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The Future of Human Evolution

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OUTLINE

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How humans will evolve in the future is highly speculative because the process of evolution depends critically on random processes such as mutation, recombination, and genetic drift, and because adaptive evolution is strongly influenced by changing environments. Because the human environment includes culture, which can change quickly, it is difficult to predict future environments and hence future adaptive evolution. Nevertheless, some predictions can be made based on a basic understanding of evolutionary mechanisms.

GLOSSARY

Eugenics. Programs designed to direct evolutionary changes in the human population by controlled breeding, selective abortions, and sterility operations.

Gene Flow. Movement of individuals or gametes from the local population of birth to a different local population followed by successful reproduction.

Gene Pool. The set of genetic variants collectively shared by a reproducing population.

Genetic Drift. The evolutionary force associated with random sampling events that alters the frequencies of genetic variants in the gene pool.

Genetic Engineering. The deliberate modification of characteristics of an organism by manipulating its genetic material.

Heterozygosity. The condition in which the two homologous segments of genetic material inherited from the parents are of a different state.

Mutation. A variety of molecular-level processes by which the genetic material of an organism (usually DNA) undergoes a change.

Neutral Allele. An allele that is functionally equivalent to its ancestral allele in terms of its chances of being replicated and passed on to the next generation.

Recombination. The generation of new combinations of DNA segments that are unlike those that existed in the parents.

1. CAN WE PREDICT HOW HUMANS WILL EVOLVE?

The current biological state of humans is the product of our past evolution (see chapters II.18 and VIII.11). But what of our evolutionary future? We can infer to some extent what our ancestors were like 100,000 or a million years ago, but what will our descendants be like 100,000 or a million years into the future? This question is difficult to answer because the evolutionary process itself is strongly influenced by random factors. There can be no evolution of any sort without genetic variation, and this genetic variation is created by mutation and recombination. Mutation and recombination are molecular-level processes that create new genetic variants before these variants are expressed phenotypically in individuals living and reproducing in an environment. In this sense, the genetic variation that is the raw material for all evolutionary change is random with respect to environmental needs—a fundamental premise of Darwinian evolution. Moreover, once genetic variation is randomly created, sampling error further accentuates the randomness of evolution. For example, suppose a new autosomal mutation occurs such that its bearer would be expected to have 10 percent more offspring than the average for the population. Assuming the population was stable, the average number of offspring per individual would be two for the population as a whole, but for this mutant bearer, the average would be 2.2. This would be regarded as extremely intense natural selection for a highly favored

mutation. However, the actual number of offspring of the individual bearing the new mutant is not the same as the expected number. Perhaps this individual died from an accident or a disease unrelated to the mutant effect before he or she could reproduce; perhaps this individual failed to find a mate; perhaps this individual had fewer or more than 2.2 children. It is impossible to predict the exact number of children any particular individual will have even if the average number of children is known. At best what is known is the probability distribution of the offspring number. Suppose this offspring probability distribution is a Poisson distribution (a standard, commonly used probability distribution) with an average of 2.2 offspring. Then, despite the large fitness value this mutant individual has, there is still an 11 percent chance that he or she will have no offspring at all, and hence the mutant will be lost. Moreover, there is the randomness of meiosis. Suppose the mutant individual had three children. Each child would have a 50:50 chance of receiving the mutant, so with a chance of $(1/2)^3 = 1/8$, none of the children would receive the mutant, and the mutant would be lost even though the bearer had more children than the population average. Using a more thorough mathematical analysis, the probability that this strongly favored mutant gene is ultimately lost by chance despite being strongly favored by natural selection is 82 percent! Thus, even strong natural selection cannot completely overcome the randomness inherent in the evolutionary process. These random events affecting the fate of a particular mutant gene are occurring for all genes in the population, and can strongly influence the course of evolution. The evolutionary force associated with these random sampling events that affect existing genetic variation is known as *genetic drift* (see chapter IV.1). Genetic drift, mutation, and recombination ensure that evolution can never be completely predictable.

Another factor that makes future evolution difficult to predict is the environment. Adaptive evolution (see chapter III.1) is always with respect to an environment, and it is difficult to predict what our environment will be like in the distant future. This is especially true for us, because we define much of our environment through our culture (see chapter VIII.10). Culture in turn can change rapidly in unforeseen ways. Therefore, even the evolutionary trajectory of the nonrandom evolutionary force of natural selection is difficult to predict because the raw material on which natural selection operates has a large random component and because our environment, particularly our cultural environment, can change in a manner that is difficult to predict. Nevertheless, some predictions are possible using general evolutionary principles, but specific details must always be regarded as speculative.

2. HAS HUMAN EVOLUTION STOPPED?

One of the more popular predictions about future human evolution is that there is none; that is, human evolution has already stopped. For example, the distinguished evolutionary biologist Stephen Jay Gould (2000) stated:

> There's been no biological change in humans in 40,000 or 50,000 years. Everything we call culture and civilization we've built with the same body and brain.

The basic rationale behind the conclusion that human evolution has stopped is that once the human lineage had achieved a sufficiently large brain and had developed a sufficiently sophisticated culture (sometime around 40,000–50,000 years ago according to Gould, but more commonly placed at 10,000 years ago with the development of agriculture), cultural evolution supplanted biological evolution through natural selection; that is, humans no longer adapt to their environment through natural selection (see chapters III.1, III.3, and III.5) but rather alter the environment to suit human needs through cultural innovations. However, other evolutionary biologists have come to exactly the opposite conclusion. For example, Cochran and Harpending (2009) concluded that "human evolution has accelerated in the past 10,000 years, rather than slowing or stopping, and is now happening about 100 times faster than its long-term average over the 6 million years of our existence."

There are two fundamental flaws in the proposal that human evolution has stopped. First, it ignores the fact that evolution can occur owing to factors other than natural selection. This flaw is discussed in the next section. The second flaw is the premise that cultural evolution eliminates adaptive evolution via natural selection. All organisms adapt to their environment, and we define much of our environment by our culture. Hence, cultural change can actually spur adaptive evolution in humans. Since the development of agriculture, the human population has grown in a roughly superexponential fashion. Agriculture also induced a more sedentary lifestyle. As a result, even early agricultural systems resulted in large increases in local human densities. This in turn created a new demographic environment that was ideal for the spread of infectious diseases. For example, the Malaysian agricultural system, first developed in Southeast Asia, makes extensive use of root and tree crops that are adapted to wet, tropical environments. This tropical agricultural system was introduced to the African mainland about 1500 years ago, and malaria has become a common disease in these new agricultural areas. Because of agriculture, malaria became a major selective agent in African, and other, human populations. The result was that human populations began to adapt to

malaria via natural selection. In sub-Saharan Africa, natural selection favored an increase in frequency of the sickle-cell allele at the hemoglobin β-chain locus, which confers resistance to malaria in individuals heterozygous for the sickle-cell allele. Similar selective forces were introduced wherever agriculture created the conditions to allow malaria to become a sustained, epidemic disease, and human populations in turn adapted to malaria by increasing the frequency of a number of alleles at many different loci in addition to the sickle-cell allele. In terms of the numbers of people affected, these antimalarial adaptations alone constitute the vast bulk of the classical Mendelian genetic diseases that afflict current humanity.

Agriculture produced a selective environment that also favored genes associated with risk for common systemic diseases in current human populations, one of the more common of which plaguing humans today is type 2 diabetes. Much of the increased incidence of diabetes is due to environmental changes in diet and lifestyle. However, phenotypes (see chapters I.4 and V.10) arise from the interaction of genes with environment, so a strong environmental component to type 2 diabetes, and many other systemic diseases, does not preclude a genetic component owing to adaptive evolution in recent human history. The idea that genes predisposing an individual to type 2 diabetes could represent recent adaptive evolution was first proposed by James V. Neel in 1962 as the *thrifty genotype hypothesis*. This hypothesis postulates that the same genetic states that predispose one to diabetes also are advantageous when individuals suffer periodically from famines. When food is more plentiful, selection against these genotypes would be mild because the age of onset of the diabetic phenotype is typically after most reproduction has occurred and because the high-sugar, high-calorie diets found in modern societies that help trigger the diabetic phenotype are very recent in human evolutionary history. There is now much evidence for the thrifty genotype hypothesis, including the genomic signatures of strong natural selection at genes shown to increase risk for diabetes in populations with a recent history of exposure to famines or calorie-restricted diets. The thrifty genotype hypothesis has often been portrayed as an example of past adaptation to a Paleolithic lifestyle despite the fact that the populations used to test this hypothesis all suffered from famines in historic times. Hence, the thrifty genotypes present in current human populations are an adaptation to recent events in agricultural systems prone to periodic failures and are *not* a legacy of human evolution having stopped in the Paleolithic.

Agriculture also induced positive selection for humans to adapt to the products of agriculture. For example, with the domestication of cattle and goats, milk and its derivatives became not only a source of nutrition but also a dietary component that protects against nutritional rickets, a common disease associated with high-cereal diets, another by-product of an agricultural environment. The phenotype of adult lactase persistence is determined by a single gene that allows the digestion of milk sugar. This specific allele shows one of the more powerful signatures of strong, recent natural selection in the human genome.

As the preceding examples demonstrate, agriculture—and culture in general—did not stop human evolution via natural selection but rather induced it through its direct and indirect effects on the human environment. Cultural innovations indeed shield some traits from natural selection, but cultural evolution will likely induce further adaptive evolution of many other traits in humans.

3. FUTURE NONADAPTIVE EVOLUTION

Not all evolution is adaptive. Evolution within a species is a change in the type or frequencies of genes or gene combinations in the gene pool over time, with the *gene pool* being the set of genes collectively shared by a reproducing population. Natural selection is a powerful mechanism for altering the frequencies of genes in the gene pool, but developmental constraints (see chapter III.8, patterns of dispersal (see chapter IV.3), system of mating (see chapters IV.6 and IV.8), population size (see chapter IV.1), mutation (see chapter IV.2), recombination (see chapter IV.4), and other factors can also cause alterations in the gene pool. Evolutionary change is determined not by one evolutionary mechanism operating in isolation but rather by several mechanisms operating in concert.

Because evolution emerges from the interaction of multiple evolutionary forces, even a relaxation of natural selection induces further evolution. Many traits are developmentally correlated, so if one trait is made selectively neutral by a cultural innovation, that in turn will alter the evolutionary balance at other, correlated traits, which in turn can induce further nonadaptive evolution via developmental correlations for the neutral trait. For example, most animals adapt to their diet in part through their teeth and jaws, but humans increasingly used tools and fire to prepare their food. These cultural innovations reduced the importance of jaw and tooth evolution as a means of adapting to the dietary environment. Rebecca Ackerman and James Cheverud (2004) tested the hypotheses of selected versus neutral evolution of human teeth and jaws by comparing various hominin fossil measurements with the expected developmental correlations among relative brain size, tooth size, and jaw size as inferred from modern-day humans, chimpanzees, and gorillas. Their analysis indicated the intensity of selection on the face diminished

with time in the human lineage, and by 1.5 million years ago there was no longer any detectable selection on human teeth and jaws. This conclusion supports the hypothesis that cultural evolution in the human lineage had indeed eliminated natural selection on these traits. However, this does *not* mean that human teeth and jaws have not evolved over the last 1.5 million years. During the last 1.5 million years, there was a large increase in brain size in the human lineage driven by natural selection, and given the developmental constraints common to humans, chimpanzees, and gorillas, human jaws and teeth continued to evolve as a correlated effect of brain size evolution. In particular, jaws and teeth became relatively smaller for overall human head size as a correlated response to increased brain size, with the jaw becoming relatively smaller more rapidly than the teeth. The result of this correlated evolution is that humans have a small, flat face compared with those of chimpanzees and gorillas, and humans have jaws that tend to be too small for their teeth, leading to tooth crowding in the jaws. This nonadaptive evolution in turn favored the cultural evolution of the profession of orthodontics. One major past selective constraint on brain size has been the difficulty of passing a large-brained baby through the mother's birth canal. With the widespread use of cesarean sections, this selective constraint is being reduced in intensity. If this trend continues and if there is still selection for increased brain size, human jaws will become even smaller relative to the teeth. Therefore, the profession of orthodontics has a secure evolutionary future. As this example shows, the release of traits by culture from natural selection leads to further nonadaptive evolution of these traits—not evolutionary stasis.

As culture makes more mutant alleles effectively neutral with respect to natural selection, then genetic drift and mutation become the evolutionary forces that influence the evolutionary fate of these neutral alleles. As discussed in chapter V.1, the rate of neutral evolution equals the mutation rate to neutral alleles. Hence, to the extent that cultural evolution reduces selective forces in humans, the mutation rate to neutral alleles will increase, which in turn will result in an increase in the rate of neutral evolution in humanity. At first this may seem to be a trivial factor in future human evolution, since by definition this accelerated evolution involves only alleles that have no adaptive significance. However, when a gene has many potential selectively neutral mutations, it is possible for that gene to accumulate many functionally equivalent alleles differing by a series of neutral mutations. In this manner, new forms of the gene can evolve via neutrality that are several mutational steps away from the ancestral gene form. The phenotypic effects of a mutation often depend on other mutations that have occurred previously, so that a mutation that would have been deleterious or neutral on the ancestral allelic background may be selectively favored on the new, derived allelic background. In this manner, neutral evolution can actually increase the adaptive potential of a population and allow for adaptive transitions that would otherwise be unlikely. Hence, cultural evolution that reduces natural selection can increase the long-term adaptive potential of the human species.

Another consequence of cultural evolution is that humans have experienced superexponential growth for the last 10,000 years. The resulting large population size interacts strongly with the random forces of mutation and genetic drift. A small population will have very few new mutations at any given time. For example, suppose a specific nucleotide mutation has a probability of 10^{-9} of occurring per gene per generation at an autosomal locus. In a diploid population of 500, there are 1000 copies of an autosomal gene, so the expected number of new mutations to this specific form in any given generation is 10^{-6}; that is, there is only one chance in a million of this mutation occurring in any given generation. Hence, the randomness of mutation plays a large role in the evolution of this population. The human population size is now at 6.8 billion, so for an autosomal locus we would expect 13.6 occurrences of this specific mutation every generation. The large human population size is causing humans to enter an evolutionary zone that few eukaryotic organisms have ever reached—the zone in which virtually every single-step mutational change occurs in every generation. This in turn greatly reduces the randomness of evolution induced by the mutational process. Recall that the sickle-cell allele became selectively favored in sub-Saharan Africa after the introduction of the Malaysian agricultural complex 1500 years ago. What is more remarkable is that this specific sickle-cell mutation went to high frequency in sub-Saharan African populations from at least four independent mutations of this specific nucleotide. The ability of large populations to produce a huge reservoir of mutational variants means that human populations are more evolutionarily responsive than ever to changes in the environment. As long as the human population size remains large, it will remain in this rare evolutionary zone that increases its adaptive potential.

An expanding population also increases the probability of long-term survival of a new mutant, thereby enhancing the reservoir of mutational variants beyond that of a population of fixed size. For example, consider a mutant with a 10 percent advantage in a stable population in which an individual had an average of two offspring with a Poisson offspring distribution. As indicated earlier, the chances of this highly favorable mutation being lost by chance alone is 82 percent. Now suppose this mutant occurs in a growing population in which the average number of children is three. Then, the

probability of loss of the favorable mutant is reduced to 33 percent. However, there is an evolutionary price to be paid for this enhanced survival of favorable mutations. Consider a deleterious mutant that reduces the fitness of its heterozygous bearers by 10 percent. In a constant-size, large population, such a deleterious mutant is eliminated by natural selection with a probability of 1, but in the growing population its chance of elimination is reduced to 53 percent. Hence, beneficial, neutral, and deleterious mutations all accumulate in the human gene pool owing to our unique demographic history. Indeed, recent studies in which the entire DNA sequence of some genes was determined in a sample of nearly 15,000 individuals reveal a large excess of rare variants due to recent mutations in the human gene pool, and many of these recent variants appear to be deleterious.

Exponential population growth cannot be sustained indefinitely in any world with finite resources, so it is inevitable that this phase of human demographic history will end in the future. Indeed, the rate of growth is already dropping. The only question is whether human population will continue to grow to a larger stable size, decrease in size, or fluctuate up and down. The change in demographic environment associated with population size stability or decline will end the era of enhanced survival of mutants, particularly deleterious ones. Indeed, natural selection will in the future start acting to eliminate the reservoir of deleterious variants that have accumulated in the gene pool during the last 10,000 years of population growth. However, as long as our population stabilizes at a large number, the reservoir of genetic variation will remain high, conferring a high degree of adaptability to the human species.

The changing demographic environment will also alter the balance of local genetic drift with gene flow. Although genetic drift causes random fluctuations in allele frequencies, it has some very predictable properties. First, genetic drift causes genetic variation to be lost, and the smaller the population size, the more rapidly genetic variation is eroded (see chapter IV.1). Second, when a species is split into multiple local populations with little genetic interchange between them, genetic drift causes random changes in allele frequencies in all of them. Because the changes are random, they are unlikely to be in the same direction in every local population. Hence, genetic drift leads to genetic differences among local populations, and the smaller the local population sizes, the greater the expected differences among them. *Gene flow* occurs when either individuals or gametes disperse from one local population to another through reproduction. Gene flow can introduce a mutation that arose in one local population into the gene pool of another local population. Hence, gene flow tends to increase the amount of genetic diversity found within local populations. The genetic interchange associated with gene flow also reduces the genetic differences among local populations. Note that genetic drift and gene flow have exactly opposite effects on genetic variation *within* local populations (decreased by drift, increased by gene flow) and genetic differences *among* local populations (increased by drift, decreased by gene flow). As a result, the balance of genetic drift to gene flow is the primary determinant of how a species' genetic variation is distributed within and among its local populations.

There is no doubt that the balance of genetic drift to gene flow has been greatly altered in recent human evolution and continues to change at a rapid pace. The increased human population size associated with the development of agriculture weakens the evolutionary force of genetic drift, and a wide variety of cultural innovations have greatly increased the ability of people to move across the globe and thereby augment gene flow. In addition, our system of mating is changing in response to cultural changes. Currently, about 10.8 percent of human couples on a global basis are related as second cousins or closer, and this subset of human couples is associated with an increased incidence of genetic disease and systemic diseases with a genetic component, as well as increased susceptibility to infectious diseases. Preference for mating with a relative decreases the amount of gene flow, but this preference is rapidly declining with increased urbanization, improved female education, and smaller family sizes. If these cultural trends continue, gene flow and outbreeding will become even stronger in future human populations. All these alterations are increasing the level of genetic variation within local human populations and decreasing the genetic differences among human populations. As long as the ability to disperse over the globe remains high and the trend toward outbreeding continues, much of future human evolution over the next tens of thousands of years will be dominated by decreased local genetic drift and increased gene flow. The result will be increased levels of individual *heterozygosity* (that is, the two copies of an autosomal gene borne by an individual are increasingly likely to be of different allelic states). This rapid and ongoing shift to increased levels of heterozygosity in humans is already having discernible health effects. For example, in studies that control for diet, socioeconomic status, and other factors, several clinical traits have significant beneficial changes with increasing heterozygosity. Similarly, areas of the human genome that lack heterozygosity are associated with diseases with genetic components, such as schizophrenia and late-onset Alzheimer's disease. As heterozygosity levels continue to increase in humans owing to vastly increased abilities to disperse, these beneficial effects are expected to increase even more. This increased heterozygosity will also

reduce the deleterious consequences of the many rare, deleterious variants the species has accumulated during its phase of superexponential population growth.

The second effect of this new balance between drift and gene flow will be the eventual fusion of all human local gene pools into a single species-wide gene pool. As described in chapter VIII.11, humans already are one of the most spatially homogeneous species on this planet in a genetic sense. The modest genetic differences observed today among different human populations will be further eroded, and with continual gene flow and large population sizes will eventually be eliminated. The only genetic differences that will be biologically meaningful in the human species will be the differences among individuals, which will be high because of the high levels of genetic variation in the common human gene pool.

One nonadaptive consequence of this genetic fusion of human populations will be the loss of local adaptations. For example, skin color in humans is an adaptation to the local level of ultraviolet radiation and is not a good indicator of "race" or overall genetic differentiation among populations (see chapter VIII.11). The degree of local adaptation reflects the balance of local selective forces favoring genetic differentiation versus gene flow favoring homogenization. If gene flow and outbreeding continue to increase, human populations will display less local adaptation and more genetic homogeneity across the globe.

4. FUTURE ADAPTIVE EVOLUTION

Adaptive evolution is always with respect to an environment, and it is difficult to predict the details of the future human environment. However, much of the past evolution induced by cultural changes has been associated with the alteration of the human demographic environment, and some predictions can be made there. Continued exponential growth is ultimately unsustainable. Two extreme scenarios are possible. The optimistic scenario is that human population size will stabilize, perhaps at a level smaller than today but still quite large, without any major collapse of human civilization. Under this scenario, it is likely that the current trends toward increased dispersal and outbreeding will continue. The level of heterozygosity will increase, improving the overall genetic health of the human species. This demographic environment will also yield a large human population with an immense reservoir of genetic variation of neutral and beneficial mutations but fewer deleterious mutations than at present. The genetic differences among human populations, already small, will become even less significant, and there will be far less local adaptation. However, because of the large reservoir of new mutations and because culture-induced neutrality will allow greater exploration of the mutational state space, the adaptive potential of the human species as a whole will be enhanced. This may be important in adapting to global climate change.

There is a caveat about this greater adaptive potential of future human populations. Although the randomness of genetic drift has been emphasized until now, Sewall Wright, the man most responsible for the development of the theory of genetic drift, emphasized its significance for adaptive evolution. Evolution, including adaptive evolution, arises from the interaction of multiple evolutionary forces, including genetic drift and natural selection. Just as a series of mutationally linked neutral alleles can augment adaptability by allowing a more thorough exploration of the mutational state space, genetic drift can allow a more thorough exploration of the adaptive gene pool state space when there are multiple ways of adapting to the same environment. Multiple adaptive solutions are particularly common when adaptive traits emerge from interactions among multiple genes. Selection in large populations where genetic drift is weak therefore tends to fine-tune a single adaptive solution, whereas populations with stronger genetic drift are more likely to undergo major adaptive innovations. Hence, future humans under this optimistic demographic scenario will have greatly enhanced potential for fine-tuning human adaptations but are unlikely to make major or radical adaptive breakthroughs unless there are also major environmental changes affecting humans at the global level.

The pessimistic demographic scenario is that human population size and civilization will both crash. This will reverse the trends to increasing dispersal and outbreeding, leading to much population subdivision. Because of 10,000 years of population growth, the current human gene pool has a disproportionate number of recent, deleterious mutations. With population fragmentation, some of these globally rare deleterious variants will become locally common, causing a major decline in the overall genetic health of the human species and inducing a period of strong natural selection against deleterious variants after the population crash. Balancing this negative selection, the enhanced reservoir of neutral and beneficial mutations that were also accumulated during the period of population growth when coupled with increased genetic drift makes it likely that some human populations will undergo major adaptive breakthroughs. The nature of these breakthroughs is difficult to predict because of the strong random role that genetic drift will play in this process.

5. EUGENICS AND GENETIC ENGINEERING

The success of agriculture in sustaining 10,000 years of population growth was possible because humans became strong and effective selective agents on crop and livestock

species. More recently, the ability to manipulate agricultural species has been augmented with genetic engineering in which humans directly manipulate the genetic material of domesticated species. One possibility for future human evolution is that humans will choose to direct their own evolution by selective breeding (eugenics) and/or genetic engineering.

Eugenic proposals and programs have a long history in human societies. However, this history does not engender much confidence in such an approach to controlling human evolution. For example, the "genetics" used by the American eugenics movement is ludicrous in light of modern genetics, yet this pseudogenetics led to forced sterilizations and major changes in immigration laws, and served as a model for the eugenic excesses of the Nazi regime. When people turn principles of selective breeding and genetic manipulation on themselves, scientific objectivity is frequently lost, and nonscientific social theories and prejudices dominate in shaping eugenic proposals. Moreover, current knowledge of human genetics indicates that the successes attained in plant and animal breeding for agricultural purposes are not likely to be replicated in humans. Phenotypes arise from genes interacting with one another and with the environment. Agricultural breeding is almost always done in stocks or lines that are far more homogeneous genetically than humans. Thus, the effects of any one gene are far more predictable in agricultural breeding and engineering than they would be in humans. The same gene could have dramatically different phenotypic effects on different human genetic backgrounds. Second, phenotypes emerge from genotype by environment interactions (see chapter III.10). In agriculture, humans select and engineer crop and livestock strains specifically for how their genes interact with simple, homogeneous environments. Human environments are not simple or homogeneous, so once again the impact of a single gene can vary tremendously. For example, the single gene locus most predictive of risk for coronary artery disease, the number one killer in the developed world, is the *Apoprotein-E* locus (*ApoE*), which has three common alleles in most human populations: ε2, ε3, and ε4. A retrospective study indicated that individuals bearing the ε4 allele had the highest incidence of coronary artery disease on average. The same study revealed that individuals in the highest tertile for total serum cholesterol level had the highest incidence of coronary artery disease compared with the middle and lower tertiles for cholesterol level. Cholesterol level in turn is affected by many interacting genes (including *ApoE*) and environmental variables such as smoking, diet, and exercise. When genotype and cholesterol levels were combined, the group of people with the highest incidence of coronary artery disease by far were people with high cholesterol levels and the ε2/ε3 genotype. Note that the genotype with the highest absolute incidence of coronary artery disease has the "good" alleles only at the *ApoE* locus. This is the main problem with eugenic and genetic engineering programs for humans: the genetic background and environment is highly heterogeneous in humans, so the consequences of manipulations can never be accurately predicted. Moreover, environments change very rapidly for humans, making eugenic predictions even more prone to error. Unless it is decided to create separate castes of relatively genetically homogeneous human strains and keep them in highly restricted environments, eugenics and genetic engineering is unlikely to play a significant role in future human evolution.

FURTHER READING

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Templeton, A. R. 2010. Has human evolution stopped? Rambam Maimonides Medical Journal 1(1): e0006, doi:10.5041/RMMJ. 10006. *Gives additional details on some the examples used in this chapter. It also argues against the idea that human evolution has stopped, using arguments not found in the book by Cochran and Harpending.*