
Scant evidence of periodic starvation among hunter-gatherers

Dear Sir,

In the April issue of *Diabetologia* Reaven [1] proffered an alternative hypothesis to Neel's thrifty genotype hypothesis [2]. His proposal, called the 'not-so-thrifty' genotype hypothesis, argues that the gene was not one which conferred exceptionally efficient storage of food energy but instead conserved muscle protein during periods of starvation by reducing gluconeogenesis from amino acids. In our opinion the basis of both hypotheses – periods of food scarcity in pre-agricultural populations – is not supported by the scientific literature.

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Implicit in both Neel's and Reaven's hypotheses is the assumption that pre-agricultural people must have gone through regular, periodic episodes of starvation that had a negative impact on reproductive potential and hence resulted in the selection of a gene or genes which would have survival value during the fluctuations between 'feast and famine'. This concept is frequently invoked to explain the high incidence of diseases of insulina resistance [Type II (non-insulin-dependent) diabetes mellitus, hypertension, obesity and coronary artery disease] among recently acculturated populations.

Although Neel's hypothesis has become 'one of the orienting concepts of nutritional and biomedical anthropology', it is founded upon an assumption which cannot be corroborated by the available ethnographic data derived from living hunter gatherer populations nor by the fossil record. Indeed, periodic starvation became more frequent and nutritional status declined when hunter gatherer populations made the transition to agriculture less than 10000 years ago [3, 4]. Starvation among early agriculturists was quite common because of the

dependence upon a few staple cereal crops. If one staple food crop failed, farmers ran a greater risk of starvation than did hunter gatherers who could use a much broader range of wild plant and animal foods. Modern studies of hunter gatherers show that there is a seasonal fluctuation in body weight, but these studies do not indicate evidence of periodic starvation or chronic malnutrition [5, 6]. In a review of 51 references examining human populations from around the earth and from differing chronologies, Cohen [7] concluded that there was an overall decline in both the quality and quantity of life during the transition from hunting and gathering to farming.

Generally, in most parts of the world, whenever cereal based diets were first adopted as a staple food, replacing the rich variety of wild animal and plant based foods of hunter gatherers, there was a characteristic reduction in stature [3], an increase in infant mortality [3, 4], a reduction in life span [3, 4, 7], an increased incidence of infectious diseases [3, 4, 7, 8], an increase in iron deficiency anaemia [3, 4, 7, 8], an increased incidence of osteomalacia, porotic hyperostosis and other bone mineral disorders [3, 4, 7, 8] and an increase in the number of dental caries and enamel defects [3, 4, 7]. Clearly, early farming brought on not a reduced mortality from starvation and nutritionally related diseases, but to the contrary, an increase [3, 7]. If either Neel's and Reaven's hypothesis is correct, then the advent of agriculture would not have reduced the selection for a thrifty genotype, but would have actually increased it. Obviously, population and epidemiological studies of Type II diabetes suggest that this is not the case. Europeans have had a relatively long exposure (5000–7500 years) to agriculture, including regular periods of severe famine right up to historical times, yet they have the lowest prevalence of Type II diabetes on a world wide basis [9]. Therefore, the assumption that starvation was the single and only factor selecting for a putative 'thrifty' or 'not-so-thrifty' genotype could not be correct.

Brand, Miller and Colagiuri [10] have suggested that the high protein intake and low carbohydrate intake of pre-agricultural diets would have represented a more likely environmental pressure responsible for selecting for multiple genes originally hypothesized by Neel to be 'thrifty genes'. Their hypothesis, 'the carnivore connection', proposes that an insulin-resistant genotype evolved to provide survival and reproductive advantages to populations adapted to a high meat, low plant food (low carbohydrate) nutritional environment. Unlike true carnivores, humans have a limited capacity for gluconeogenesis even on a high protein diet [11]. Insulin resistance would have conveyed a selective advantage for populations consuming high protein and low carbohydrate diets long-term because it would have maximized gluconeogenesis and thereby

redirected glucose away from muscles, facilitating the preferential use of glucose by the brain, fetus and mammary gland [10]. It is likely that Neel's concept of 'thrifty' and Reaven's concept of 'no-so-thrifty' are a misinterpretation of the true function of the gene(s) which produce insulin resistance.

Yours sincerely,

L. Cordain, J. Miller, N. Mann

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Insulin resistance, the key to survival: a rose by any other name

Dear Sir,

My purpose in suggesting that muscle insulin resistance was once of evolutionary use to our species and is now responsible for the world-wide epidemic of Type II (non-insulin-dependent) diabetes mellitus [1], was quite simple. I believe the initi-

al suggestion by Neel [2] that the basic abnormality that now increases risk of Type II diabetes must at one time have had survival value for primitive man. In his initial presentation, Neel suggested that a "quick insulin trigger" was the relevant physiological event. I believe this view to be physiologically incorrect and that muscle insulin resistance was the abnormality – not a primary increase in insulin secretion – and was at one time useful but now greatly increases the risk of Type II diabetes. It is obvious from the letter by Drs. Cordain, Brand-Miller and Mann that they are in fundamental agreement with the survival value of insulin resistance. Specifically, they state "... humans have a limited capacity for gluconeogenesis even on a high protein diet. Insulin resistance would have conveyed a selective advantage for populations consuming high

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protein and low carbohydrate diets long-term because it would have maximized gluconeogenesis and thereby redirected glucose away from muscles, facilitating the preferential utilization of glucose by the brain, fetus and mammary gland." I will put off debating physiology with them for another day, but simply indicate in this context that they seem to agree with me that the goal was to prevent glucose from being used by muscle for energy, i.e. muscle insulin resistance was the survival trait. Thus, as far as I can tell, the only difference between the position I formulated and the view expressed in the letter by Drs. Cordain, Brand-Miller, and Mann, is the reason why insulin resistance was of evolutionary value. They argue that insulin resistance did not emerge because of the threat of starvation, but rather because it would have survival value for populations consuming a "high meat, low plant food" diet. I don't think a great deal would be gained by continued debate over whether the evolutionary pressure that led to the emergence of insulin resistance as a useful survival feature was secondary to periods of inadequate nutrition, as compared with the consistent consumption of high protein, low carbohydrate diets. On the other

hand, it would be a step forward if there were general agreement as to the fact that insulin resistance was once evolutionary useful and that explains why the health-related risks of this abnormality are so pervasive now. If Drs. Cordain, Brand-Miller, and Mann agree that insulin resistance was the genotype that Neel initially proposed as providing survival value, I am quite willing to welcome them to the ranks.

Yours sincerely,
G. M. Reaven

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