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The Reluctant Calf

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You only live once, but some people stay juvenile forever.

"Capricious irrationality" is how the leading ethnologist Robert Lowie (1883–1957) referred to many aspects of culture in 1918—behaviors that showed the essential nature of culture. Culture is based on arbitrary symboling. Lowie was a Boasian particularist, who generally refused to extrapolate past the boundaries of a particular culture. At an opposite pole in the golden age of ethnology was Leslie White (1900–1975). He was an arch advocate of culture as a universal evolutionary phenomenon, who stressed two fundamental points: 1) culture evolves *sui generis,* as a self-determining process rather than by the will of individual humans, and 2) culture is *abiological* in the sense that cultural traits are not based in specific human biological traits.[1] In respect to the arbitrary nature of cultural traits, Lowie and White agreed.

"Take, for instance, the Chinese loathing for milk," White said to our 1968 class in ethnological theory. "This cultural trait goes directly against their interests, given the nutritional value of milk." White used the example, first cited by Lowie 50 years earlier,[2] to show a fundamental tenet of his "science of culture" (what he called culturology): humans are one beast worldwide, diversified by culture.

We teach that much of human anatomy—traits like thumbs, lack of sharp canines, and upright posture—evolved with or because we had culture, or to enable culture, at the least in the sense of an increasing dependence on manufactured tools. But specific cultural traits, like classificatory kinship, languages, and religions seemed clearly unrelated to anything biological. People of every hue can speak English or be Buddhist. It was the *ability* to symbol that had evolved biologically, an open-ended ability that *freed* us from the brutish reliance on muscle and instinct.

But then spake borborygmus.[1]

CULTURAL RELATIVITY: WHEN SICK IS NORMAL

Marvin Harris took a cultural materialist perspective to make much of the study of food taboos,[2,3] showing the complex sources of attitudes even toward the most important aspects of survival. Material influences are not inconsistent with the notion that culture is biologically arbitrary. A cow may become sacred nominally for religious reasons, but those reasons may reflect economic considerations such as usefulness as beasts of burden. Milk taboos don't require genes for loathing or loving milk.

In 1954 the U.S. government, not noted for being culturally savvy even at the level of Ethnology 101, inaugurated the well-intended Food for Peace program. One of the most widely distributed items was powdered milk (a surplus politicians liked subsidizing). Unfortunately, most of the world's adults do not drink milk, and some of this food aid ended up as whitewash for buildings, and may even have contributed to *mal*nutrition.[4]

Another Ethnology 101 lesson is that power affects worldviews. One of the few populations in which adults *do* drink milk—Europeans—also happens to have controlled science. As a result, adult milk consumption is viewed by science as the normal human condition, and lactose *intolerance* becomes abnormal—a disease (it *is,* of course, to those who suffer it). But every reader of this article knows that the truth is very different.[4–6] By the mid-60s, studies of digestive problems in adult African Americans found that these patients did not produce the enzyme *lactase* that digests the main milk sugar *lactose,* leading to various intestinal discomforts including diarrhea. Anthropologists noticed that even populations without a history of milk taboos had strong negative reactions to the great act of American beneficence in the form of powdered milk. Subsequent testing of individuals from many populations showed that lactase is not produced in adults of most populations. What is normal for humans, as for most other mammals, is to stop producing lactase after weaning.

A SINGLE GENETIC STORY WITH MULTIPLE PLOTS

Lactose is not easily absorbed across the intestinal wall. In the colon (large intestine), undigested lactose draws water from the intestinal wall and bacteria ferment lactose to produce gases and other products, lead-

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[1]The rumbly gut.

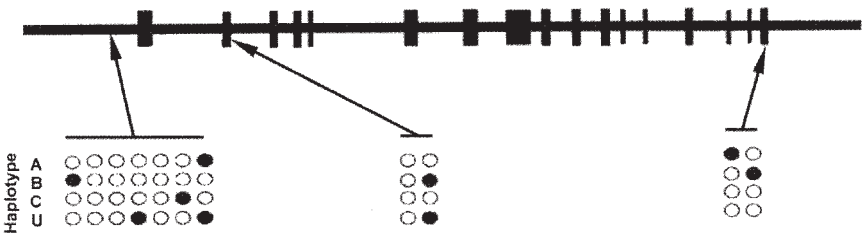

Figure 1. Gene structure and SNPs of the LCT gene on chromosome 2. Black boxes are exons and the solid line is the intervening introns. The chromosomal locations of 11 of the 13 common variant positions are shown below the line (the other two are off this scale). The allelic states of the 4 globally common haplotypes are shown; an open circle denotes the ancestral variant, darkened circle the more recent human variant. (Modified from Swallow, 2003.)

ing to symptomatic pain or diarrhea. But lactase, which is expressed in the small intestinal cells, digests lactose into the sugars galactose and glucose, which are readily absorbed.

Lactase is encoded by a gene called LCT (Figure 1). This gene contains 17 exons (sections of protein code) interspersed with non-coding introns. Common variants have been found in 13 different positions along this region, at each of which a given copy of the gene has either the ancestral nucleotide—found in the chimpanzee—or a derived (new to humans) nucleotide. The particular set of variants along a given copy of LCT is called its *haplotype,* which we can represent by 0's for the ancestral variant and 1's for the human-specific variant. For example, 0000001001000, called haplotype A, is the most common of the four major haplotypes, that make up 89% of non-African and 51% of African copies of the gene. Africans, as usual, are more variable than non-Africans.[7]

Adult lactase persistence (lactose tolerance) segregates in families as a dominant trait. Tests have shown that the problem is generally one of regulation rather than of variation in the LCT protein itself. In other words, the coding sequence is the same in persistent and non-persistent individuals, but lactose-intolerant individuals produce much less of the enzyme than tolerant individuals. Most lactose-tolerant individuals in Europe, where LCT variation was first studied intensively, carry haplotype A, but none of the 13 haplotype-defining variants is itself directly responsible for this tolerance difference. Indeed, many lactose-intolerant Europeans also carry copies of A.

However a recent study looked farther along the chromosome and found a site 14 kb (13,910 base pairs) upstream of the LCT gene itself in which a **T** (thymine) occurred in place of the normal **C** (cytosine) and was exclusively found on haplotype A and in perfect association with lactase persistence in a large sample from Finland.[6,8] This is somewhat strange because the **C**/**T** variant site is in a non-coding intron of *another* gene with no known relationship to lactase. Yet this **T** allele is associated with lower LCT production;[9] generally, people carrying even a single copy of the **T** allele produce enough lactase as adults to give them near-"normal" milk tolerance. DNA samples from other European and some non-Europeans were consistent with this Finnish finding[6–8] and it seems that the **T** mutation occurred early in human evolution and was drifting around in the human gene pool until being favored by natural selection for reasons I'll discuss below.

However, the story is not totally simple. A few exceptions have been claimed, of lactose-tolerant Europeans without the expected **T** allele.[6,10] This may indicate genetic heterogeneity, but a new study has found a pattern of chromosomal haplotype-sharing that extends much farther around the LCT gene, raising the possibility that the **T** mutation arose on a larger haplotype subsequent to some other undiscovered mutation that was already present and is the truly causal one.[11] And there is circumstantial evidence in some African dairying populations that the **T** allele may not be as frequent as selective arguments would predict.[5] Perhaps something else is genetically going on at this or other genes in Africans.

OF CALVES AND KIDS, DOWN ON THE FARM

The reason for the global distribution of lactose persistence alleles seems basically clear. There is a high correlation between the prevalence of lactase persistence and a long history of milk production—dairying—among the world's populations. The data have been well publicized as a classic case of gene-culture *coevolution.*[4,6] Where there has been a long history of dairying, adult lactose tolerance is prevalent, but in other populations that have not used dairy products, tolerance is rare or absent (as is said for those milk-loathing Chinese). Animal husbandry, the prevalence of persistence genotypes, and cultural traits related to milk (mythology, food taboos, preparation and dietary techniques) are temporally, spatially, and causally correlated. The pattern of DNA sequence variation associated with LCT alleles in Europeans suggests a strong, recent selection history affecting that chromosome region,[5] and a selective advantage of a few percent would suffice to raise a tolerance allele to its present frequency in about 10,000 years, which fits the archeological evidence for cattle husbandry in the Near East that dates back about that far (see Durham, 1991; Beja-Pereira et al., 2003).

Bill Durham has systematically evaluated a range of plausible coevolutionary scenarios for this pattern.[4] The association between prevalence and culture might simply reflect a longer dairying history leading to higher lactose tolerance prevalence, coevolving with cultural practices. The selective force favoring milk tolerance could have been due to the nutritional value of milk as a foodbank for hard times, or perhaps a source of liquid in drought-prone regions. Archeological evidence suggesting that calves were weaned early supports this idea in a general way.[12] However, a number of loose ends cast at least

Figure 2. A very northern, very hairy cow—a Scottish Highland Coo. Photo by the author.

some doubt about such a simple nutritional explanation. Some populations use dairy products only after processing them into yogurt, cheese or in other ways that reduce or eliminate lactose so anyone can consume them without ill effects. Only some of these populations have high prevalence of lactase persistence. Why would natural selection favor the persistence allele if a population could *culturally* digest the lactose, as many populations do?

A second possibility is that the persistence allele, which probably predated any husbandry, was present in the ancient pastoralists who first began to manage animals. Originally with no useful function, but not particularly harmful, persistence alleles were favored and rose in frequency as dairying expanded into Europe. This would be consistent with the **T** allele's presence outside of Europe. But why would the frequency in southern regions of Europe and the Fertile Crescent region, where it all began and where dairying has been part of the culture for the longest time, not be higher than in northern Europe, the most distant part of the cultural expansion zone of ancient pastoralists?

Durham argued that a third explanation was more compelling. Milk is a great source of calcium ions that are important for many functions including the formation of bones and teeth. Northern life means low sunlight exposure and thus low induction by UV radiation of vitamin D production in the skin. This is likely to be at least a partial explanation for the evolution of lighter skin in the northern latitudes. Vitamin D circulates in the blood and has been shown to increase the permeability of intestinal cells to the absorption of calcium ions in the gut, from any dietary source, including milk with its high calcium content. Potentially connecting this to adult lactose consumption is that experiments have shown calcium to be better absorbed in the presence of lactose in the gut. Milk has its other nutritional benefits as well. It's good to have the milk at your upper end, but it's pathologic at your lower. Interestingly, lactase might be beneficial at both ends, at the upper end allowing lactose to help in calcium absorption in milk-drinkers, then digesting the lactose before it gets farther down the line. This argument seems plausible but would mainly apply to periods of bone growth that occur after weaning, when lactase production historically has ended. But, as is so often the case, the evidence that lactase producers absorb more calcium is controversial.[13]

These findings are at least consistent with selection favoring persistence alleles most strongly in the north, leading to a zone of higher prevalence there than in the south and Middle East, as has been observed. And recently a different kind of evidence has emerged, that is generally consistent with this idea. This coadaptive story was examined from the *cow's* point of view.[12] Variation in genes coding for six important milk proteins was studied in 70 cattle breeds sampled from across Europe. A three-way correlation was found, between specific milk-protein gene variants and the overall amount of that variation in the cows, the prevalence of lactase persistence and the **T** allele in humans, and the time depth of archeological evidence for dairy use since the Neolithic period about 5000 years ago (Figure 3). Cattle in north-central Europe, where lactose tolerance is most common and dairying most ancient have the highest genetic diversity and genetic uniqueness (rare alleles not found elsewhere), suggesting that these genes reflect a history of selection affecting milk proteins. The argument is that large herds and artificial selection on milk proteins, most intensely or for the longest time in northern Europe, have produced genetically more varied and distinct cattle in that region.

This correlation has been seen as strong supporting evidence for the co-evolution story, if northerners specifically engaged in selection related to their cows because they were so important. However, as with most evolutionary tales, we must be aware of potential limitations. The tested cattle were a mix of dairy and beef breeds present in various parts of Europe today, and the breeding selection and distribution that produced the cattle in their current locations might reflect economics in recent times rather than a steady history of in *situ* evolution.

Sampling on "breeds" ascertains a de facto history of population separation and artificial selection that affects the pattern of diversity. And improved milk proteins may be favored for reasons having nothing to do with milk. They may be advantageous to the calves' health, and/or may mean more hefty calves and ultimately more beef for the pastoralists unrelated to human milk-drinking. The tested genes included those for calcium binding caseins, and whey proteins whose function is unclear, but may have to do with mammary function or secretion rather than calf nutrition. I know of no evidence that variants of these proteins are more nutritious for humans or calves. Nor is it obvious that

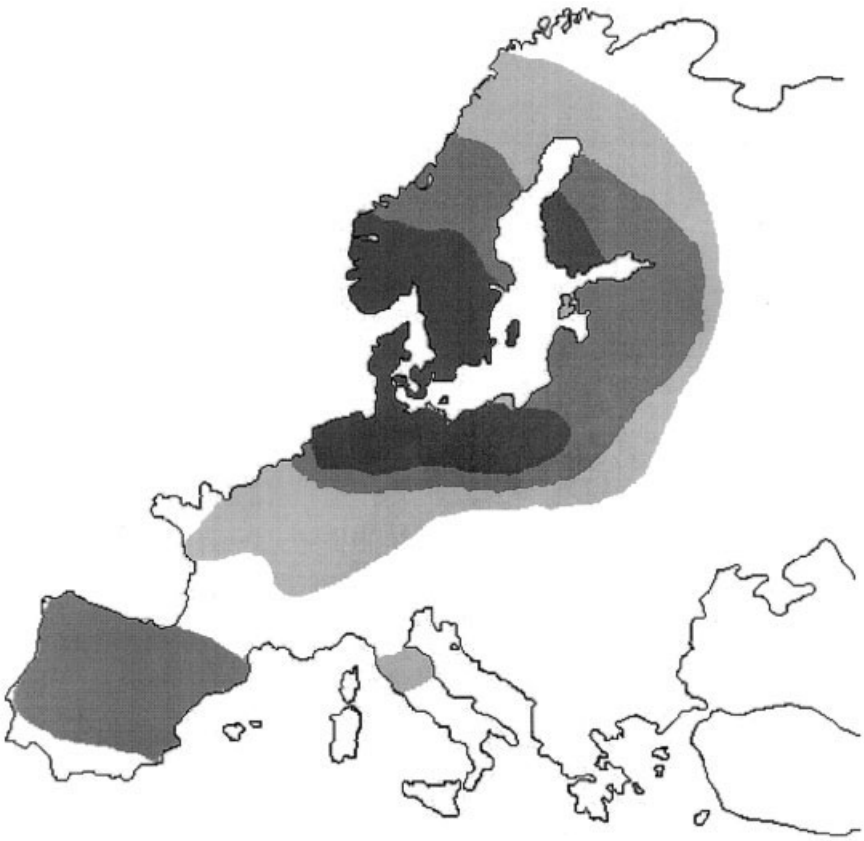

Figure 3. Distribution of bovine genetic variation and adult lactose tolerance are correlated in Europe. Shade darkness is associated with increasing genetic distinctiveness, and increased prevalence of adult lactose tolerance. The darkest patch from Denmark south indicates area of earliest archeological evidence of pastoralism in Europe. Patches of high frequency of lactose tolerance are found in Near East and Africa, but the latter are more isolated. By A. Buchanan; for details, see Durham, 1991; Swallow, 2003; Beja-Pereira et al., 2003.

such selection would lead to more rather than less diverse protein genes within the northern region. The north can be a harsh and occasionally limiting environment for cows as well as humans. So the selective argument is problematic in its details.

There is also the classical danger of using population (geographic) data to infer causation from correlation. However, it is at least reassuring that persistence and dairying-history correlations are found elsewhere in the world,[6,10,14] and that European lactose intolerance is specifically associated with the tolerance allele. And there's yet more to this story.

MORE CULTURAL AND GENETIC SUBTLETIES

Like a good, integrative anthropologist, Durham asked whether the areal distribution of *cultural* traits among relevant populations showed any evidence for a kind of historical continuity consistent with his favored northern-calcium-absorption hypothesis. He compared various linguistic and mythological "memes," and found they fell into two major regional patterns of cultural correlation, a northern one roughly coinciding with his expectations based on the vitamin D argument, and a southern one. This indicates a twofold culture history reflecting two independent and different kinds of selective advantage and culture histories, for humans living in the north and in the south.

These arguments are at least consistent with another new aspect of this story. Durham's study was published in 1991 before the gene or its details were known in this context. But he and others have argued that the pockets of African lactase persistence may have had a different history, for different reasons, than the "main" story in Europe. Some of these populations rely on cheese or other preparation techniques, for example. This fits well with the possibility mentioned earlier that the genetic variation associated with lactase persistence may be heterogeneous. Specifically, the general heterogeneity in genomic as well as culture history between Africans and non-Africans is compatible with a difference in the genetic mechanisms associated with lactase persistence, which itself may have had a largely independent history from that in Europe.

In a general sense such differences would be expected unless by some process like the "ancient pastoralist" model a common source of dairying and lactase persistence allele had expanded globally. But this seems not to be the case, for reasons described above. It is often said in textbooks that natural selection for a trait leads to genotypic convergence as well as phenotypic similarity. But this is actually not the general rule: even when there is selection, different alleles associated with the same favored trait are found in different populations.

The reason is simple: selection raises the frequency of whatever alleles associated with a favored trait happen to be found in each area. There are usually many such alleles. Millennia later, the same trait can be found in different global regions, produced by different genotypes. This is consistently what we see. The classic example is the geographic variation in mutations in the globin genes that are associated with resistance to malaria. Lactase persistence may be yet another example, in which the cultural trait "milk consumption" produced the selective force, working on different genes, perhaps in different ways, in the north and in the south. Consistent with this is the finding that I mentioned earlier that Africans may have other alleles than the **T** allele, that are associated with lactase persistence on that continent.[5] This finding was presented as if it were surprising, but in fact that is just what we should expect and predict.

ONE NEW FACT . . .

Science cannot work without some form of organizing matrix, or theory. Indeed, the search for theory about the world may be the definition of science. But we should not be so captured by our theory that we are blinded to other explanations. It was a core tenet of ethnologic theory that culture is biologically arbitrary, and this is still the prevailing view. This axiom is in the professional interest of ethnology, which holds that culture is a key aspect of human uniqueness—the reliance on an abiological force that overcomes the laws of brutish nature. Indeed, such a view has been adopted even by some of the most staunch defenders of biological evolution, ranging from Thomas Huxley and Alfred Wallace to E. O. Wilson, Daniel Dennett, Richard Dawkins and others.[15,16]

A critical question that any thoughtful scientist should ask is "Could my view be shown to be wrong by just one new fact?" If the answer is positive, a bit of circumspection is in order. The simple fact of a genetic explanation for lactase persistence showed that the "obvious" cultural inference was wrong.

Though Leslie White was combative, as a scientist he would have accepted the evidence had he known of it. However, I think he would have argued that this is a narrow physiological exception, and that culture made the gene come along for the ride as much as the other way around: coevolution rather than genetic determinism. Still, the lactase story cannot provide comfort to the a priori assertion that culture is genetically arbitrary.

Culture can make a biological organism behave contrary to what on the surface seems to be its own interests. But what's in whose interest can be subtle. We make the cow give up its calf and still produce milk, a huge energetic cost to the cow and perhaps some risk to the calf (especially males who soon become veal). The farmer persists in his juvenile diet, a *human* calf reluctant to give up the cozy taste of infancy. Yet, this change of behavior is good for humans, and it must be good for the evolutionary success of cows (until cola commercials give us a loathing for milk after all), because there are certainly a lot more of them around as a result. If giving your essential elixir to a predator who will milk you and then eat you can be good for your evolutionary fitness, then almost anything is possible in life. We learn again and again in evolutionary biology that there are many ways to be "fit," and they don't have to be fun.

Theories of cultural determinism, like biological determinism, can result from a herd mentality among scientists, asserting that their theory simply *must* be true. But we should beware of that one new fact. Following cattle around the world has shown both biological and cultural components of this nutritional story. The biologists were right, and the cultural critics classically wrong. Yet the specifics of the story are not clear, nor is it entirely genetically determined, showing once again how we can get lost by just following the herd.

NOTES

I welcome comments on this column: kenweiss@psu.edu. I have a feedback and supplemental material page at http://www.anthro.psu.edu/weiss_lab/index.html. I thank Anne Buchanan, Bill Durham, John Moore, and John Fleagle for critically reading this manuscript.

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