by Paul M. Ribisl, Ph.D., FACSM

Darwin Was Wrong: The Thrifty Genotype and Demise of the Fittest

Last year, in a column entitled: "Darwin Was Right: Survival of the Fittest," I wrote about the protective effect of physical fitness on cardiovascular mortality, suggesting that Darwin's theory about the survival of the fittest through natural selection had modern day relevance (1). However, the natural selection that Darwin referred to was a phenomenon that took tens of thousands of years to show results, whereas the study that I cited by Jonathan Myers, Ph.D., FACSM, and colleagues (2) took place within one generation. The Myers study demonstrated that the most physically fit individuals lived longer and that for each increase of 1.0 metabolic equivalent (MET) in exercise capacity, there was a 12% improvement in survival. In that study, the influence of genetics was minimal because the protection came primarily from fitness and a healthy, active lifestyle rather than genetic influence.

In this column, I will take a different approach and show how a genetic advantage that has served Homo sapiens well for thousands of years may actually lead to our early demise, rather than an extended life span. The background for this column comes from a recent paper by Manu V. Chakravarthy, M.D., Ph.D. and Frank W. Booth, Ph.D., FACSM, (3) entitled: "Eating, Exercise, and 'Thrifty Genotypes': Connecting the Dots Toward an Evolutionary Understanding of Modern Chronic Disease." In this important and revealing paper, the authors demonstrate that our ancestors, who were hunter-gatherers, were exposed to repeated cycles of feast and famine, and they depended upon superior physical fitness and extended physical activity in their search for food. But to ensure survival during periods of famine, certain genes evolved to regulate efficient food intake as well as the efficient utilization of fuel. These genes were identified as "thrifty genes" in 1962 by Neel (4), who related these genes to the development of type 2 diabetes.

Our Genetic History

Although it is difficult to trace our genetic history precisely, it is believed that most of our present genome was developed through natural selection during the Late Paleolithic era (50,000–10,000 BC), at a time when humans existed as Hunter-Gatherers (5). This time was characterized by daily physical activity in which man needed to forage for food in the form of fruits, vegetables, nuts, etc., as well as fish and hunt for animals. It is believed that our human genome has changed little if at all in the past 50,000 years. Support for this viewpoint is that no genetic differences have been discovered between primitive people who have retained the hunter-gatherer lifestyle and those who adopted agriculture in the distant past. Therefore, modern man retains the "thrifty genes" genetic makeup of the Hunter-Gatherer, a genetic makeup that served man well for these millennia in times where the "kilocalories-in" were balanced with "kilocalories-out." But today, man is faced with a drastically different scenario where the kilocalories-in/kilocalories-out ratio is unbalanced.

Our Physical Activity History

It has been estimated (6) that the physical activity level of Paleolithic man was approximately 1,000 kcal/day^{-1} whereas the total kcal/day intake was typically around 3,000 kcal/day^{-1}. This provides a subsistence efficiency of 3:1. However, in contemporary affluent societies like the United States and most Western nations, we consume approximately 2,100 kcal/day^{-1} while only expending about 300 kcal/day in physical activity, yielding a subsistence efficiency of 7:1. It is clear from these figures that even though modern man consumes fewer kcal/day, he would

need to increase his physical activity level to 700 kcal/day^{-1} to reestablish the 3:1 subsistence efficiency of Paleolithic man. Modern technology and mechanization have engineered most of the physical activity out of our daily lives and a sedentary lifestyle is now the rule rather than the exception.

Our Dietary Intake History

There has been a great deal of research, debate, and speculation about the composition of the diet of the "hunter-gatherer" recently, especially since the onset of the obesity epidemic (7) and various other nutrition-related disorders. The Paleolithic hunter-gatherer diet was originally thought to be predominantly carnivorous with a significant meat intake—but then other studies suggested that gathered plant foods formed the majority of food energy; however, most recently Loren Cordain, Ph.D., et al. (8) has proposed that animal food formed the major (~65%) portion of the hunter-gatherer diet with the remainder coming from plant foods. The Paleolithic period preceded the Neolithic period but the latter period coincides with the adoption of agriculture approximately 10,000 years ago. The Neolithic period included the cultivation of plants and the domestication of animals for readily accessible food and could be thought of as the precursor to our current diet. But some have concluded that humans are maladapted to the relatively recent diets of domesticated and processed foods (9) and have suggested a return to a so-called Paleolithic (preagricultural) diet, which is similar to the recent and popular Adkins diet. But is it simply the composition of the diet that makes a difference or is there more to the equation that must be considered?

Our Present Lifestyle Pattern

Throughout man's early existence, physical activity was linked to survival and it has been estimated that men may have hunted for one to four nonconsecutive days per week, whereas women were estimated to have gathered food every two to three days (3). This pattern of feast and famine characterized our early lifestyle but differs greatly from our present day pattern. Our current lifestyle pattern is one of near-perpetual physical inactivity coupled with abundant food. Thus, we have the reversal of the "high physical activity and famine" pattern of our ancestors to an unhealthy pattern today of "feast and rest." This is not the lifestyle that our genetic selection process prepared us to confront.

Thrifty Genotype Paradox

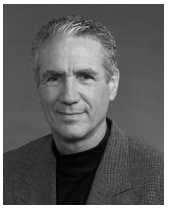
Although our genes were adapted to alternating periods of "feast/famine" and "physical activity/rest," we now have a lifestyle pattern with only half of the equation: "feast and rest." The thrifty genotype allowed us to store excess energy in times of feast and to conserve energy in times of famine—it was thrifty because it was extremely efficient in the intake and/or utilization of food (4). The more excess energy one could store, the longer one could survive a long period of famine, whereas those who could not store significant amounts of excess energy were unlikely to survive and thus were unable to pass along their "inefficient" genes to later generations. As Drs. Chakravarthy and Booth (3) have noted: "...the genes of our ancestors were not selected for sedentary existence. In fact, those individuals whose genes only supported sedentary living were likely eliminated from the gene pool during evolution because of their inability to gather food or hunt." These authors point out that there are similarities in the patterns of change in certain parameters during the "feast/recovery-from-exercise" phase and the "famine/exercise" phase. In the feast/recovery from exercise phase, blood glucose, insulin, and skeletal muscle glycogen are increased while skeletal muscle fatty acid oxidation decreases; the opposite occurs during the famine/exercise phase. As long as there are regular and alternating repeats of these cycles, the body remains in homeostasis; however, prolonged and extended periods of either phase are detrimental to survival.

Due to the limited supply of food

and the physical demands of everyday life in the past, there was little risk of an extended period of feast and rest. It has only been recently that our society has been able to engineer most of the physical activity out of our daily lives at the same time that food has been made abundant, accessible, and cheap. It is safe to say that we currently have a lethal mix of the wrong genetic makeup to cope with a toxic environment of declining physical activity and increasing caloric consumption. What is the solution?

The Need to Adapt Our Behavior to Our Genes

At the present time, if we cannot change our genes, then we must change our behavior. The change in behavior must occur on both sides of the energy balance equation. Consuming a large number of calories and/or a high fat intake, in and of itself is not problematic—because individuals who are engaged in heavy physical labor, either occupational or recreational, can consume 5,000 to 8,000 kcal/day and still retain a normal body mass index with no ill effects upon their health and well-being. These individuals are in energy balance and they also benefit from the physiologic benefits of vigorous physical activity. The problem occurs when we combine the Westernized sedentary behavior with the Westernized diet of calorically dense foods in excess, allowing our "thrifty genes" to express themselves in the efficient storage of the excess calories as fat. Unfortunately, we have not progressed to the next cycle of famine or exercise but have remained stalled in our cycle of "feast and rest." The healthy solution is not to use the "famine" approach to this problem, which is essentially a starvation tactic similar to anorexia. Given the trend toward automation and removal of all physical exertion from our occupations and activities of daily living, the only practical solution is to program regular physical activity back into our lives and the lives of our clients.



Paul M. Ribisl, Ph.D., FACSM, is a Professor and Chair in the Department of Health and Exercise Science at Wake Forest University. He is an exercise physiologist who was a cofounder of the Cardiac Rehabilitation Program at Wake Forest University, which he directed from 1975 to 1991. In 1997, he completed a mini-fellowship in gerontology at Stanford University and is now involved in three research trials. Dr. Ribisl currently serves as an associate editor for ACSM's Health & Fitness Journal®.

References

1. Darwin, C. *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*. London: John Murray, 1859.
2. Myers, J., M. Prakash, V. Froelicher, et al. Exercise capacity and mortality among men referred for exercise testing. *New England Journal of Medicine* 346(11):793–801, 2002.
3. Chakravarthy, M.V. and F.W. Booth. Eating, exercise, and "thrifty" genotypes: connecting the dots toward an evolutionary understanding of modern chronic diseases. *Journal of Applied Physiology* 96:3–10, 2004.
4. Neel, J.V. Diabetes mellitus: a "thrifty" genotype rendered detrimental by "progress"? *American Journal of Human Genetics* 14:352–353, 1962.
5. Cordain, L, R.W. Gotshall, S.B Eaton, et al. Physical activity, energy expenditure and fitness: an evolutionary perspective. *International Journal of Sports Medicine* 19(5):328–35, 1998.
6. Saris, W.H.M., S.N. Blair, M.A. van Baak, et al. How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st Stock Conference and consensus statement. *Obesity Reviews* 4:101–114, 2003.
7. Richards, M.P. A brief review of the archaeological evidence for Palaeolithic and Neolithic subsistence. *European Journal of Clinical Nutrition* 56:1270-1278, 2002.
8. Cordain, L., J. Brand-Miller, S.B. Eaton, et al. Plant-animal subsistence ratios and macronutrient energy estimations in worldwide hunter-gatherer diets. *American Journal of Clinical Nutrition* 71:682–692, 2000.
9. Cordain, L., S.B. Eaton, J. Brand-Miller, et al. The paradoxical nature of hunter-gatherer diets: meat-based, yet non-atherogenic. *European Journal of Clinical Nutrition.* 56: S42–S52, 2002.