GENETIC FACTORS IN NUTRITION

Edited by
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Genetic Factors in Nutrition

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Introduction

During the nineteenth century, one of the forefathers of human genetics, Francis Galton, used the terms "nature" and "nurture" to refer to biological heredity and to the environment, the two opposing forces which mold a living being and determine its phenotype. Although it is generally recognized that genes play a role in the use of nutrients, Galton's choice of words emphasizes the frequent perception of nutrition as a condition modulated essentially by the environment. The environmental aspects of nutrition have been amply studied, whereas studies on genetic factors are scarce.

For a long time now, scientists from both fields have recognized the enormous variation in all human populations. Genetic polymorphisms are widespread and essential for survival and evolution. On the other hand, nutritionists have been hindered by great individual variation in their subjects when establishing minimum nutritional requirements adequate for achieving optimal levels of health in various populations.

This great variability, seen both from the genetic and nutritional points of view, generates an enormous degree of individuality. But to what extent is nutritional individuality a consequence of genetic individuality? How do genes and food interact to determine nutritional state? How does this interaction influence health and disease? Why are some people obese without being gluttons or lazy, while others can eat almost limitless amounts without becoming obese? Why do some children fall victim to kwashiorkor or marasmus while others, seemingly equally undernourished, manage to adapt, survive, and reproduce? How in nutrition might we quantitatively interpret Ortega y Gasset's phrase "I am I and my circumstances?"

For many of these questions we lack even tentative responses. Finding the answers will depend on the joint interdisciplinary effort of nutritionists and geneticists. There have not been many such collaborations; geneticists and nutritionists have usually followed separate paths. For example, we know something about the importance of genotype in susceptibility to obesity, but we know nothing at all about the importance of genotype in predisposition to serious forms of malnutrition. We have the results of countless nutritional surveys carried out throughout almost the entire world. But students interested in the role of family factors will have a hard time finding anything useful because these factors are almost never considered in the questionnaires.

It is time for this situation to change. This book contains the proceedings of the International Workshop on Genetic Factors in Nutrition, sponsored by the National Autonomous University of Mexico and the National Institute of Nutrition ''Salvador Zubirán'' to promote the opening of communication between the two disciplines and to help develop a link between them. We aimed to define questions rather than answers, inventory methodological tools and strategies, and identify some of the most promising lines of interdisciplinary research.

The first papers establish the framework for consideration of genetic–nutritional interplay, utilizing the unifying perspective of biological evolution. Afterward, some examples of successful interaction between the two disciplines are reviewed. This is followed by a discussion of some aspects of nutrient requirements and utilization and consideration of methodological approaches to assess nutritional status, with emphasis on malnutrition. Finally the proceedings are summarized and genetic prospectives are presented. The discussions held by the participants during the meeting have been summarized by the chairmen of each session.

The editors were extremely fortunate in having the advice and support of the members of the program committee: Héctor Bourges, Stephen Cederbaum, Phillip P. Cohen, James V. Neel, Cecilia Salgado, Antonio Velázquez, and Richard Ward. They helped us plan the conference, define the approach, develop the program, and convince the participants, all of them very busy scientists, to temporarily set aside some of their obligations, prepare their manuscripts, and attend the meeting. This workshop on genetics and nutrition would never have come to fruition had it not been enthusiastically accepted and generously supported by the National University of Mexico's Coordinator de la Investigación Cientifica, Jaime Martuscelli; by the Director del Instituto de Investigaciones Biomédicas, Kaethe Willms; and by the Secretario Ejecutivo del Consejo de Estudios de Posgrado of the University, José Manuel Berruecos. We also want to acknowledge the valuable help of the Programa Universitario de Investigación Clínica, of the Dirección General de Asuntos de Personal Académico of the University, and the Consejo Nacional de Ciencia y Tecnología.

Special thanks go to Dr. P. P. Cohen and Cecilia Salgado, whose help and cooperation both before and during the workshop contributed greatly to its success, and to Paulina Rostín, whose constant and efficient work always made our job easier.

It is appropriate that this Workshop on Genetic Factors in Nutrition should be held in Mexico. For 40 years now, many excellent, internationally recognized nutritional research projects have been carried out here; the country has several mature groups of nutritionists.

The work sessions took place in Teotihuacán, near Mexico City. Two thousand years ago, the archeological site was the principal city on the American continent, a crucible in which the arts and sciences peacefully flourished. It is appropriate to point out that Teotihuacán was one of the few great metropolises never surrounded by defensive walls. Could there be a better place, then, for scientists from many countries to meet in harmony, as surely wise men of that ancient civilization often did, to work together for the advancement of knowledge?

A. VELÁZQUEZ
H. BOURGES

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PART I

EVOLUTIONARY AND GENETIC FRAMEWORK

GENETICS AND NUTRITION: AN EVOLUTIONARY PERSPECTIVE

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INTRODUCTION

The diet of our ancestors

Humans are exceedingly omnivorous animals. In the early stages of hominoid divergence from the other primates, we may presume the diet was very similar to that of present day chimpanzees. Our ancestors would have been scavengers, living on nuts, berries, fruits, roots, and an occasional small animal or egg, but, they posessed simple tools, and gathering was therefore much more efficient than in chimpanzees por example. As they began to develop hunting skills (as opposed to scavenging skills), perhaps 1,000,000 years ago, the amount of animal protein in the diet increased. Then came plant domestication, beginning some 20,000 years ago, and, even with early agricultural practices, a radical change in the diet occurred.

There are very few surviving human populations depending on pre-agriculture-type hunting-and-gathering for their livelihood, and such as there are - Australian aborigines - have usually been so displaced from their customary range that they do not project a very satisfactory picture of the nutritional balance of a hunting-gathering population. On the other hand, there still exist - or did until recently - relatively intact populations combining hunting-and-gathering with primitive agricultural practices. Two such groups are the Yanomama Amerindians, occupying the region drained by the Upper Orinoco and the two principal northern tributaries of the Amazon River, the Rio Branco and the Rio Negro, and the Xavante of the Brazilian Mato Grosso. In addition to our studies of these two groups, we have by now done field work among 10 other Amerindian tribes in various but more advanced stages of acculturation.

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In this presentation, I shall tend to concentrate on findings among Amerindians, not only because this is the group with which I am most familiar but also because it seems especially appropriate to a meeting of this type in this hemisphere.

Although the studies of our group on the Xavante and Yanomama were never specifically dietary in nature, some aspects of their subsistence patterns were obvious. With respect to general nutritional status, we never encountered true obesity but an occasional young woman was 'pleasingly plump'. Neither, on the other hand, did we encounter the stigmata of chronic protein malnutrition. Although the Yanomama still are extensively engaged in hunting and gathering, the majority of their calories are derived from the cultivated cooking banana *(Musa paradisica)*. This is grown in gardens by the slash-and-burn technique, new gardens being started frequently. There may be periods of acute food shortages, when the old gardens are not yielding well and the new gardens are not yet mature, but I doubt if any undisturbed tribal population ever endured the chronic malnutrition which is a problem for so much of the world today. No group would voluntarily occupy an area that would not adequately support it.

In their efforts to achieve nutritional balance, the Xavante and Yanomama are most adaptable as to protein source. Although game - tapir, capybara, monkey, armadillo - are preferred, caterpillars, beatle larvae, turtle eggs in season, and small fish obtained by poisoning streams with rotenone, are quite acceptable.

In general, a child is breast fed for some 3 years, until the arrival of the next child. If an adult woman is not nursing her own child, she is nursing the child of some relative. The nutritional status of infants is by inspection usually excellent. The gamma-globulin levels of tribal populations are by the standards of civilized populations quite high; we have argued for a *relatively* smooth transition from passive to active immunity against the local pathogens [1]. By the time the child is weaned, its dentition enables it to cope with the local foods. It is our impression that the weanling diarrhea so characteristic of civilized tropical agrarian populations is a much less serious problem in a tribal group such as the Yanomama.

It is, in this connection, relevant that almost all primitive groups which have been adequately studied can be shown to have customs which sharply limit population growth. To what extent this results from a conscious effort to reconcile numbers with available resources is a much debated question among anthropologists. The prolonged lactation mentioned earlier may serve to suppress ovulation for some time following parturition; this can scarcely be seen as a conscious measure to limit population growth. An Indian mother will nurse her child several times an hour during the day, and several times in the course of the night. McNeilly [2] has argued that frequent nipple stimulation leads to regular prolactin surges and a suppression of estrogen and progesterone production, which is much more effective than the suppression induced by widely-spaced nursing.

In addition, however, there are conscious efforts to control the birth rate. There are often intercourse taboos for at least a year following the birth of a child. Further, abortion, induced by direct trauma to the abdomen, and infanticide are not uncommon among the Yanomama. Although precise figures are very difficult to obtain, we estimate, on the basis of anecdotal information plus the markedly unbalanced sex ratio among the very young, that approximately 30 percent of liverborn female infants and 5 percent of liverborn male infants are killed [3]. One stated reason for the abortion and infanticide is that the nursling is not yet ready to leave the breast. In addition, deformed children are customarily killed. The basis for the custom of such preferential female infanticide has no simple, compelling explanation.

Recently it has been argued that the apparent child-spacing among primitive populations may also be due to the fact that women below critical levels of fat storage do not conceive [4, 5, 6,]. This is a hypothesis that cannot-unfortunately-be pursued in many contemporary populations. As already suggested, the apparent nutritional level of the Yanomama and other relatively undisturbed tribes is such, that I dou'›t whether this is an important factor in Amerindian child spacing.

The ecology of disease is quite different in unacculturated Amerindians than in civilized communities [7, 8]. Of particular interest to us in the context of nutrition should be the parasitic and diarrheal diseases. I have already indicated the belief that weanling diarrhea is relatively uncommon among Amerindian infants. Our studies of parasites reveal a high prevalence of *Ascaris lumbricoides,* hookworm, *Trichuris trichiura, Strongyloides stercoralis, Entamoeba hartmanni, Entamoeba coli, Entamoeba histolytica, Iodamoeba buschlii, Giardia lamblia* and *Chilomastix mesnili,* plus several other less frequent parasites [9, 10]. But despite the high prevalences, the parasitizations, as judged from very limited stool samples, were not heavy. In the instance of hookworm, the custom of changing the village site every 3 or 4 years plus lack of a fixed place for defecation undoubtedly prevented the super-infection characteristic of many rural agricultural populations. The vicious combination of recurrent diarrhea, intense parasitization, and chronic malnutrition seen among the caboclos and campesinos of Central and South America is much less apt to occur amongst unacculturated Amerindians. On the other hand, in some areas parasitization by microfilaria of *Mansonella ozzardi* is very heavy [11, 12]; it has never ceased to amaze me how the tissues (at least as judged by the skin) can so swarm with these worms with so little apparent medical consequence.

The result of all this is for the Yanomama a life curve rather different from those encountered in civilized populations (Fig. 1) [3]. We estimate that, aside from death due to infanticide, some 22% of liveborn males and 13% of liverborn female infants die during infancy. This is high by the standards of developed countries, but well below the situation in most peasant populations until rather recently. The continuing mortality during the childhood and adult years has a large traumatic component. Approximately 10% of liveborn infants can expect to reach age 60. An analysis of skeletal material from Indian burial mounds suggests prehistoric mortality patterns very similar to those of the Yanomama [13, 14, 15]. We suggest that with this population structure, the natural rate of population

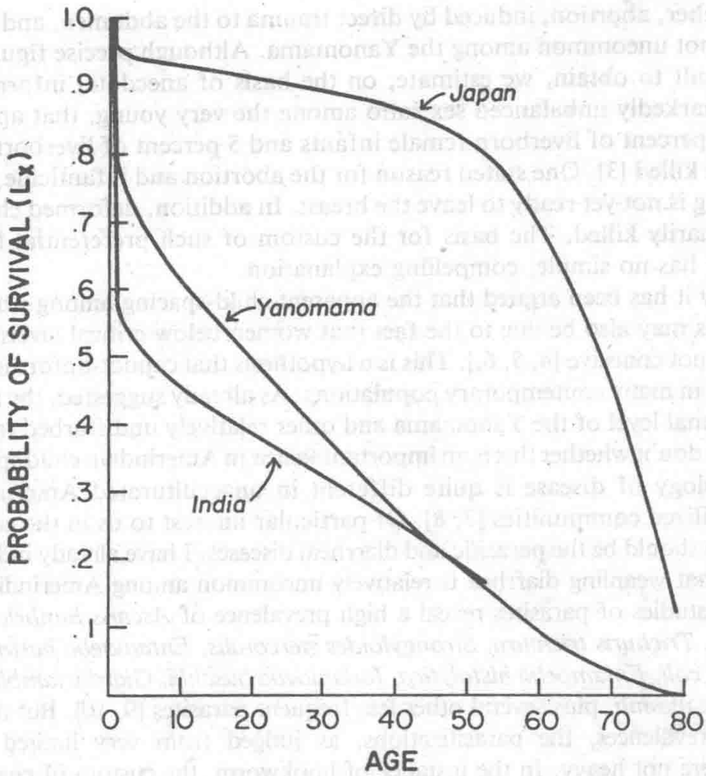

Figure 1. Life curve of the Yanomama compared to other populations.

increase per year is 0.5 -1.0% per year. Howell [16] reports similar findings among the contemporary !Kung San. We believe that because of the decimation of their neighbors plus the relatively recent acquisition of steel tools, the Yanomama are expanding more rapidly than characterized Indian tribes during prehistory. Even lower rates of increase - say 0.3% - were presumably periodically offset by a variety of disasters - the most important probably being intervillage warfare -otherwise given 20,000 years and even a very small founding population, the total numbers of Indians at the time of first contacts [estimated at 20,000,000 for South America [17]] would have been larger.

Our altered nutritional circumstances

I hardly need dwell on how dramatically the nutritional circumstances of modern man depart from those of his ancestors. The most obvious differences are, on the one hand, the emergence, all over the world, of groups who are chronically malnourished, but, on the other hand, a striking frequency of