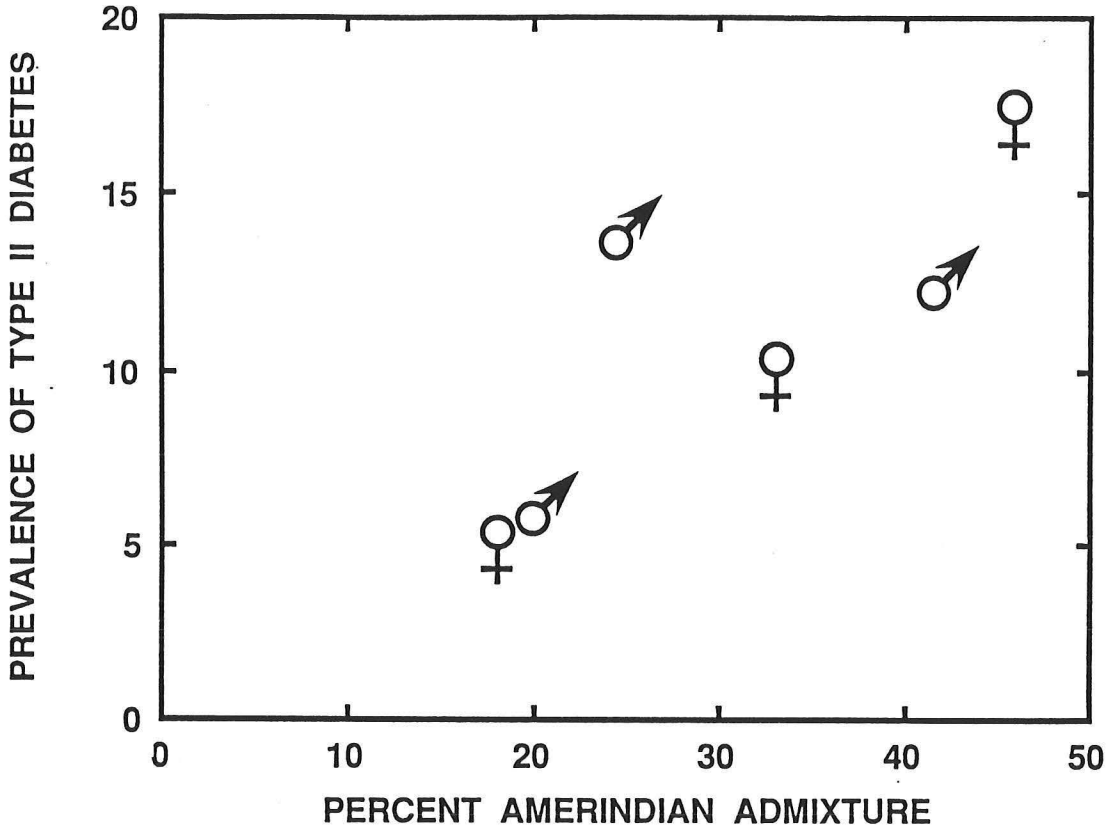


Figure 19

levels are markedly elevated in approximately 60 percent of Mexican-Americans but in only about 10-15 percent of Caucasians.

As with central obesity and gallbladder disease there is also a direct relationship within the Mexican-American community between the prevalence of Type II diabetes and the percentage of Amerindian admixture. For example, Fig. 19 shows age-adjusted prevalence rates as a function of the Amerindian gene content in different populations of Mexican-Americans in Texas. It is clear that for both men and women the prevalence of diabetes is nearly 4-fold greater in those individuals having nearly 50 percent Amerindian genes as opposed to those who have only 5 percent.

Not only is there evidence that the hyperglycemia is more severe in Mexican-American diabetics than in Caucasian diabetics, data has been collected in the San Antonio Heart Study suggesting that complications of diabetes such as retinopathy are also more severe in Mexican-American patients. For example, in diabetic patients, retinopathy is present 1.7 times more commonly in Mexican-Americans than in non-Hispanic whites. Furthermore, severe retinopathy is 2.4 fold more likely to occur in the Mexican-American population. Similarly, the incidence of proteinuria is significantly greater in Mexican-American diabetes than in Caucasians. Recent data have also illustrated that Mexican-Americans have a disproportionately high incidence of end-stage renal disease. Both Mexican-Americans and Blacks have an excess treatment rate for end-stage renal disease (incidence ratios of 3 and 4, respectively) when compared to Caucasian control groups. For diabetes-related end-stage renal disease the incident ratio is 6 for Mexican-Americans compared to Caucasians. In contrast to these findings, the prevalence of diabetic neuropathy and

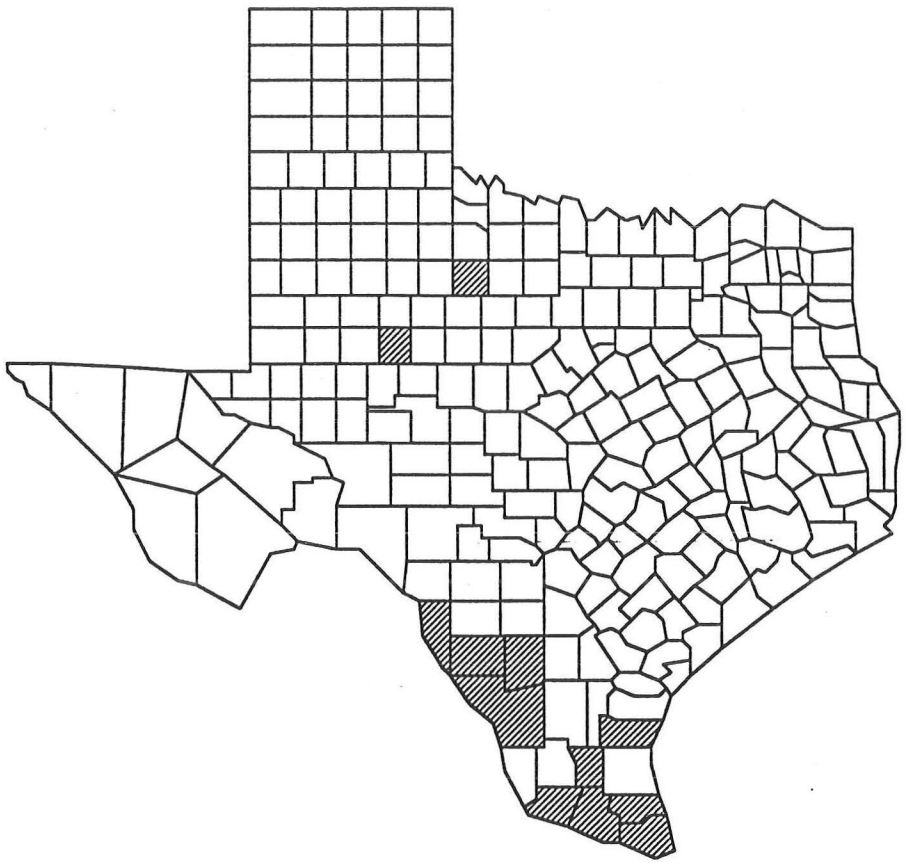


Figure 20

---

macro-vascular disease appears to be no more prevalence in Mexican-Americans diabetics than in non-Hispanic patients.

Thus, all of these lines of evidence suggest that not only is the prevalence of Type II diabetes in Mexican-Americans elevated several-fold but, in addition, the incidence of serious complications from this disease may also be disproportionately high in Mexican-American patients. This high complication rate is reflected in the crude mortality data shown for the various counties of Texas in Fig. 20. The major concentration of Mexican-Americans in the state of Texas is in the 30-40 counties that lie just north of the Texas-Mexico border. In these counties about 35 percent of the people have Spanish surnames. The shaded counties in this figure show those areas of Texas where death is attributed to the complications of diabetes in > 30 patients per thousand. These exceptionally high mortality figures are clearly found in those counties of far south Texas where greater than half of the population is Mexican-American. Thus, it seems clear that Type II diabetes represents a major health problem in the Mexican-American population.

5) End-stage Renal Disease

As noted above a disproportionately high percentage of the Mexican-American population requires treatment for end-stage renal disease. The incidence ratio (Mexican-American/non-Hispanic white) is approximately 1.5-2 in the 10-40 year old age range. During the next four decades, however, this ratio increases to 3, 10, 14 and 20. Blacks also have a high incidence ratio for the development

	MEN							
	25-35		36-45		46-55		56-65	
	MA	CA	MA	CA	MA	CA	MA	CA
Triglycerides	150	132	181	164	187	163	196	165
Cholesterol	197	190	206	204	217	213	212	215
HDL-C	44	44	42	43	43	43	42	44
BP	117	115	119	117	122	119	130	123
	73	72	76	74	76	74	75	73

Figure 21

of end-stage renal disease: in this case the renal disease is primarily due to hypertension. In contrast, much of the end-stage renal disease seen in Mexican-Americans is related to their high prevalence of Type II diabetes.

6) Cardiovascular Disease

Rather extensive public health surveys have been carried out in Mexican-American populations in several Texas cities. A portion of this data is summarized is Fig. 21. Serum triglyceride concentrations tend to be slightly higher in Mexican-Americans than in Caucasians at any age. In general, these higher triglyceride concentrations are consistent with the higher body weights seen in these same patients. In contrast, serum total-cholesterol concentrations are not significantly different in the two groups. Similarly, mean blood pressure levels do not really differ significantly between Mexican-Americans and Caucasians. This similarity of blood pressures is of particular interest since the Mexican-American population is typically more obese than the Caucasian control patients. These findings, along with other factors such as the presence or absence of diabetes, obesity, smoking, etc., can be used to calculate cardiovascular risk scores for the Mexican-American population. These are summarized in Fig. 22. In women, as is apparent, Mexican-Americans and Caucasians have similar cardiovascular risk scores. This is also true in Mexican-American men up to the age of 45. Above this age there is a slightly increased risk for cardiovascular disease that attains statistical significance.

These data are consistent with crude mortality data in Hispanic groups from California, New Mexico and Texas. In general, death rates from cardiovascular disease are approximately equal in women of Mexican-American and non-Hispanic derivation and are significantly lower in Mexican-American men than in non-Hispanic men. In a survey of nearly 3,000 Mexican-American subjects, the age-adjusted prevalence rates of angina were 5.4 percent in Mexican-American women and 6.3 percent in Caucasian women. In men these figures equalled 2.8 (MA) and 3.9 (Caucasians). Thus, these figures are remarkably in that Mexican-Americans do not seem to differ significantly from Caucasian populations

	CARDIOVASCULAR RISK SCORES							
	25-35		36-45		46-55		56-65	
	MA	CA	MA	CA	MA	CA	MA	CA
MEN	1.4	1.4	3.2	3.0	7.2	6.0	15.3	11.4
WOMEN	0.3	0.2	0.9	0.7	3.1	2.3	8.4	6.2

Figure 22

with respect to mean blood pressure levels and the prevalence of atherosclerotic complications even though they have significantly greater body weights and very high prevalences of Type II diabetes. Such figures have lead some investigators to postulate that Mexican-Americans may be relatively protected from developing atherosclerotic disease by something in their gene background.

6) Bone Disease

Interestingly, several papers have now provided data suggesting that metabolic bone disease is significantly less important in Mexican-Americans than in Caucasians. For example, the risk of post-menopausal hip fracture in Mexican-American women was calculated to equal only 35 percent of the risk seen in Caucasian controls. In another series the relative risk for developing vertebral fractures in Mexican-American women was calculated to be only about 55 percent of that seen in Caucasians.

F. SUMMARY

These data demonstrate very clearly that modern populations that contain a significant percentage of Amerindian genes are seriously at risk for the development of major chronic diseases including cholesterol gallstone disease, carcinoma of the gallbladder and Type II diabetes. These complicating diseases may arise as a result of, or in addition to, development of post-pubertal, central obesity. Presumably, during migration through Beringia some 20,000 years before the present, most migratory groups died or were turned back by the extremely harsh climate. A few immigrants succeeded, probably because they had subtle metabolic differences that favored the rapid storage of metabolic energy in central fat stores. Presumably such individuals had a energy utilization system that was tightly coupled and that provided the means for rapidly synthesizing fatty acids in the liver from dietary carbohydrates and amino acids and for then storing these fatty acids in the central fat stores. This metabolic system was subsequently distributed to the thousands of subgroups of Amerindians derived from this original, very small founding group. Later migrations into North American (the Athapascan-speaking people and the Eskimo-Aleuts) presumably did not acquire this metabolic set. This highly efficient storage system served the hunter-gatherers well since it provided the metabolic means for rapidly metabolizing and storing calories from infrequent and erratically spaced meals. However, once food intake became relatively constant, there was inappropriately high fatty acid and cholesterol synthesis in the liver, increased very low density lipoprotein secretion and excessive delivery of fatty acids to central

stores. Thus, on a relatively normal caloric intake (compared to Caucasians) there is inappropriate overproduction of cholesterol, the production of cholesterol gallstones and the development of carcinoma of the gallbladder. There is also continuous deposition of lipids into the central stores and, ultimately, the development of insulin resistance and Type II diabetes. The prevalence of these events in any population appears to be directly related to the proportion of genes in that population that are derived from the Amerindian population.

FURTHER READING

A. THE EVOLUTION OF HOMO SAPIENS

1) Tattersall I, E Delson, and J Van Couvering. Encyclopedia of Human Evolution and Prehistory. Garland Reference Library of the Humanities, Vol. 768. Garland Publishing, New York, 1988.
2) The Motherhood of Man. The Economist, August 13, 1988, 71-74.
3) CB Stringer and P Andrews. Genetic and fossil evidence for the origin of modern humans. Science, 239:1263-1267, 1988.
4) Wolpoff MH. Modern human origins. Science 241:772-774, 1988.
5) Lewin R. Modern human origins under close scrutiny. Science 239:1240-1241, 1988.

B. THE MOVEMENT OF MAN INTO THE NEW WORLD

1) Lewin R. New views emerge on hunters and gatherers. Science 240:1146-1148, 1988.
2) Lewin R. American Indian Language Dispute. Science 242:1632-1633, 1988.
3) Nelson DE, RE Morlan, JS Vogel, et al. New dates on Northern Yukon artifacts: Holocene not upper pleistocene. Science 232:749-751, 1986.
4) Lewin R. The first Americans are getting younger. Science 238:1230-1232, 1987.
5) Morell V. Confusion in earliest America. Science 248:439-441, 1990.

C. "RELATEDNESS" AMONG MODERN AMERINDIANS

1) Kraus BS and CB White. Micro-evolution in a human population: A study of social endogamy and blood type distributions among the Western Apache. American Anthropologist 58:1017-1043, 1956.
2) Szathmary EJE and NS Ossenberg. Are the biological differences between North American Indians and Eskimos truly profound? Current Anthropology 19:673-701, 1978.
3) Szathmary EJE. Dogrib Indians of the Northwest Territories, Canada: genetic diversity and genetic relationship among subarctic Indians. Ann. Hum. Biol. 10:147-162, 1983.
4) Szathmary EJE. Blood groups of Siberians, Eskimos Subarctic and Northwest Coast Indians: The problem of origins and genetic relationships. In The First Americans: Origins, Affinities, and Adaptations. 185-209, 1979.
5) Szathmary EJE. Peopling of Northern North American: Clues from genetic studies. Acta Anthropogenetica 8:79-109, 1984.
6) Szathmary EJE. Population of genetics of aboriginal North America. In Genetique et Histoire du Peuplement. A. Langaney (ed), Ordina, Bruxelles, 1987.
7) Szathmary EJE. Genetic and environmental risk factors. In: Diabetes in the Canadian Native Population: Biocultural Perspectives. T.K. Young (ed), Canadian Diabetes Association, Toronto, Canada. 27-66, 1987.
8) Szathmary EJE. Modelling ancient population relationships from modern population genetics. In Proceedings of the First World Congress of the Peopling of the Americas. R. Bonischen, K. Turnmire, and J. Tomenchuk (eds), 1990.

D. CULTURAL DEVELOPMENT IN THE NEW WORLD

1) Fagan BM. The Great Journey: The Peopling of Ancient America. Thames and Hudson Ltd, New York. 1987.
2) Covarrubias M. Indian Art of Mexico & Central America. Alfred A. Knopf, New York, 1957.
3) Waldman C. Encyclopedia of Native American Tribes. Facts on File Publications, New York, 1987.
4) Kopper P. The Smithsonian Book of North American Indians: Before the Coming of the Europeans. Smithsonian Books, Washington, D.C., 1986.
5) Coe M., D Snow, E Benson. Atlas of Ancient America. Facts on File, Inc., New York, 1986.
6) Parson LA. Pre-Columbian Art. The Morton D. May and The Saint Louis Art Museum Collections. Harper & Row, New York, 1980.

E. GENETIC MIXTURE IN MEXICAN AMERICAN

1) Roberts L. Disease and Death in the New World. Science 246:1245-1247, 1989.
2) Hanis C, R Chakraborty, RE Ferrell, and WJ Schull. Individual admixture estimates: Disease associations and individual risk of diabetes and gallbladder disease among Mexican-Americans in Starr County, Texas. Am. J. Phys. Anthropol. 70:433-441, 1986.
3) Weiss KM, RE Ferrell, and CL Hanis. A New World syndrome of metabolic diseases with a genetic and evolutionary basis. Yearbook Phys. Anthropol. 27:153-178, 1984.
4) Diehl AK. The melting pot: Examine before stirring. J. Gen. Int. Med. 3:90-91, 1988.
5) Weiss KM, RE Ferrell, CL Hanis, and PN Styne. Genetics and epidemiology of gallbladder disease in New World native peoples. Am. J. Hum Genet. 36:1259-1278, 1984.
6) Szathmary EJE. Genetic and environmental risk factors. In Diabetes in the Canadian Native Population: Biocultural perspectives. T.K. Young (ed), Canadian Diabetes Association, Toronto, Canada. 27-66, 1987.
7) Hanis CL, R Chakraborty, RE Ferrell, and WJ Schull. Individual admixture estimates: Disease associations and individual risk of diabetes and gallbladder disease among Mexican-Americans in Starr County, Texas. Am. J. Phys. Anthropol. 70:433-441, 1986.

F. DISEASES OF MEXICAN-AMERICANS

1) Neel JV. Diabetes mellitus: a "thrifty" genotype rendered detrimental by "progress"? Am. J. Hum. Genet. 14:353-362, 1962.
2) West KM. Diabetes in American Indians and other native populations of the New World. Diabetes 23:841-855, 1974.
3) West KM. Diabetes in American Indians. Adv. Metab. Dis. 9:29-48, 1978a.
4) Stern MP, SP Gaskill, CR Allen, Jr., et al. Cardiovascular risk factors in Mexican Americans in Laredo, Texas. Am. J. Epidemiol. 113:546-555, 1981.
5) Diehl AK, MP Stern, VS Ostrower, and PC Friedman. Prevalence of clinical gallbladder disease in Mexican-American, Anglo, and black women. South. Med. J. 73:438-442, 1980.
6) Hanis CL, RE Ferrell, SA Barton, et al. Diabetes among Mexican Americans in Starr County, Texas. Am. J. Epidemiol. 118:659-672, 1983.

7) Gardner, Jr. LI, MP Stern, SM Haffner, et al. Prevalence of diabetes in Mexican Americans: Relationship to percent of gene pool derived from Native American sources. Diabetes 33:86-92, 1984.
8) Hanis CL, RE Ferrell, BR Tulloch, and WJ Schull. Gallbladder disease epidemiology in Mexican Americans in Starr County, Texas. Am. J. Epidemiol. 122:820-829, 1985.
9) Chakraborty R, RE Ferrell, MP Stern, et al. Relationship of prevalence of non-insulin-dependent diabetes mellitus to Amerindian admixture in the Mexican Americans of San Antonio, Texas. Genet. Epidemiol. 3:435-454, 1986.
10) Haffner SM, MP Stern, HP Hazuda, et al. Do upper-body and centralized adiposity measure different aspects of regional body-fat distribution? Relationship to non-insulin-dependent diabetes mellitus, lipids, and lipoproteins. Diabetes 36:43-51, 1987.
11) Haffner SM, AK Diehl, MP Stern, and HP Hazuda. Central adiposity and gallbladder disease in Mexican Americans. Am. J. Epidemiol. 129:587-595, 1989.
12) LaCroix AZ, SG Haynes, DD Savage, and RJ Havlik. Rose questionnaire angina among United States black, white, and Mexican-American women and men. Am. J. Epidemiol. 129:669-686, 1989.
13) Diehl AK and MP Stern. Special health problems of Mexican-Americans: Obesity, gallbladder disease, diabetes mellitus, and cardiovascular disease. Adv. Intern. Med. 34:73-96, 1989.
14) Burchfiel CM, RF Hamman, JA Marshall, et al. Cardiovascular risk factors and impaired glucose tolerance: The San Luis Valley diabetes study. Am. J. Epidemiol. 131:57-70, 1990.
15) Mitchell BD, MP Stern, SM Haffner, et al. Risk factors for cardiovascular mortality in Mexican Americans and non-Hispanic whites. The San Antonio Heart Study. Am. J. Epidemiol. 131:423-433, 1990.