

## Strong and weak linkages in the thrifty genotype hypothesis

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Evidence for a substantial variability in the frequency of NIDDM among Pacific island populations is now well documented. Data from the published studies support the hypothesis that this variability is in part the result of genetic differences between the populations. In the past it has been hypothesised that these differences were the result of variation in a single gene. This hypothesis appears now to be abandoned. Hopefully the high level of research currently proceeding on the human genome will soon produce some clear loci linkages to the disorder.

Whether there are one or several genes involved in producing the population differences, a major evolutionary question is how natural selection processes resulted in such population differences. Indeed, major population variability in NIDDM frequency has been recently observed in a wide variety of identifiable populations and ethnic groups. Given the clear evidence that a reasonably affluent life style is a prerequisite for the high levels of NIDDM it seems probable that even more variability in population frequency rates will soon appear as new populations increase in affluence.

The close association of increased wealth to altered diets, increased body weight and rising rates of NIDDM has made James Neel's thrifty genotype hypothesis a very attractive explanation for the very high rate in such groups as Polynesians, Micronesians, Native Americans and Australian Aborigines. Neel has in recent years become more dubious of his own hypothesis and in a 1989 publication termed it a soft hypothesis noting that "non-insulin dependent diabetes mellitus is undoubtedly quite heterogeneous in aetiology".

In a 1984 publication I explored in a preliminary fashion the inter-relationship between the demographic and genetic history of the Pacific islanders and the degenerative disorders which had become common by that time. The conceptual structure of the "thrifty" genotype seemed to fit well with the rapid and massive weight gains demonstrable in Polynesians and Micronesians. However, the linkage of NIDDM to a feast and famine history fit only some of the groups. This evidence, along with the more recent studies which demonstrate a lack of consistent physiological and biochemical linkages, suggests that a detailed examination of the Pacific populations in terms of the postulated steps of the selected process is desirable.

It has been shown that the Polynesians, and to a lesser extent Micronesians, have very heavy weights and large BMIs. Indeed it appears that Samoans are, as a population, the heaviest group in the world with the greatest average BMI. Extensive studies of the possible causes for these high weights have been conducted and will be described in detail in the

lecture. The evidence suggests an ability to gain weight with a rapidity which only occurs under conditions of forced feeding in other groups. Exercise reduction below critical levels and binge eating appear the most significant behaviour associations with high body weights.

The survival and reproductive advantages which are presumed to exist for individuals who can rapidly increase in fatness is that the energy stored will keep them alive and active during periods of food shortage. Such food shortage periods can be documented for small island groups in the typhoon areas of the Pacific and can be assumed to have occurred numerous times during voyaging.

A second advantage which has not been fully considered in relation to the level of fat is the insulative value during cold exposure. Data showing the insulation and calorie saving value of subcutaneous fat will be presented at the lecture. This may also be quite significant for the explanation of high fat levels in North American natives since their ancestors passed through quite cold areas and mortality from cold exposure was possible. However, for Pacific islanders the important aspect would have been the caloric savings gained during voyaging and fishing. It should be noted that sea mammals, including those restricted to tropical waters, have very heavy subcutaneous layers of fat which are used for insulation and for energy during travel without food.

These behavioural and physiological data provide strong evidence for the suggestion that evolutionary selection would have favoured genes that produced rapid fat and muscle gain. However, it is not obvious to me why this should result in high levels of NIDDM. Certainly there is an association between BMI and NIDDM in some populations, but the linkage appears to be weak. Thus the Nauru population which has a much lower average BMI than the Samoan group with a similar exposure to affluence and imported food have a frequency of NIDDM which is several times the Samoan rate. These findings do not mean that the unusually high levels of NIDDM among some Pacific populations lack a strong genetic basis but it is likely that the selection for the ability of some Pacific populations to rapidly increase body fatness is not a sufficient cause for the unusually high frequencies occurring in selected populations.

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