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Diabetes Mellitus and Cardiovascular Disease in Developing Populations: Hunter-Gatherers in the Fast Lane

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With the control of infectious diseases in many developing countries, there was every reason to expect a significant improvement in life expectancy. Although this has been the case in some populations, an epidemic of noncommunicable diseases (NCD), including non-insulin-dependent diabetes mellitus (NIDDM) and cardiovascular disease (CVD), has reduced the expected gains in many others (1).

This situation is well illustrated in the Pacific region, where rapid socioeconomic development over the past 50 years has resulted in a change of lifestyle from traditional to modern. With the accompanying improvements in public health, mortality from infectious disease has fallen dramatically. Somewhat paradoxically, however, there has been a marked increase in the prevalence of risk factors for NCD, including NIDDM and CVD.

Apart from some isolated communities where contact with Europeans has been absent or minimal, the disease profile has changed dramatically. Social and cultural changes resulting from modernization have caused a change in diet, physical activity, and smoking habits, as well as increasing obesity and alcohol consumption (1). Coincidental with these lifestyle changes, NIDDM, coronary artery disease (CAD), strokes, hypertension, and certain cancers (particularly cervix and lung) have now become major contributors to morbidity and mortality (1,2). The emergence of these NCD appears to be a result of socioeconomic and demographic change in the region, since they are predominantly lifestyle related (1–3).

NON-INSULIN-DEPENDENT DIABETES MELLITUS

Since a major focus of our studies has been the epidemic of NIDDM in Pacific islanders, it will be used here to illustrate the adverse effects of lifestyle change.

TABLE 1. *Age-standardized prevalence of non-insulin-dependent diabetes mellitus (age >20 years) using WHO (1985) criteria in Pacific populations surveyed by our group*

	Diabetes prevalence (%)[a]	
	Males	Females
Micronesians		
Nauru (1982)	33.4 (29.5–37.2)[b]	32.1 (28.4–35.8)
Kiribati		
Rural	3.7 (1.9–5.4)	3.9 (2.2–5.6)
Urban	11.7 (8.6–14.8)	11.1 (8.4–13.8)
Polynesians		
Western Samoa		
Rural	1.7 (0.3–3.0)	4.2 (1.9–6.5)
Urban	8.2 (5.3–11.1)	8.5 (6.0–11.0)
Wallis Islanders		
Wallis Island, rural	2.0 (0.3–3.7)	4.1 (1.6–6.5)
Noumea (25–64 years), urban	10.0 (5.9–14.1)	14.0 (9.3–18.7)
Rarotonga	5.5 (3.6–7.4)	8.5 (6.1–11.0)
Niue	5.6 (3.6–7.6)	8.9 (6.7–11.2)
Tuvalu	0.8 (0.0–1.9)	8.4 (4.6–12.3)
Ouvea (Loyalty Islands: part-Polynesians)	7.3 (3.3–11.4)	6.5 (3.5–9.4)
Melanesians (NAN)		
PNG highlands, rural	0.0	0.0
PNG highlands, periurban	0.0	0.0
Melanesians (AN)		
Ouvea (Loyalty Islands)	0.0	4.2 (1.9–6.5)
Touho (New Caledonia)	1.8 (0.0–4.2)	1.4 (0.0–4.1)
Fiji		
Rural	2.1 (0.0–4.2)	2.1 (0.0–4.1)
Urban	5.9 (3.4–8.3)	10.3 (7.2–13.4)
PNG coastal (Tolai)		
Rural	1.8 (0.0–4.1)	0.0
Periurban	4.7 (1.0–8.4)	7.0 (1.4–12.7)
Indians (Asian)		
Fiji		
Rural	15.1 (9.8–20.3)	13.6 (8.9–18.2)
Urban	17.5 (13.5–21.6)	16.3 (12.5–20.1)

[a] Age-standardized using the direct method and weights derived from Segi's world population for the age groups 20–24, 25–34, . . . 65+.
[b] 95% confidence intervals in parenthesis.

The Pacific region provides a unique natural situation for the investigation of genetic and environmental determinants of NIDDM, given the wide range in the extent of modernization of its peoples and their genetic diversity.

From these studies, the following facts have emerged: (a) Diabetes is almost exclusively of the NIDDM type (4). (b) A range of prevalence exists (Table 1) from extremely low [0% in Papua New Guinea (PNG) highlanders] to high (8–12% in Western Samoa and Kiribati) to extremely high (15–33% in migrant Asian Indians in Fiji and Nauruans). The prevalence (5) and incidence (6) of NIDDM in Nauru are

the second highest yet recorded in the literature, after the Pima Indians of Arizona (7). (c) Diabetes prevalence is much lower in traditional living compared to urbanized and migrant communities of the same ethnic group (8). (d) Within countries, there are large differences in prevalence between ethnic groups. For instance, in Fiji, the prevalence is almost 4 times higher in urban Indian than in Melanesian males (9). (e) Cross-sectional studies have shown pronounced heterogeneity of behavioral, environmental, and social risk factors for NIDDM, for example, physical inactivity, obesity, and modernization (10). (f) Hyperinsulinemia, a hallmark of insulin resistance, is present in the high prevalence Micronesian population of Nauru. Its presence predates NIDDM and is predictive of its development (11). (g) Microvascular complications are common with similar risk factors as in other populations (i.e., duration of diabetes and degree of hyperglycemia) (5,6). (h) There is considerable morbidity and premature mortality from NIDDM in Nauru and a fourfold increase in risk of mortality in diabetics compared with subjects with normal glucose tolerance (2). (i) Certain ethnic groups (Micronesians, Polynesians, and Asian Indians) appear to have an increased genetic susceptibility to NIDDM (4), whereas some Melanesian populations appear to have a low susceptibility (12).

EVOLUTIONARY AND ANTHROPOLOGICAL PERSPECTIVE

A fascinating aspect of this marked change in disease profile is that it may well have an evolutionary basis. Almost 30 years ago, the American geneticist James Neel raised the question of why NIDDM, a disease associated with considerable morbidity and reduced life expectancy, had reached such high prevalence in certain populations. To explain this apparent paradox, he proposed the thrifty genotype hypothesis (13), which suggested that people with a hereditary tendency to obesity and NIDDM were better able to store food as fat during times of plenty. The Pacific islanders were subjected to periodic food deprivation associated with long migratory canoe voyages and natural phenomena, such as droughts and cyclones. Therefore, the thrifty gene would have offered a survival advantage under these conditions, through efficient storage and utilization of energy. This predisposition to obesity and NIDDM may have been maintained selectively in communities, such as Polynesians, Micronesians, and Australian Aborigines, where feast and famine conditions were present. However, with modernization and plentiful food supplies, this inherited survival factor has become disadvantageous, to such an extent that obesity and clinical diabetes have now become prevalent (Fig. 1).

Although the nature of the responsible gene(s) remains elusive, Neel's proposal has provided stimulus for research into the etiology of NIDDM. There is compelling evidence that Micronesians, Polynesians, American Indians, and Australian Aborigines have a heightened genetic susceptibility to NIDDM (4,6), which appears to be unmasked by environmental change. Obesity, reduced physical activity, dietary changes, and stress have been invoked as major environmental factors (3,4,6).

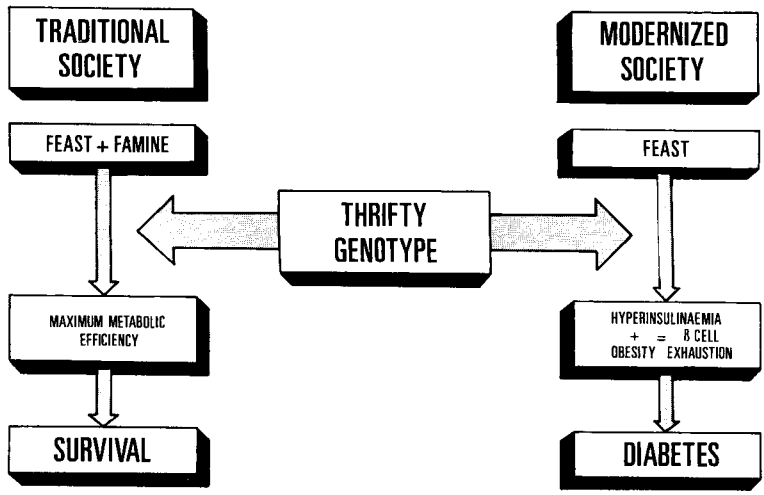

FIG. 1. The suggested mechanism for operation of the "thrifty" genotype in the etiology of non-insulin-dependent diabetes mellitus in developing populations.

GENETIC CONNECTION

There appear to have been three major migrations from South East Asia, and archeological evidence suggests that New Guinea was first settled over 50,000 years ago by Australoid populations (14). Approximately 10,000 years ago, Papuan-speaking migrants reached New Guinea from the west and then spread further east to Fiji. Between 3,500 and 5,000 years ago, Austronesian speakers arrived in New Guinea and intermarried with the Australoids who were resident in coastal areas. However, Austronesian genetic elements did not penetrate into the PNG highlands (12).

The Austronesian speakers spread to, and intermarried with, the coastal people of New Britain, the New Hebrides (now Vanuatu), and New Caledonia. By 3,000 years ago, the Austronesian speakers had moved on to Fiji, the most eastern point in Melanesia. Some of these Austronesians continued to move further east into Polynesia and colonized Samoa and Tahiti and later migrated to other parts of Polynesia. The highlanders of PNG are survivors of the earlier migrations and are referred to as non-Austronesian (NAN)-Melanesians. The majority of the people of the rest of Melanesia show genetic diversity as a result of ancestral Austronesian penetration and are referred to as Austronesian (AN)-Melanesians.

As a result of these various migrations, there is now a gradient of proportional NAN and AN genetic admixture across the Pacific from west to east ranging from the PNG Highlanders (0% AN) to the Polynesians and Micronesians (100% AN). This pattern of genetic admixture of NAN and AN elements has been used to study glucose tolerance in six semitraditional Pacific populations from the PNG Highlands, New Caledonia, Fiji, Wallis Island, Western Samoa, and Kiribati (15). We observed a gradient of increasing NIDDM prevalence through the six populations after con-

trolling for age and obesity. Differences in physical activity, diet, and degree of modernization were not considered a sufficient explanation for these findings, which lends support to the hypothesis of a genetic component to variability in glucose tolerance.

Within PNG itself, King et al. (16) demonstrated an absence of diabetes in traditional living and urban PNG highlanders (NAN-Melanesians), but in the Tolai of New Britain (AN-Melanesians), the prevalence of diabetes was 4%. Since it is well documented that Polynesians—an AN ancestral group—have an increased genetic susceptibility to NIDDM (6,17), the higher prevalence of diabetes in Melanesians with AN admixture is probably due to their Austronesian ancestry.

The Micronesians and Polynesians (AN) have been subject to periods of considerable privation associated with their arduous migratory voyages between islands and natural phenomena (droughts, hurricanes), which have adversely affected the productivity of their often rather barren coral atoll soils. These circumstances are compatible with the selective process envisaged by the thrifty genotype hypothesis. In contrast, the AN-Melanesians of highland PNG have lived settled lives for many thousands of years, with well-developed agricultural habits taking advantage of reliable high rainfall and fertile soils. In their situation, the thrifty genotype was probably unnecessary.

It also is possible, however, that the highland Papua New Guineans have not yet been subject to sufficient modernization to expose their susceptibility (16). Certainly, Australian Aborigines, who are also of NAN descent, seem very susceptible to NIDDM (6). Nonetheless, it is convenient to suggest that Austronesians at least may carry the thrifty gene(s), consistent with the high NIDDM prevalence seen in their urbanized populations (3). Just as increasing AN-admixture is associated with increasing NIDDM prevalence in the Pacific, increasing Caucasoid admixture is associated with declining NIDDM prevalence in Nauruans (3), American Indians (3), and Australian Aborigines (18). Thus, the marked change in diet and other environmental factors, set against a background of genetic factors, including admixture, can explain much of the variation of NIDDM prevalence in the Pacific and other developing populations.

RISK FACTORS FOR NIDDM AND THEIR MODULATION BY LIFESTYLE CHANGE

There are a number of recent reviews on the role of risk factors other than genetic susceptibility in triggering the development of NIDDM (3,4,6). These include constitutional factors, such as increased longevity, obesity, and reduced physical activity, as well as more obvious environmental variables, such as changes in nutrition and levels of stress.

Age and Increased Longevity

Both the prevalence and incidence of NIDDM increase with age (4,6). In developed populations, the rise in prevalence is slow initially but increases more rapidly with

TABLE 2. *Comparison of hunter-gatherer, peasant agriculturist, and modern diets*

Constituent	Hunter-gatherer	Peasant agriculturist	Modern
Energy (kcal/day)	1,800	2,000	2,400
Carbohydrate (%)			
Complex	50–70	60–75	25–30
Refined	0	5	20
Fat (%)	15–20	10–15	40
Protein (%)	15–20	10–15	12
Fiber (g/day)	40	60–120	20
Sodium (g/day)	1	5–10	10–15

advancing age. In highly susceptible developing populations such as Nauruans, however, the prevalence tends to rise linearly from an already high level in young adults and peaks around the age of 60 years, after which it declines. This fall may be indicative of a survival effect but also might reflect the recent appearance of epidemic glucose intolerance in these populations, with the older cohort retaining more traditional lifestyle habits (6).

Given the strong association of age with NIDDM, it is readily apparent that with the control of communicable diseases in many developing countries, more people are living to older age. This fact alone will result in an increasing prevalence of NIDDM with time in these populations.

Dietary Change

Since humans first evolved as a species, there have been continuing changes to the physical and social environment. Until 10,000 years ago, when agriculture was developed, food was obtained by hunting and gathering. Although hunter-gatherers now constitute less than 0.001% of the world's population, there are considerable data available regarding their biological characteristics (19). Certainly, obesity, NIDDM, and other degenerative disorders are rare or nonexistent in these traditional populations.

Despite marked environmental change, the human genetic constitution has not changed very much since the appearance of modern human beings about 40,000 years ago (20). The original genetic constitution of the hunter-gatherers did not adapt to the development of agriculture some 10,000 years ago, let alone the modern diet, which has progressively evolved over the last 100 or so years. Thus modern man in general is still genetically and biochemically programmed for the preagricultural diet, and this has major implications for our health.

A comparison of the major components of the diets of the hunter-gatherer, peasant agriculturalist, and modern man are shown in Table 2. The most obvious changes are the increase in contribution of fat (15% to 40%), refined carbohydrate (0% to

20%), decrease in complex carbohydrate (50–70% to 25–30%), and increase in salt consumption.

Dietary factors have long been considered important as possible determinants of NIDDM (4). However, no specific dietary component has yet been implicated, and West concluded that dietary factors exerted their effect through their tendency to promote obesity (21). A dietary study in Nauru in 1976 (22) found no association between NIDDM prevalence and any particular dietary component (carbohydrate, fat, or protein). However, the Nauruans were consuming almost exclusively high-calorie refined imported foods, and their mean caloric intake was at least twice that recommended for Australians. In association with their low levels of physical activity, this large positive energy balance almost certainly contributed to the marked obesity and the high prevalence of NIDDM found in Nauruans.

Similar dietary studies were carried out in Tuvalu (23), Fiji (24), and Kiribati (25), and again, only the overall nature of the change in diet emerged as a possible indirect etiological factor. Thus, the change from a high-complex carbohydrate, low-fat, and high-fiber diet to a high-energy, refined carbohydrate, high-fat, and low-fiber diet appears to be related to the emergence of NIDDM. It is still possible, however, that specific dietary components may have direct importance. The inability to show direct associations may reflect the crude nature of measurement techniques and cross-sectional analyses and/or the fact that epidemiological surveys have been too late to document the crucial change.

Obesity

Obesity certainly was present in Pacific populations in earlier times, as evidenced by the writings and illustrations of early European navigators and later photographic records (26). Large body size has been regarded as a sign of high social status and prosperity in Pacific islanders for many centuries. It is quite clear, however, that the obesity seen today is both more prevalent and of greater degree than that seen traditionally (26).

Although the 1980 WHO Expert Committee on Diabetes Mellitus concluded that obesity was the most powerful risk factor for NIDDM (27), there is still considerable controversy on this point (3,4,6). Both NIDDM and obesity are heterogeneous states, and data from the Pacific and other regions suggest that the impact of obesity on NIDDM may also be heterogeneous (10). This phenomenon may reflect other risk factors that are either closely associated or interact with overall body mass. Identical twin studies indicate that the genetic component of NIDDM may act independently of obesity (3). Similarly, studies in Pima Indians have demonstrated a marked interaction between obesity and parental history of diabetes, with the genetic component being particularly important (28).

A number of studies have demonstrated that differences in obesity cannot explain variation in the prevalence of NIDDM between populations (4,10,15,21). Migration studies have shown that differences in obesity do not account for all of the variation

in diabetes prevalence between migrants and sedentees (4). Supportive results are seen also in rural-urban comparisons of diabetes prevalence (4,6). The marked difference in prevalence of abnormal glucose tolerance between rural and urban Polynesians from Western Samoa persisted after age and weight standardization of the two groups (29).

Studies within Pacific populations have shown an inconsistent relationship between diabetes and obesity. The cross-sectional relationship between obesity (measured as body mass index, BMI) and NIDDM was studied on a comparative basis in three Pacific ethnic groups—Fiji Melanesians and migrant Asian Indians, and Kiribati Micronesians (10). Considerable heterogeneity was found in terms of the effect of obesity on NIDDM prevalence. Our 6-year follow-up study in Nauruans indicated that BMI was a significant independent predictor of subsequent diabetes in females but was of marginal predictive value in males, perhaps indicating a gender difference in the pathogenesis of NIDDM (26).

Cross-sectional and longitudinal data now suggest that a centralized or truncal fat distribution (particularly in the abdominal area) may be an important risk factor for both NIDDM and CVD. Centrally distributed fat seems to act independently of the overall body mass in determining risk of NIDDM (30). At this time, however, it appears that differences in fat distribution do not explain ethnic differences in NIDDM prevalence. Bjorntorp has proposed that intraabdominal fat is uniquely involved in the pathogenesis of NIDDM (30), although further evidence is required to prove this hypothesis.

Currently, body mass *per se* is not considered to be quite as important as a cause of NIDDM as previously thought. It seems more likely that it acts as a potentiator in those with genetic susceptibility, particularly in individuals with a centralized distribution of fat stores and an appropriate duration of obesity (3). Future epidemiological and experimental studies may be better able to define the relationship of the metabolic associations of centralized fat depots with the development of hyperinsulinemia and insulin resistance, as well as the importance of age of onset and duration of obesity.

Physical Activity

Results from several cross-sectional Pacific studies (Table 3) suggest that increased physical activity may have an independent protective effect against the development of NIDDM (31–33). In Melanesian and Indian Fijian males, we found that the prevalence of NIDDM was more than twice as high in those graded as sedentary or undertaking light activity as in those classed as performing moderate or heavy exercise (31). Similar differences were observed in Wallis Islanders (32) and in Kiribati (33), where physical activity remained an independently associated factor in females after age, obesity, and rural-urban status were taken into account. These findings have been confirmed in our recent study of three ethnic groups in Mauritius, an Indian Ocean island nation (unpublished data). Moreover, the gender differences in

TABLE 3. *Prevalence of non-insulin-dependent diabetes mellitus in inactive and active male subjects, from our studies in Pacific and Indian Ocean populations*

Country	Ethnic group	Age (years)	Prevalence (%)	
			Inactive	Active
Fiji[a]	Melanesian	20+	8.4	2.6
	Indian	20+	17.2	9.1
Wallis Island[a]	Polynesians	20+	4.1	1.5
Mauritius	Indian (Hindu)	25+	19.3	10.2
	Indian (Muslim)	25+	16.7	7.1
	Creole	25+	13.2	4.1
	Chinese	25+	21.4	13.0
Kiribati	Micronesians	20+	8.9	5.0

[a] Age-adjusted.

NIDDM prevalence observed in some of our earlier studies may have been due to differences in physical activity.

In less developed populations where NIDDM is rare, plasma insulin levels are also low, suggesting that insulin sensitivity is high (16). These populations have high levels of habitual physical activity related to food gathering and agricultural practices. Several clinical studies have shown that physical activity may result in lower plasma insulin levels and improved insulin sensitivity and glucose tolerance in both normal and NIDDM subjects (3). O'Dea noted similar results in a group of Australian Aboriginal subjects who reverted from a modern to a more traditional lifestyle (34). This encompassed changes in both diet and level of physical activity.

Populations with high NIDDM prevalence and in which hyperinsulinemia also has been documented—such as Nauruans (11), Pima Indians (35), Mexican-Americans (36), and Australian Aborigines (37)—have undergone considerable change in lifestyle. A major component of their modernization has been the decline of traditional hunter-gathering and agricultural practices and the adoption of sedentary lifestyles. The resulting physical inactivity may either directly cause or promote hyperinsulinemia (and insulin resistance) and initiate the cycle leading to diabetes, particularly in those who are obese (Fig. 2). In the context of our present knowledge from observational and clinical studies, this is a plausible hypothesis. However, the mechanisms by which physical activity modulates insulin secretion and/or sensitivity remain to be elucidated.

Earlier etiological studies often have ignored levels of habitual physical activity and, hence, may have overestimated the effect of obesity. In future prospective epidemiological studies, the effect of physical activity should be controlled for when the impact of obesity (and fat distribution) on NIDDM prevalence and other parameters, such as insulin sensitivity, is assessed. Such data have important ramifications for strategies directed toward prevention of NIDDM.

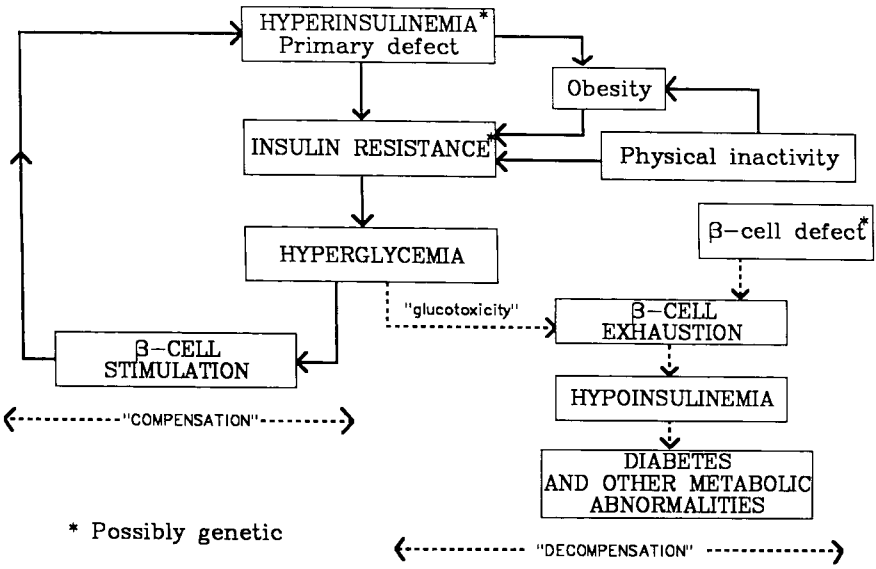

FIG. 2. How hyperinsulinemia may operate as the primary defect for the development of non-insulin-dependent diabetes mellitus. From Zimmet P, et al. (3).

Stress

The role of stress in NIDDM causation remains elusive. A major problem is the difficulty of developing meaningful parameters to study the association (4). Despite speculation of central nervous system involvement in the etiology of NIDDM, there are as yet few supportive data for such a view (4,6). Certainly, it can be argued that stress, in one form or other, has always been a part of life in Pacific island societies.

IS NIDDM A DISCRETE SYNDROME OR PART OF AN NCD COMPLEX?

The epidemic of NIDDM noted in many developing countries has occurred in association with the emergence of the major risk factors for CVD, among which is glucose intolerance itself. It has been suggested that NIDDM may not be a discrete disease entity, and, in fact, the term glucose intolerance may be more appropriate (38).

Glucose intolerance, hyperinsulinemia, hypertension, hyperlipidemia, and obesity often are found together, and it has been suggested that they may share a common etiology (38,39). If this were the case, NIDDM (or glucose intolerance) would appear to be just the tip of the iceberg. In some individuals, it may be the first metabolic abnormality to appear, whereas in others, it may appear later. If this is the case, one would expect that there eventually would be an escalation of CVD in high-

prevalence NIDDM populations. Evidence indicates that this is occurring in Pacific populations (1,26).

Reaven has suggested that resistance to insulin-stimulated glucose uptake and hyperinsulinemia are involved in the etiology and natural history of three major NCD-NIDDM, hypertension, and CAD (39). He proposed that a series of related variables exists (syndrome X), which may be of importance in the genesis of CAD. These variables include resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinemia, increased very-low density lipoprotein triglyceride, decreased high-density lipoprotein cholesterol, and hypertension. Although not included in the original hypothesis, there is sufficient evidence to suggest that central obesity (30,40) and hyperuricemia (41) should be included as part of this syndrome.

Hyperinsulinemia has been suggested as the primary determinant of this chronic disease complex. The hyperinsulinemia may be genetically determined and could be explained on the basis of the thrifty genotype hypothesis (3). In a number of populations, hyperinsulinemia predates the development of glucose intolerance by many years (11,35–37).

The concept of an NCD risk factor cluster, with possible common etiology, has very important implications for the primary prevention of NCD (38,42). An integrated lifestyle approach to prevention aimed at all of the risk factors would be more cost- and health-effective than tackling each factor separately. The epidemiological basis for an integrated approach to the prevention of NCD has been discussed in detail elsewhere (40,43). This is based on the evidence for common risk factors in the etiology of the main NCD, that is, CAD, NIDDM, hypertension, strokes, and certain cancers. The recent evidence strongly suggests that the relationship between some of these disorders is even more closely linked through a common mechanism, possibly hyperinsulinemia or insulin resistance. The most likely situation is that syndrome X (or the chronic risk factor cluster) is genetically determined and that the genetic defect is unmasked through lifestyle-related environmental precipitants—almost certainly involving diet (38). This would be quite compatible with the available data from rapidly modernizing populations, such as the Polynesians, Micronesians, Australian Aborigines, and migrant Asian Indians.

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DISCUSSION

Dr. Diamond: A question about the comparison between the New World and the Pacific: if you look at the Pacific results, I am struck by the fact that the New Guinea Highlanders, settled agriculturists who have not been recently derived from overwater colonizing ancestors, seem to be much less susceptible to diabetes than other Pacific islanders. If, however, you turn to the New World, the proportion of American Indian genes is linked with the frequency of diabetes, yet most American Indians are settled agriculturists, as much so as the New Guinea Highlanders. Those New World results seem not compatible with the New Guinea results. How would you reconcile them?

Dr. Zimmet: I agree; that is one of the loose ends. The "thrifty gene" hypothesis does fit the feast-and-famine situation. I am not sure to what extent this affects some of the American Indian tribes that lived in relatively arid conditions because when we are talking about thrifty genes, we are not only talking about food or changes in food availability but about wide changes in the temperature in the desert setting. There may have been no changes in the genetic constitution, and the body is still programmed to the hunter-gatherer diet. That does not seem to fit in with the concept of natural selection, which is the basis for the thrifty gene hypothesis.

Dr. Truswell: One of the unanswered questions is what it is in the diet of the people in Nauru and Fiji and Australian Aborigines that has precipitated diabetes in people who have some genetic tendency, which may be hyperinsulinism. There is another aspect—the glycemic index. Bush foods, which Aborigines would have eaten before white settlements, have a very low glycemic index (1). Apparently, traditional foods that the Pima Indians would

have eaten, various types of tempere beans and maize, also have a very low glycemic index (2). This suggests that these people have changed from foods that gave a slow rise of blood glucose after they ate it to foods where the blood is quickly flooded with glucose when they have a meal.

Dr. Zimmet: It would be simplistic to look at changes in nutrition or the diet as being the sole factor. It may be that physical inactivity may be much more important as a major etiological contributor. In different populations, the risk factors may be different in greater or lesser proportions.

Dr. Truswell: The genes may be different as well.

Dr. O'Dea: Attitudes to overeating change when you have to go out and get the food, digging for yams or chopping down a tree for honey. No matter how much you love that food, your enthusiasm wanes rather quickly! There is a very close interrelationship between physical activity and food intake in that sense as well.

Dr. Zimmet: There probably might have been considerable intermarriage. There are only 6,000 inhabitants on Nauru. I think the population of Western Samoa is 150,000. The genetic component is very important, but it does not express itself in the traditional setting, and in rural Western Samoa, the rates are much less than in the urban setting. The prevalence of diabetes starts to fall in American Indians with increasing Caucasoid genetic admixture, and so it is with the Australian Aborigines and the Pacific islanders. The best intervention program to improve their glucose tolerance would, in fact, be by introducing the genes of a low prevalence group.

Dr. Lentze: As a pediatrician, I would like to know when this cascade of risk factors starts in the children in these areas.

Dr. Zimmet: I would have paid you $300 to ask that question, but fortunately I did not have to. I have a slide ready. We, along with Michael Gracey and Norman Kretchmer, have been investigating this in young Aborigines and in Papua New Guinea, and there are data emerging. We found higher insulin levels, that is, hyperinsulinemia, in urban children in Papua New Guinea. Whether this is a good marker for the effect of acculturation we do not know. In the Pima Indians, non-insulin dependent diabetes occurs in children as early as 13 to 14 years of age.

Dr. Lentze: But what about weight and height or weight for height curves? Have there been significant changes over the last 10 to 20 years?

Dr. Gracey: I can comment on the available information about growth and body size in young Aborigines in remote parts of Australia. However, there is little well-documented, prospectively collected information available to help answer your question. My strong impression is that females, in particular, in Aboriginal communities tend to change from teenage to early and midadult years from being very thin scrawny girls to being very obese females within about 10 to 15 years. This is quite a remarkable transformation, which occurs very quickly in these young women. Such a change in body composition does not appear to be so prevalent in Aboriginal males.

Dr. Kretchmer: Dr. Gracey and I studied children starting at the age of 7 to about 18 in remote parts of northwest Australia (3). We measured insulin, C-peptide, growth hormone, and a panorama of fatty acids as well as lipids. The data we have are very similar to those reported by Hilary King and Paul Zimmet. Of about 100 children, approximately 10% showed evidence of hyperinsulinemia and about 3 showed frank diabetes. We have not analyzed all the data, but we did do BMIs and have plotted three-dimensional curves that involve BMI, suggesting that, insofar as the females are concerned, the BMI was correlated with the insulin response.

The Pimas have confused everybody about the American Indians. The Pimas were, historically, agriculturists not hunter-gatherers. They lived in the Gila River Valley, and they have been farming for a thousand years. We talk of them as hunter-gatherers. Bear in mind that most of the American Indian tribes and groups do show this kind of diabetes but not at the rate of the Pimas, who seem to have the highest rate of diabetes in the world. There are certain groups, such as the Northern Athabascan Indians, who are more related to Eskimos than to more southern Indians. They have practically no diabetes. The Eskimos have a low rate of diabetes. They are the primeval hunter-gatherer, and they have practically no diabetes except when they move into urban areas. My own prejudice is that once we are dealing with a genetic thing, I personally like to think of it as a survival situation. It makes good sense to me. I have spoken to Jim Neel about this theory,and he believes that no one has sufficiently tested his hypothesis—not he, not we. He has revised it once since the original inception of the theory. It is a wonderful theory, and it makes very good sense in thinking of insulin as a survival hormone. Being a pediatrician, too, I believe we should look for all chronic diseases in children, not in aging people. This is the prejudice of a pediatrician, but that is where we will find the roots of chronic diseases—in children.

Dr. Gracey: To complete the answer for Michael Lentze, if I am not mistaken, the youngest child with hyperinsulinemia and impaired glucose tolerance in our study of Kimberley Aborigines was 11 years of age (*Proceedings of the Nutrition Society of Australia*, 1989).

Dr. O'Dea: We have found hyperinsulinemia independent of age, from 15 to over 70, and pretty much independent of BMI. Hyperinsulinemia can occur in very thin people, and good insulin sensitivity can occur in very fat Aboriginal people. The fasting insulin is much more correlated with the BMI but not the insulin response.

Dr. Truswell: It would be good to have another workshop like this, to look at all the different groups of mankind that have an increased tendency to diabetes. For example, there are migrants from the Indian subcontinent, in different parts of the world, in Africa, also in parts of Europe, who have a much higher rate of diabetes than the host population.

Dr. Zimmet: I can comment on that because we have studied the migrant Asian Indians in Fiji and Mauritius. Obesity is not the whole story because, in general, these people are not obese, but they are hyperinsulinemic. All the groups that have been studied, migrant Asian Indians in Singapore, Great Britain, Fiji, Mauritius, and Africa, exhibit hyperinsulinemia in the presence of normal glucose tolerance. They have quite high rates of cardiovascular disease, but they tend to have normal lipids. Factors that have emerged as major risk factors of the cardiovascular diseases in these groups consistently are glucose intolerance, hyperinsulinemia, and, in some of the groups, hyperuricemia. Obesity usually is not a major factor.

Dr. Diamond: To return to the hypertension issue, although it has not been our focus here, there is a possible interest in an African/New Guinean comparison. People of West African descent have a high incidence of essential hypertension. An evolutionary interpretation has been that, at least in the interior of Western Africa as one gets away from the coast, it is clear that historically salt availability was very low. Salt came in by caravans from far away. Similarly in the New Guinea Highlands, where I started to work in 1964, the people with whom I worked told me how they had got salt before it became available from salt shakers through contact with Europeans. It was excruciatingly difficult and involved gathering, burning, and leaching of selected leaves. Salt availability was extremely low, so one could speculate that people like New Guineans and West Africans, living on a chronically low salt diet, would have evolved salt thriftiness, a heightened ability to conserve salt. That ability would then give them hypertension on a high-salt diet. If that were the case, however, one would

then expect New Guinea Highlanders to be developing a high incidence of hypertension now that they have access to salt shakers. What can you say about the incidence of hypertension in the New Guinea Highlanders?

Dr. Zimmet: In brief, in the Papua New Guinea Highlanders and in the rural setting, hypertension is rare, and there is not the age-related rise in blood pressure that one sees in Western populations. However, hypertension is emerging in the urban populations. Further out into the Pacific, in Micronesia and Polynesia, there are rates of hypertension almost twice that seen in Caucasoid populations, the prevalence of which is around 10%. We have not been able to correlate salt intake with this. There may be social stresses that play a major role in these communities as part of the migration and urbanization process.

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