Survival of the Sickest

INTRODUCTION

BRIEF BIOGRAPHY OF SHARON MOALEM

Moalem was born in Israel before his family immigrated to Toronto, Canada, when he was 18 months old. Moalem then studied biology at the University of Guelph in Ontario, Canada before receiving a PhD in human physiology, specializing in neurogenetics, from the University of Toronto. He went on to earn his Doctor of Medicine from Mount Sinai School of Medicine in New York City. After his junior year in college, he and four other students worked with the King of Thailand to run an orphanage for infants and young children who came from HIV-positive mothers. Moalem's subsequent research also led to developments in genetic understanding of Alzheimer's disease and several rare inherited syndromes. Moalem has also founded two biotechnology companies and been awarded 25 patents for inventions related to biotechnology and human health. He has also written several bestselling books intended to make science accessible to the general public, including *Survival of the Sickest* (2007). Moalem currently lives in New York City.

HISTORICAL CONTEXT

Moalem's theories build upon the theory of evolution by natural selection, which received a breakthrough with Charles Darwin's publication of *The Origin of Species* in 1859. This book drew on findings by Darwin while traveling aboard the *HMS Beagle* for geological research. The ship sailed to various places in Africa, South America (including the Galapagos Islands), and Australia. In observing both the diversity of life and some commonalities among disparate species, Darwin proposed the theory of natural selection: that individuals in a species have genetic variation due to reproduction, and that those with genetic variations that provide them with advantageous traits are more likely to survive and reproduce, thereby allowing those advantageous traits to be passed on. This principle is referred to as "survival of the fittest," and it is from this phrase that Moalem adapts his title. More recent research has also been vital in understanding genes' role in evolution. The Human Genome project was a global research effort launched in 1990, its goal being to map all of the genes of the human genome from a physical and a functional standpoint. The project was completed in April 2003, and it's useful in a variety of ways: identification of mutations linked to different forms of cancer, the design of more effective medication, and the genotyping of viruses to direct treatment. Additionally, the development of epigenetics has also been an important breakthrough in understanding how the expression of genes can vary based on one's environment, even when one's genes have not changed. The term epigenetics was coined in the 1940s, but its biggest breakthroughs have come since the 1980s and 1990s. Moalem notes that there is a lot we still don't understand about how epigenetics works, and the field continues to develop—but findings have shown that the expression of one's traits can be altered both in the womb and even after birth.

RELATED LITERARY WORKS

Moalem's other popular science books on biology and genetics include *How Sex Works*, *Inheritance*, *The DNA Restart*, and *The Better Half*. Other books that examine how illness is related to evolution and genetics include Randolph M. Nesse and George C. Williams's *Why We Get Sick* and Nesse's *Good Reasons for Bad Feelings*, the latter of which looks the evolutionary factors that may have caused certain mental illnesses. Richard Dawkins's *The Selfish Gene* is another book that examines evolution from a genetic perspective. For a more in-depth look at epigenetics, a relatively new field that Moalem touches on, Nessa Carey's *The Epigenetics Revolution* and Richard C. Francis's *Epigenetics: How Environment Shapes Our Genes* are two good starting places. Daniel E. Lieberman's *The Story of the Human Body* also provides more detail as to how humans have evolved over millions of years. Additionally, Moalem's work (and the work of all evolutionary biologists) would be non-existent without the first book that proposed the theory of natural selection in evolution: Charles Darwin's *On the Origin of Species*.

KEY FACTS

- **Full Title:** Survival of the Sickest: The Surprising Connections Between Disease and Longevity
- **When Written:** 2004–2007
- **Where Written:** Toronto, Canada
- **When Published:** February 6, 2007
- **Literary Period:** Contemporary
- **Genre:** Nonfiction; Popular Science
- **Point of View:** First Person

EXTRA CREDIT

Teamwork. *Survival of the Sickest* was written with the help of Jonathan Prince, a senior advisor and speechwriter for the Clinton administration.

PLOT SUMMARY

Sharon Moalem states that *Survival of the Sickest* is about medical mysteries, and he shares a personal anecdote of one such mystery: when Moalem was 15, his beloved grandfather was diagnosed with Alzheimer's. His grandfather also loved to donate blood because it inexplicably relieved his aches and pains. Distraught by his grandfather's memory loss and confused by this strange healing effect of blood donation, young Moalem decides to do some research at a medical library. Through reading about iron, he discovers that his grandfather has hemochromatosis, a hereditary disease in which excess iron builds up in the body and can cause major organ damage. One of the most effective way of treating this condition is through donating blood to reduce iron levels, which explains the relief his grandfather feels after doing so.

Despite others' doubts, Moalem intuits that hemochromatosis and Alzheimer's are somehow related, since the former condition must have a negative effect on the brain. He pursues biology in college and dedicates the early part of his medical education and research to proving that this is, in fact, the case. Moalem reveals that he, along with 30 percent of people with Western European ancestry, also have hemochromatosis. This is what motivated him to write *Survival of the Sickest*: he wants to answer the question of why seemingly harmful inherited diseases like his persist in the gene pool. The book will also delve into the interconnectedness of all life and all evolution on Earth, and it will show that genetics is much more nuanced and fluid than people tend to assume. In doing so, Moalem hopes to instill a sense of curiosity in the reader and to help them better understand and take control of their own health.

Moalem begins the first chapter with another case study on hemochromatosis. Moalem then explains that iron is necessary for life—but that bacteria, cancer cells, and other parasites also need iron and have evolved to use the iron in our blood and tissue to survive. In particular, pathogens use the iron in our macrophages (white blood cells responsible for fighting biological invaders). However, in a person with hemochromatosis, the iron builds up everywhere *except* the macrophages. Thus, when facing something like the Black Plague (which is caused by a bacterium), hemochromatosis could provide an advantage because there is no iron in the macrophages of a hemochromatic person, and therefore the bacterium is unable to grow stronger using that iron. This theory is supported by the fact that hemochromatosis is particularly common in people of Western European descent—exactly the population that faced the plague.

In the second chapter, Moalem focuses on diabetes, which is a chronic disease that over 171 million people had when the *Survival of the Sickest* was written in 2007. For diabetics, the process through which insulin helps the body use glucose is broken, and sugar builds up to dangerously high levels in the blood. Studies of other plants and animals show how this might have been helpful in the past. Grapes, when experiencing a frost, offload water and increase their sugar content in order to lower their freezing point. The wood frog, which has the unique ability to completely freeze in winter, then spark back to life in the spring, also increases the glucose in its blood and decreases the amount of water in its bloodstream. These adaptations to the cold lead Moalem to argue that humans with diabetes had an advantage during the Younger Dryas, Earth's last ice age. With a higher glucose content in their blood, diabetics were less likely to freeze to death. As further proof of the connection, Moalem points out that Type 1 diabetes is much more common in people of Northern European descent—the population that would have faced the harshest conditions during the ice age.

The third chapter examines humans' relationship to the sun, and how the sun affects our health and skin color. Too little sun prevents people from producing vitamin D (which is essential to bone health), but too much sun destroys humans' reserves of folic acid (which is important in cell growth and DNA replication). Thus, human skin color adapted to achieve a balance: people who lived in places with large amounts of sun exposure produced more melanin, resulting in a darker skin tone. This prevents ultraviolet light from being absorbed and destroying folic acid. People who have less sun exposure produce less melanin and have lighter skin tones. But for people who have developed very dark skin (and therefore can't absorb enough ultraviolet light), or for people who don't receive enough sunlight, they have adapted in another way. These two groups increase the amount of cholesterol in their bloodstream, which can then be converted to vitamin D. As a result, people of African descent and Northern European descent are both at risk for heart disease and stroke from their high cholesterol.

The fourth chapter examines the relationship between fava beans, anemia, malaria, and a condition called favism. Moalem explains that favism causes a deficiency in the G6PD enzyme, which helps to rid the body of chemical elements (like free radicals) that destroy red blood cells. Without this enzyme, people experience anemia, particularly when they eat fava beans, which have free radicals in them. But, Moalem notes, favism is most common in places where malaria is also prevalent, like Northern Africa and Southern Europe. This is because anemia offers some protection against the protozoa that causes malaria. Moalem then shifts gears to explore how plants and animals frequently affect one another's evolution. Plants, for example, develop chemical toxins to ward off predators, while mammals in turn develop mechanisms to detect those toxins and to avoid them, focusing on eating plants' fruit or other edible parts instead.

Next, Moalem focuses on organisms like the Guinea worm, bacteria, and other parasites. He recounts how many parasites

have adapted "host manipulation," in which parasites evolve behaviors that provokes their hosts to behave in a way that helps the parasites to survive and reproduce. The Guinea worm, for example, leaves the human digestive tract when it is ready to reproduce and secretes acid to burn its way out of the skin. This causes humans to seek relief through water, which in turn serves as a signal to the Guinea worm to secrete a milky fluid with thousands of larvae into the skin. But Moalem notes that by spreading understanding, we can prevent these parasites from harming humans. Former president Jimmy Carter led an effort to spread information about the Guinea worm's transition methods, and infections dropped from 3.5 million in 1986 to 10,674 in 2005. Moalem also examines how we can use parasites' and diseases' need to survive and reproduce to our advantage. Cholera, for example, can be transmitted by physical contact, or through infected water. Cholera that is transmitted through water is much more virulent (deadly to the host) than that which is transmitted through humans, because cholera that is transmitted through humans needs those humans to be mobile. Thus, by developing ways to protect the water supply, countries can put evolutionary pressure for the bacteria to evolve to be less virulent.

The sixth chapter examines an area of research that looks at "jumping genes," which were first discovered by Barbara McClintock as she researched corn genetics. McClintock found that in times of stress, sequences of DNA would copy themselves and insert themselves into other genes in order to trigger mutations that might be beneficial. Moalem writes that jumping genes have been found in other organisms like bacteria, fleas, and even humans. He also posits that jumping genes may have been descendants of retroviruses, which are a subset of viruses that can insert themselves into our DNA. Because retroviruses are "master mutators," they can help spur adaptations at a much greater rate than we would be able to achieve without their help. Retroviruses and jumping genes prove that our DNA is not always set in stone.

The seventh chapter explores another way in which DNA can change, or at least how the *expression* of our DNA can change. The relatively new field of epigenetics suggests that certain compounds can "turn genes on or off," changing the expression of those genes (a process called methylation). This was the focus of a study of *agouti* mice, whose genetic expression for coat color and size was completely changed when their mothers were fed vitamins during pregnancy. Many species have been observed to do this naturally: for example, one species of lizard is born with a large body and long tail or a small body and short tail, depending on whether the mother smells a lizard-eating snake while pregnant. Epigenetics may even account for rising obesity in children: when a mother eats junk food during pregnancy, the embryo may receive signals that it's going to be born in a harsh environment with scarce nutrients. It would then develop a "thrifty" metabolism and would be more efficient at hoarding energy. Then, when the child is surrounded by calorie-rich food after being born, they become overweight. Studies have also suggested that our genetic expression can be affected throughout life, not only in early stages of development.

In the final chapter, Moalem argues that even aging may be preprogrammed as a safeguard against cancer. Cells can only reproduce a certain amount of times before losing crucial genetic information, which causes aging. This goes some way to prevent cancer cells (which grow and reproduce uncontrollably) from developing, though cancer cells have developed some mechanisms to circumvent this limit. He also likens aging to planned obsolescence in technology (like **iPods**): it helps us "upgrade" faster, which ultimately helps our species adapt and evolve. Moalem then shifts to exploring two different hypotheses as to how humans might have evolved: first, the widely-held "savannah hypothesis," which suggests that humans adapted due to conditions found in the savannah and the development of hunting techniques. Second, marine biologist Alister Hardy proposed a different theory called the "aquatic ape hypothesis" which argues that humans evolved by living in and around water—this, Hardy believed, is why we lost our hair and have fat on our skin, like other marine mammals. Moalem posits that water births offer additional evidence that water played into our evolution, citing statistics that water births are just as safe as conventional births and are often easier on mothers.

In his conclusion, Moalem asks readers to take away three ideas from his book: first, that life is undergoing a constant process of creation. Second, that nothing on Earth is isolated from other things. And third, that human disease is highly complex. He emphasizes that we should keep asking questions and that we should appreciate "the miracle of evolution."

CHARACTERS

MAJOR CHARACTERS

Sharon Moalem – The author of *Survival of the Sickest*, Moalem is a physician, scientist, and biotechnology inventor who is an expert in a variety of scientific fields, including rare diseases. As such, he advocates for the importance of interdisciplinary research and collaboration among different fields of study. Moalem's clinical research primarily focuses on neurogenetics and has led to the discovery of rare genetic syndromes as well new insights about Alzheimer's. In *Survival of the Sickest*, Moalem traces the origins of several diseases (such as diabetes) which modern society generally sees as disadvantageous in order to show that these illnesses are actually evolutionary adaptations that developed in response to extreme environmental conditions. He also provides insight

on the relatively new field of epigenetics to show that people's genes aren't set in stone because genetic expression depends upon environmental and nutritional conditions. Through this book, Moalem aims to provide a better understanding of why diseases develop in the first place with the ultimate goal of helping his fellow doctors and researchers find more effective treatments and preventative measures for these conditions. Moalem is also the author of several other popular science books, including *How Sex Works* and *Inheritance*, which further delve into the evolutionary mechanisms behind human behavioral patterns and health conditions.

Aran Gordon – Gordon is a long-distance runner with hemochromatosis (an inherited disease in which the body stores too much iron). In 1997, as Gordon trains for the Marathon des Sables, a 150-mile race across the Sahara Desert, he starts to experience joint pain and heart problems. He goes to several doctors, who are unable to explain his symptoms or who misdiagnose him. After three years, they finally discover that Gordon has hemochromatosis. Gordon is given five years to live if he does not treat the condition. He starts giving blood—the treatment of choice for hemochromatosis—and he goes on to run the Marathon des Sables twice. Gordon's story illustrates how an increased understanding of how iron functions in the body proved tangibly beneficial for people with hemochromatosis, and it also shows that previously-dismissed treatments for the condition (like bloodletting) may have actually been beneficial.

Charles Darwin – Darwin was a 19th-century biologist and the originator of the theory of natural selection, which he published in his 1859 book *On the Origin of Species*. The theory of natural selection, which is now widely accepted by the scientific community, holds that evolution is spurred by mutations which confer an advantage on an individual in a species. That individual is thus more likely to survive and reproduce, thereby passing that trait on to its offspring and making the trait more widespread as it continues to be passed on in subsequent generations. Natural selection provides the foundation for many of Moalem's arguments, as Moalem writes how certain illnesses actually confer advantageous traits when facing deadly environments or diseases and thus make it more likely for the people who have them to survive and reproduce.

Jean-Baptiste Lamarck – Lamarck was an 18th- and 19th-century French biologist who is largely remembered for the theory of inherited acquired traits. The theory holds that a physical characteristic acquired by a parent can then be passed down to its offspring. The theory is often contrasted with Darwin's theory of natural selection. However, the theory of inherited acquired traits predates Lamarck and was not the primary focus of Lamarck's theory of evolution. Additionally, Darwin did believe in some aspects of the inherited acquired traits theory. In Survival of the Sickest, Moalem illustrates how the theory of inherited acquired traits may not have been entirely incorrect, as he examines how jumping genes can change an organism's traits over the course of their life and how those traits can then be passed on to its offspring.

Alister Hardy – Hardy was the marine biologist who proposed the aquatic ape hypothesis. Hardy suggested that a band of woodland apes became isolated on an island and adapted to the water, and that these were humans' predecessors. He noted that humans have no hair and have fat attached to their skin, much like marine mammals such as hippos, sea lions, and whales. This theory is widely refuted by anthropologists—instead, most hold to the more mainstream savannah hypothesis, which states that humans evolved due to conditions found in the savannah and the development of hunting techniques.

Elaine Morgan – Morgan was a writer who became interested in evolution in the 1970s. She was skeptical of the savannah hypothesis, which stated that humans adapted due to conditions found in the savannah and the development of hunting techniques. Morgan then discovered and became a proponent of Alister Hardy's aquatic ape hypothesis, which argued that humans evolved as they did because they lived in and around water.

David Barker – Barker was a British medical professor who examined the effect of junk food on epigenetic signals and childhood obesity. He suggested that when mothers eat junk food that lacks nutrients, the embryo may receive signals that it will be born into a "harsh environment." The embryo then develops a "thrifty" metabolism and hoards energy to help it survive amid scarcity. However, when the child is born and is surrounded by high-calorie junk food, their slow metabolism causes them to become obese.

Barbara McClintock – McClintock was a scientist who discovered "jumping genes" by studying corn genetics. McClintock found that when the corn was stressed, sequences of DNA moved from one place to another and triggered changes in the genome. Though she met much skepticism throughout her career, she was awarded the Nobel Prize in 1983, at age 81, for her work.

Paul Ewald – Ewald was a pioneer of evolutionary biology who focused on the transmission of diseases. He developed a theory that by making diseases (cholera, for example) more reliant on human transmission, they would evolve to be less virulent (i.e., less harmful to the hosts) because they would need humans to be mobile in order to spread.

MINOR CHARACTERS

August Weissman – Weissman was a 19th-century biologist who divided the body's cells into two categories: germ cells (egg and sperm cells) and somatic cells (all other kinds of cells). Weissman's theory held that information in somatic cells is never passed on to germ cells, a concept called the Weissman

barrier.

Edward Jenner – Jenner was a doctor living in 18th-century England who developed the first vaccine. He scraped a cowpox sore from a milkmaid and purposefully infected teenage boys with it, who as a result were protected from smallpox—a much more dangerous disease.

Carl Djerassi – Djerassi was a chemist who developed the first birth control pill, modeling its chemicals on the phytoestrogens in the Mexican yam.

Ken Storey – Storey is a biochemist who studied wood frogs and their ability to freeze in the winter before sparking back to life in the spring.

TERMS

Anemia – Anemia is a condition in which people lack enough healthy red blood cells to carry adequate oxygen to the body's tissues. Anemia can often be caused by a lack of iron. In *Survival of the Sickest*, **Moalem** illustrates how anemia can be helpful in two examples: first, a lack of iron prevents pathogens from gaining access to that iron in our bodies and thus makes people less susceptible to other diseases. Second, anemia can be helpful in combatting malaria, because the parasitic protozoa that cause the disease can only infect normal, healthy red blood cells. This is why favism can be helpful in people around the Mediterranean, because it leads to anemia and can help prevent malaria.

Epigenetics – Epigenetics is a developing scientific field which suggests that certain compounds can attach themselves to specific genes and suppress their expression. For example, in *agouti* mice, feeding pregnant mice vitamins led the mice babies to have brown coats and thin bodies because a compound in those vitamins "turned off" the *agouti* gene. This field provides further evidence for the idea that DNA (or at least the *expression* of DNA) may not be as fixed as was once thought.

Favism – Favism is an inherited disorder that affects 400 million people around the world. Favism results in a G6PD enzyme deficiency. The G6PD enzyme is designed to protect the integrity of red blood cells, including by mopping up free radicals (which can be found in fava beans). Free radicals frequently destroy red blood cells, which can in turn result in anemia. However, **Moalem** illustrates that favism is actually helpful in places in which malaria is prevalent, because the parasite that causes malaria cannot invade damaged red blood cells—like those of people with favism.

Folic acid – Folic acid is a B vitamin that is an integral part of cell growth. Folic acid helps DNA replication when cells divide, and thus it's particularly important during pregnancy. Too little folic acid during this period can result in serious birth defects. Folic acid is destroyed by ultraviolet light, and so humans have adapted to find a balance between getting enough sunlight to produce vitamin D and but not so much that their levels of folic acid are diminished.

Free radicals – Free radicals are molecules with unpaired electrons that can disrupt cellular chemistry. Such molecules can be found in fava beans, and when people with favism eat fava beans, the free radicals within wreak havoc on those individuals' red blood cells, resulting in severe anemia.

Hayflick limit – The Hayflick limit is the maximum number of times a cell can divide, because each time a cell reproduces it loses DNA. This limit was discovered by Leonard Hayflick in the 1960s, who found that chromosomes within the cell had extraneous DNA at their tips (called telomeres). But by the time a cell divides between 52 and 60 times, the telomeres have disappeared and important genetic information is lost, causing aging. **Moalem** posits that this limit is meant to serve as a safeguard against cancer.

Hemochromatosis – Hemochromatosis is a condition that causes iron to build up in the body. Without treatment, it can lead to liver failure, heart failure, diabetes, arthritis, cancer, and ultimately death because of the damage it causes to major organs. Iron doesn't build up in white blood cells called macrophages, however, which fight disease. In people without hemochromatosis, infectious agents feed on the iron in our macrophages, which actually makes the infectious agents more deadly. This becomes a key point in **Moalem**'s argument, as he uses hemochromatosis as his first example of how diseases can provide evolutionary benefit. When the Black Plague began in 1347, people who had hemochromatosis more likely to survive it because the bacteria were unable to access their iron and grow stronger.

Transposons ("jumping genes") – Transposons, or "jumping genes," are sequences of DNA that can "copy and paste" or "cut and paste" itself into other parts of an organism's DNA, thus changing the individual's genome. Jumping genes were discovered by **Barbara McClintock** when she was studying corn genetics. Jumping genes offer evidence for the idea that DNA is not fixed and can change particularly in times when organisms are stressed. **Moalem** also notes that jumping genes may have descended from retroviruses that wrote themselves into our DNA.

Macrophage – Macrophages are a type of white blood cell which helps fight disease by finding and destroying pathogens. In people with hemochromatosis, macrophages have less iron than usual, which prevents pathogens from gaining access to that iron and growing stronger. This adaptation, **Moalem** argues, proved advantageous during the Black Plague.

Malaria – Malaria is a disease common to tropical climates which infects almost 500 million people and kills more than one million people every year. Malaria is caused by parasitic protozoa which infect mosquitoes, and the disease is then

transmitted by mosquito bites through the blood of humans. Malaria causes joint pain, vomiting, and anemia. Ultimately, it can lead to coma and death, especially in children and pregnant women. Having anemia provides some resistance to malaria, because without healthy red blood cells, it is difficult for the protozoa to infect the cells. This is why favism, which leads to fewer healthy red blood cells, can provide some advantage against malaria.

Methylation – Methylation is the process by which genes are turned on or off by certain compounds without changing the genes themselves. Methylation is the key process that is studied in the field of epigenetics.

Retrovirus – A retrovirus is a virus made out of RNA which can copy itself into the DNA of an organism. **Moalem** posits that jumping genes are likely descended from retroviruses.

Phytoestrogens – Phytoestrogens are chemicals developed by plants which mimic the effects of sex hormones like estrogen and act as a defense against animals. When animals eat plants with phytoestrogens, they disrupt animals' reproductive capability. Chemist **Carl Djerassi** also modeled the first birth control pill on phytoestrogens produced by the Mexican yam.

Weissman barrier – The Weissman barrier is the idea, put forth by **August Weissman**, that mutations in a person's somatic cells (cells except for egg and sperm cells) would not be passed on to germ cells (egg and sperm cells) and therefore would not be acquired by successive generations. This was largely accepted wisdom until researchers discovered that jumping genes and retroviruses are able to write themselves into the DNA of germ cells, thereby affecting later generations, and that methylation can also change the expression of genes in germ cells.

Younger Dryas – The Younger Dryas was Earth's last ice age, which began around 12,000 years ago and lasted around 1,000 years. Its onset only took a decade. By that point, humans had started to migrate out of Africa and into Europe, and so when temperatures dropped an average of 30 degrees, many people starved or froze to death. **Moalem** posits that those with diabetes who lived in these northern places were able to better survive the Younger Dryas because the high sugar content in their blood acted as a kind of natural antifreeze.

THEMES

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EVOLUTION AND ILLNESS

Sharon Moalem's primary goal in *Survival of the Sickest* is to explore the evolutionary history behind certain illnesses, diseases, and genetic disorders. Many of the chapters center around the question of why, if these diseases and disorders are harmful, evolution has not simply selected for individuals who do not have them. Moalem uses the book to illustrate how many inherited conditions still exist because they historically helped fight against more dangerous and life-threatening conditions. Thus, Moalem argues that evolution sometimes selected for traits that helped people survive in the short term and allowed them to reproduce and pass on those traits—even if, in the long term, those inherited conditions might end up being deadly.

Being able to survive deadly diseases in the short term is a necessary tradeoff to having a condition that might eventually cause harm, because those conditions allow enough time for humans to reproduce and pass on those inherited traits. Moalem's first example of a disease that once provided short-term benefits is called hemochromatosis, a condition that causes iron to build up in the body. Hemochromatosis is inherited, particularly in people of Western European descent; if unchecked, it can lead to liver failure, heart failure, diabetes, arthritis, and cancer. However, in those with hemochromatosis, iron *doesn't* build up in white blood cells called macrophages, which fight disease. In people without hemochromatosis, infectious agents feed on the iron in our macrophages, which actually makes the infectious agents more deadly. Thus, when the Bubonic Plague began in 1347, people who had hemochromatosis were more likely to survive it, because the bacteria were unable to access their iron and grow stronger. Thus, people who have inherited the gene for hemochromatosis may have done so because it allowed their ancestors to survive in the short term, even if it would harm them in the long term. There is a similar tradeoff with people who have a condition called favism, which is a condition that prevents people from clearing free radicals in their bloodstream. Free radicals are molecules or atoms with unpaired electrons that can wreak chemical havoc in cells in the body, and they often cause red blood cells to break down. This results in severe anemia, which can sometimes be deadly. However, Moalem posits that favism (which is found mostly in people around the Mediterranean) helps to combat malaria, because the parasitic protozoa that cause malaria can only infect normal, healthy red blood cells. Thus, those with favism, who do not have healthy red blood cells, are more likely to survive in their malaria-prevalent environments. So while anemia can be deadly, favism and the resulting anemia actually prevents people from dying from malaria and allows them to pass on those genes.

These genetic tradeoffs are not limited to safeguards against deadly diseases: in some cases, harmful adaptations have

sprung up as a result of harsh nutritional conditions that existed thousands of years ago, which enabled people to survive even if it led to disease. Type 1 diabetes is thought to be an autoimmune disease wherein the body's defense system mistakenly attacks the cells in the pancreas responsible for insulin production, and it is much more common in people of Northern European descent. For those with diabetes, the process through which insulin helps the body breaks down sugar doesn't function properly, and the sugar in the blood builds up. Unmanaged, these abnormal blood sugar levels can lead to rapid dehydration, coma, and death. Though the theory is controversial, Moalem posits that flooding the bloodstream with sugar once acted as a kind of natural antifreeze that helped people survive in colder climates. Additionally, the extra sugar in the blood stream was not as problematic as it is today, because food and sugar were less available in general. During the Younger Dryas (a rapid period of climate change that occurred around 12,000 years ago, in which temperatures dropped significantly), people in Northern climates were particularly at risk of freezing—and those who were diabetic were more likely to survive because of their diabetes and the resulting sugar in their bloodstream. Thus, although diabetes is an unhelpful adaptation in the industrialized world, it was extremely helpful for primitive humans amid their harsh climate. Obesity may be another adaptation to harsh conditions. In 1987, British medical professor David Barker developed a theory that fetuses who experience poor nutrition develop "thrifty metabolisms that are much more efficient at hoarding energy." Ten thousand years ago, the theory explains, this metabolism helped a baby survive when it was born into relative famine. But now, when a pregnant mother eats junk food, the embryo "receive[s] signals that it's going to be born into a harsh environment where critical types of food are scarce." As a result, when that baby is born and is surrounded by calorie-rich but nutritionally poor food, the "conservationist metabolism" that would once have helped the baby survive now leads to obesity.

In Moalem's final example, he argues that everyone experiences these kinds of evolutionary tradeoffs, as even aging is an example of our bodies protecting us from something more deadly: cancer. Normally, our cells are only able to reproduce a specific number of times before genetic information begins to be lost. This prevents cells from becoming cancerous and reproducing an infinite number of times, unchecked. But as a result of these built-in controls, our cells gradually hit the limit of the number of times they can replicate, and our bodies begin to break down as a result. Thus, the aging process is the body's way of protecting us from cancer in the short term, even if it causes significant damage later in life.

As the book's title suggests, the common phrase "survival of the fittest" does not tell the whole story—Moalem illustrates in numerous examples how illness can sometimes be advantageous. In understanding why certain conditions developed and what they were fighting against, Moalem argues, humans can understand how to better treat those conditions without offsetting the advantages that the diseases proffered.

INTERSPECIES CONNECTIVITY AND ADAPTATION

Survival of the Sickest focuses on the interconnectedness of all life on Earth. Moalem examines not only how humans pass down genes from one generation to the next, but also the constant and parallel evolution of other types of beings—plants, animals, bacteria, viruses—with which we share the planet. Even though many humans might believe that we live and evolve relatively independently of other organisms, in reality we frequently cause adaptations in other beings and vice versa. Moalem thus argues that no species exists in a vacuum: our evolution can often change the organisms around us by making some of their traits more advantageous, and this in turn can spur evolutionary changes in us. As such, all species are locked in a constant feedback loop of adaptation.

Moalem describes the broader connection between evolution in the animal kingdom and evolution in the plant kingdom, and how each group has adapted to find a symbiotic relationship. Plants that produce edible fruit evolved that way for their own benefit: animals want to pick the fruit and eat it, and then those animals deposit the seeds within the fruit somewhere else. This allows plants to spread out and grow in other places. Evolution favored the plants that developed this fruit, and in turn, animals that recognized the fruit as a food source were more likely to survive. This kind of exchange introduced mutually-beneficial adaptations between the plants and animals. As more animals developed habits to eat the fruit that the plants provided, animals also began to attack other parts of the plants that were more vital to them. Subsequently, plants found defense mechanisms so that other parts of them were not eaten. Thorns are the most obvious defense mechanism plants developed, but certain species like clover, sweet potato, and soy all contain phytoestrogens, which restrict animals' reproductive capability. Thus, as animal behaviors adapted to the new food source, plants in turn evolved defense mechanisms against those animals. Other plants developed toxins and poisons, even evolving adaptations that are specific to species that will harm them. For example, chili peppers have developed a chemical called capsaicin, which stimulates the nerve fibers that sense pain and heat in mammals, but not in birds. This adaptation likely developed because mammals' digestive systems break down the chili pepper seeds, but birds' digestive systems do not. Chili plants that developed this mutation were more likely to survive, and thus that adaptation was selected for. These adaptations illustrate the ways in which

plant and animal life are connected, and how their behaviors and biology adjust based on each new adaptation.

Parasites and viruses serve as other examples of organisms that adapt to changing conditions in humans and other species. Yet unlike the adaptations between the plant and animal kingdoms, which can frequently lead to mutual benefit or simply self-preservation, these organisms frequently operate only on a parasitic level, using human adaptation to their own benefit. In the first chapter, Moalem explains how dependent humans—and most species—are on iron. He writes, "Humans need iron for nearly every function of our metabolism. Iron carries oxygen from our lungs through the bloodstream and releases it in the body where it's needed. Iron is built into the enzymes that do most of the chemical heavy lifting in our bodies, where it helps us to detoxify poisons and to convert sugars into energy." We also store iron in our macrophages (white blood cells) to help fight disease. Yet parasites, bacteria, and viruses also use our iron, and because macrophages try to fight against these kinds of organisms, those pathogens have adapted to use the iron in our bodies and grow stronger as a result. For every resource and leg up that humans have tried to gain over potential threats, infectious agents have evolved to try and combat those advantages. Parasites also try to hijack our natural responses to threats to their own advantage. For instance, when a person is infected with a Guinea worm (usually by drinking unclean water in remote tropical areas), the worm develops and makes its way to the surface of the skin. Once there, it secretes acid, burning its way through the skin to make an exit tunnel. The burning caused by the acid prompts humans to seek relief with cooling water—but the worm has evolved in such a way that as soon as it senses water, it emits a milky fluid full of thousands of larvae. Thus, it uses humans' natural adaptive response (the desire to relieve burns through cooling) to its own advantage, as a signal to reproduce. In this way, our own behaviors—which have been driven by evolution—end up changing the behaviors and adaptations of other organisms, sometimes even to our detriment.

Moalem makes it clear throughout his book that changes in any organism can have a ramification on the adaptations of many others, but his analysis does not stop there. The goal of the book is to increase knowledge about these conditions and to highlight how this knowledge can be useful. He writes, "[infectious agents] are faster, but *we're smarter*." Understanding how parasites use our behavior to our disadvantage can allow us to curb that behavior. For instance, President Jimmy Carter led a two-decade effort to spread information about the Guinea worm, which led to a drop in infections from 3.5 million in 1986 to 10,674 in 2005. Likewise, recognizing how we have impacted plants, causing them to develop phytoestrogens, helped us develop the birth control pill in turn. The more information we gain on the interconnectedness of all life, the more we can use that those adaptations to our advantage.

ENVIRONMENT, ANCESTRY, AND RACE

Just as the evolution of other organisms has had a major effect on human evolution, the environment in which people live also plays an important role in making certain genes more advantageous. Whether it is a population's exposure to sun, the climate in which one's ancestors lived 10,000 years ago, or different social customs that have developed in particular areas of the world even in the past few centuries, our ancestors' environment has been a key factor in the development of our genetics. The environment dictates different physical traits and behaviors among different groups of people, and so Moalem argues that this relationship between environment and ancestry serves as one of the building blocks to our ideas of culture and race.

In order to illustrate the idea of environment impacting human evolution, Moalem considers how the climate that early humans experienced caused them to develop certain adaptive traits. Moalem first looks at how a period of extreme cold added evolutionary pressure to those who lived in cold environments, causing them to be more likely to develop diabetes. The previous ice age, Moalem recounts, was followed by a period of warmer weather, in which human populations migrated out of Africa and into Europe, which had previously been too cold to be habitable during the ice age. Then, around 12,000 years ago, there was a rapid shift (occurring over just a decade) back to colder weather. This resulted in a period called the Younger Dryas, which lasted more than 1,000 years. During this period, it is likely that thousands of humans froze or starved to death in those colder areas. However, those who survived adapted in ways both social and biological. It is believed that diabetes may have actually allowed people to live by increasing the sugar concentration in people's blood, which provided them with a higher chance of not freezing to death. There were additional social developments from the Younger Dryas that changed parts of our genetic code as well. For instance, many scientists believe that this colder period led to the first development of agriculture in Northern Europe and the collapse of hunter-gatherer societies in the area. Moalem posits that because of the development of dairy farming over time in these Northern European areas, populations from those areas are more likely to have enzymes that can break down lactose in milk and are therefore less likely to be lactose intolerant than people from other ancestral lines—another illustration of how geographic and social conditions can affect one's genes.

The idea that geography and our ancestor's environment can affect our genetics becomes tied up in the complicated idea of what race actually represents on a biological level. While Moalem shies away from trying to define what race means, he acknowledges that "distinct populations do share distinct genetic heritages, which are almost certainly the result of different evolutionary pressures our various ancestors

experienced as they settled and resettled across the globe." He argues that the prevalence of genetic mutations in certain ethnic groups is largely based on common environments and social conditions. In our ancestors, skin color was determined largely by sun exposure. Those with more exposure produced more melanin (which causes darker skin), blocked more ultraviolet light, and therefore protected their folic acid, which is integral to cell growth. Those with less sun exposure produced less melanin because ultraviolet light absorption is crucial in one's vitamin D production. These skin color adaptations, which were developed over thousands of years, play a large role in several key health issues: for instance, people who have little access to sunlight (like Northern Europeans) have trouble maintaining healthy levels of vitamin D. People with very dark skin are also unable to absorb the necessary ultraviolet light that allows them to create vitamin D. Due to this deficiency, both groups have evolved to produce a protein called apolipoprotein E (ApoE4). This protein increases the amount of cholesterol in the bloodstream, which can then be converted to vitamin D. But this comes with a tradeoff: the extra cholesterol also puts people at greater risk for heart disease, stroke, and Alzheimer's disease. Our ancestors' varied environments thus had a major effect on our skin color, which in turn can affect one's health conditions for generations, even after leaving that environment.

Moalem also delves into how cultural factors that arise from different geographic locations can change certain people's genes in ways that are distinct from other groups. For instance, people of Asian descent frequently have a genetic variation which makes it difficult to break down alcohol, causing them to appear and often feel more drunk. People of European descent, however, rarely have this variation. This is because, as humans settled into cities and towns, the dilemma of how to clean water first arose. In Asia, people purified water by boiling it and making tea. In Europe, they used fermentation, and the resulting alcohol from that fermentation killed microbes, even when it was mixed with water. As a result, Moalem writes, "there was evolutionary pressure in Europe to have the ability to drink, break down, and detoxify alcohol, while the pressure in Asia was a lot less." Geographic location and the cultural customs that accompany that location both clearly affect the genetic makeup of populations who live there.

Moalem sums up his point about environment and ancestry as such: "One thing is clear—there is mounting evidence that where our ancestors came from, how they adapted to manage their environment, and where we live today all combine to have a significant impact on our health." His main project, as with exploring the other factors that help us understand our genetics, is to provide a greater understanding for why we have certain conditions and therefore to find more effective ways to treat ourselves if we move to new environments where those conditions are no longer beneficial.

GENETIC EXPRESSION, ACQUIRED TRAITS, AND MUTATION

As Moalem takes readers through the different factors that can affect evolution and the human genome, it appears at first that the cliché phrase "biology is destiny" might be true, as various evolutionary pressures select for advantageous genes. Yet in the later chapters of the book, Moalem makes a point of illustrating the ways in which DNA can adapt at early stages of an individual's life. Even though one's genetic information might be inherited from one's parents, Moalem illustrates how several biological processes can enable the expression of seemingly new traits and allow us to adapt at a much more rapid pace.

Epigenetics is an emerging field that studies how the resources a fetus receives when inside its mother's womb, and in the first few months after a child is born, can significantly affect how traits are expressed in a child. This suggests that even if one's genes are not altered, how those genes are expressed might not necessarily be set in stone before (or even after) birth. The first big breakthrough in the field of epigenetics came from a study of *agouti* mice, which are distinct for their yellow coats and a tendency toward obesity. A team of scientists at Duke University then separated pregnant *agouti* mice into two groups. In the control group, they gave the mice a regular diet, and their babies were also fat and yellow. In the experimental group, they fed the pregnant mice vitamin supplements of vitamin B12, folic acid, betaine, and choline. Their babies, by contrast, were thin and had a dark coat. This suggested that certain compounds in the vitamin supplements were able to "turn off" parts of their genes. Their DNA still contained the gene for pale coats and fatter bodies, but the chemicals had "attached to the gene and suppressed its instructions," a process called methylation. The results of this experiment thus suggest that even if genes are fixed, the *expression* of those genes is not. The same kinds of results have long been found in other animals in the wild, where researchers observed how the offspring of some organisms can be "custom-tailored on the basis of the mother's experiences during pregnancy." For instance, the mother of the tiny freshwater flea *Daphnia* will produce offspring with a larger helmet and spines if it's going to give birth in an environment crowded with predators. Additionally, one species of lizard is either born with a long tail and large body or a small tail and small body depending on whether its mother smelled a lizard-eating snake while pregnant. These examples serve to show how the environment and resources of a mother can greatly impact her direct offspring. These adaptations are vastly different from genetic mutations that have developed and been handed down over time; instead, these examples prove how some adaptations can develop in a single generation. Methylation is present in humans as well, and it's one of the reasons why child obesity may have become more prevalent in recent decades. If a newly-

pregnant mother eats junk food that's largely devoid of nutrients, "the embryo may receive signals that it's going to be born into a harsh environment where critical types of food are scarce." In response, various genes are turned off through methylation, and the baby is born small and with a "conservative metabolism" so that it needs less food to survive. Then, when the child grows up in a nutrient-poor but calorie-rich diet, the child gains weight. This illustrates the impact of prenatal nutrition on children throughout their lives: even if they do not inherit obesity, children can acquire traits before birth that lead to this condition.

Methylation is not the only way in which our genes can rapidly adapt. The discovery of "jumping genes" proves that even our genetic material can change in order to direct the process of adaptation, particularly under times of stress. Barbara McClintock studied genetic mutation in corn in the 1950s. Moalem describes how "Especially when the plants were stressed, McClintock discovered whole sequences of DNA moving from one place to another, even inserting themselves into active genes. When these genes cut and pasted themselves from one place in the corn's DNA to another, they actually affected nearby genes—by changing the sequence of DNA, they sometimes turned genes on and sometimes turned them off." Moalem summarizes that the corn plants seemed to be engaged in "intentional mutation," thereby uncovering another method by which organisms can alter their genetic blueprint. These "jumping genes" are called transposons; in addition to corn, they've been found in organisms like fruit flies, the bacterium *E. coli*, and even humans. For us, jumping genes are "are very active in the early stages of brain development [...] Every time one of those jumpers inserts or changes genetic material in brain cells, it's technically a mutation. And all of that genetic jumping around may have a very important purpose—it may help to create the variety and individuality that make every brain unique." Thus, jumping genes not only help us change our genetic code, but they may also allow for our individuality as a whole. Jumping genes also enable us to create antibodies—specialized proteins to target specific invaders. This idea makes a particularly strong case for how we may have adapted jumping genes, as these mutations directly lead to our enhanced survival in fighting viruses and bacteria.

Research on epigenetics and jumping genes is still in the early stages—it's not entirely clear what spurs either process or exactly how different stimuli affect mutations and genes. Moalem even writes a note of caution that "we need to be awfully careful when we start to change the choreography"—that is, the choreography of how the building blocks of our genetic code are formed. But these two new avenues of research clearly illustrate that our biological code is not set in stone, and that these adaptations allow for a vast amount of future evolutionary possibility.

INTERDISCIPLINARY SCIENCE AND RESEARCH

Moalem's book draws on a wide array of scientific research and studies—crucially, though, Moalem doesn't simply focus on studies about genetics and evolution. Instead, he demonstrates how research on a completely disparate topic might actually provide essential insight into our genetic development. And because there is so much that we still do not know about how our genes have developed, he argues that we need to continue asking questions and conducting research in all fields. That research, Moalem suggests, might in turn help us find new information about evolution and give us new ways to treat disease and illness, and vice versa: research on evolution can also unlock the key to scientific discoveries in other fields.

First, Moalem delves into how studying adaptations in plants and animals can provide insight into similar adaptations in humans. Studies of how plants and animals react to freezing helps us understand why diabetes may have insulated humans from colder temperatures during the Younger Dryas, the last period of extremely cold weather, and can lead us to develop better techniques for organ transplant. To illustrate this, Moalem discusses the frozen grapes that are used in ice wine, a drink that was created by accident 400 years ago by a German winemaker who waited too long to harvest the grapes; in the late autumn, the winemaker's fields were hit by a sudden frost. The grapes were shrunken, but when the winemaker harvested them, they were incredibly sweet. Subsequent studies proved that this was due to two different reactions: first, the grapes were trying to offload water so that they did not freeze and die. Second, sugar is also a natural antifreeze, so they were retaining sugar to lower their freezing point to survive. This provided a potential explanation for cold diuresis, the phenomenon in which humans urinate more frequently in cold temperatures (in order to similarly offload water). It also explained why humans might have developed diabetes: to fill the blood with sugar as our own natural antifreeze during the Younger Dryas. Some animals do the same thing: the wood frog lives across North America, all the way up to Alaska. Rather than hibernating and insulating itself in the winter, the frog freezes solid. It has no heartbeat, breathing, or measurable brain activity. Yet a few minutes after rising temperatures thaw the frog, it sparks into gear. It is able to do so because it has flooded glucose into its bloodstream, lowering its freezing point. The ice, on the other hand, has been sandwiched around its organs to keep them as cool as possible without actually being frozen or damaged. Understanding the wood frog not only provides us with evolutionary clues on why diabetes became an inherited trait, but it could also lend itself to the development of future techniques to freeze and transport organs for donation.

Research on babies birthed in the water also provide key

insights as to how we might have evolved from our pre-human predecessors. Studies conducted in 1999 and 2005 show that water births tend to be shorter, less painful, and with less rate of infection. Babies don't breathe until they feel air on their face, mitigating the fear of drowning and also protecting them from inhaling fecal matter or "birthing residue" that can cause an infection in their lungs during conventional deliveries. These studies offer some evidence for a controversial theory called the "aquatic ape" theory, which was first theorized by Alister Hardy. Hardy suggested that we may have descended from an ape that was aquatic or semi-aquatic, and the contemporary studies suggesting that human birth is better suited for water than land provides give new credence to older theories of evolution.

The reverse has also proven true: studies of evolution can also lead to the development of improved medications and medical practices for humans, showing a reciprocity of information from evolutionary research to other fields as well. Studies of plant evolution have illustrated that certain plants, like sweet potatoes and clovers, produce phytoestrogens, which serve as a defense mechanism for plants because they interfere with animals' reproductive systems when they are eaten. Chemist Carl Djerassi based the development of the birth control pill on this kind of chemical production by plants, modeling his chemicals on the Mexican yam. Thus, research in plant evolution has allowed humans to create medical innovations as well. Recognizing how viruses and infectious agents select for or against traits that harm their hosts can help us "influence the evolution of parasites away from virulence" (the degree to which an organism destroys its host). An example of this is cholera, which can spread through humans or through water. If sewage flows easily into rivers that people wash in or drink from, then the cholera strain would evolve toward virulence because it can multiply freely without humans and rely on its access to the water supply for transmission. But if a country develops ways to protect its water supply, the bacteria "should evolve away from virulence"—that is to say, if a bacterium needs a human to be mobile in order to spread, the disease will be less fatal. The implications of this are enormous, as Moalem writes, "instead of challenging bacteria to become stronger and more dangerous through an antibiotic arms race, we could essentially challenge them to get along with us." In this way, learning about evolutionary pressures on organisms like bacteria can ultimately help us learn to combat them.

Moalem ends *Survival of the Sickest* with the assertion that his book is all about questions—the first being, "Why?" and the second being, "What can we do with that?" Moalem emphasizes the need to be curious and to pursue research, both in evolutionary science and in other fields. As he demonstrates repeatedly throughout the book, developing science in all fields can open up new avenues of understanding about where we've come from, where we might be going, and how we can use that information to improve our future.

SYMBOLS

Symbols appear in **teal text** throughout the Summary and Analysis sections of this LitChart.

IPOD

The iPod serves as a metaphor for human aging. Moalem notes that Apple came under criticism because people accused them of employing "planned obsolescence" in their iPods (which were relatively new at the time of the book's publication), because their batteries would only last about 18 months and couldn't be replaced, forcing consumers to buy a new model.

Moalem indicates that this concept can be applied to aging in humans as well: he posits that aging is preprogrammed into human genes, because it helps prevent cancer. Normally, our cells are only able to reproduce a specific number of times before genetic information begins to be lost. This prevents cells from becoming cancerous and reproducing an infinite number of times. But our bodies begin to break down once we surpass that limit, and our cells lose genetic information. It is a tradeoff, but Moalem argues that there is still some benefit to aging. Like the obsolete iPod, "aging makes room for new models, which is exactly what creates the room for change—for evolution." Evolution, Moalem posits, is the way that a species gets "upgraded," and thus it is important for older models to be cleared away so that we can receive the benefits of the new adaptations.

QUOTES

Note: all page numbers for the quotes below refer to the HarperCollins edition of *Survival of the Sickest* published in 2008.

Chapter 1 Quotes

❝ Our relationship with iron is much more complex than it's been considered traditionally. It's essential—but it also provides a proverbial leg up to just about every biological threat to our lives. […] Parasites hunt us for our iron; cancer cells thrive on our iron. Finding, controlling, and using iron is the game of life. For bacteria, fungi, and protozoa, human blood and tissue are an iron gold mine. Add too much iron to the human system and you may just be loading up the buffet table.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 6

Explanation and Analysis

After introducing hemochromatosis, a disease that causes excess iron to build up in the body, Moalem shifts to exploring humans' relationship with iron more generally. In this quote, he illustrates how iron usage is essential for all life on Earth. Because we and other organisms rely on iron so heavily, it is also one of the ways in which we spur adaptation in other organisms, and they in turn spur adaptation in us. By "loading up the buffet table," Moalem argues, we are inviting bacteria and other parasites to access our iron—and that is exactly what they do. As he notes when he discusses the Black Plague, these parasites have adapted to access the iron in our blood and tissue because it makes them more likely to survive. This, in turn, spurs adaptation in us—Moalem goes on to describe how we then developed methods called "iron locking," in which white blood cells called macrophages limit pathogens' access to the iron in our bodies.

This is one of the reasons that hemochromatosis has been advantageous in the past, because it is a condition in which this "iron locking" occurs constantly, despite the fact that iron builds up in the body. Thus, the use of iron and the mechanisms we have developed to protect iron become a first illustration of how other organisms can greatly affect our evolution, and vice versa. Without these pathogens, we would not have needed to develop the iron locking mechanism, and hemochromatosis may not be as prevalent as it is today.

❝ Then, in 1347, the plague begins its march across Europe. People who have the hemochromatosis mutation are especially resistant to infection because of their iron-starved macrophages. So, though it will kill them decades later, they are much more likely than people without hemochromatosis to survive the plague, reproduce, and pass the mutation on to their children. In a population where most people don't survive until middle age, a genetic trait that will kill you when you get there but increases your chance of arriving is—well, something to ask for.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 15

Explanation and Analysis

Moalem explores the history of how the Black Plague of the 14th century made hemochromatosis more advantageous for people living in Europe at the time. Limiting the amount of iron in macrophages (white blood cells), as hemochromatosis does, actually provides a key advantage for people during plagues, because it prevents pathogens from using that iron to their own advantage and thus results in weaker infectious agents. This is an illustration of the thesis of Moalem's book: even though disease like hemochromatosis might ultimately be harmful for those who have them, they can also provide short-term benefits, such as when the Black Plague hit Europe. This explains the high prevalence of hemochromatosis in people of Western European descent.

Yet this quote also hints at the fact that even if hemochromatosis was once advantageous, it no longer is—especially because people are now living much longer than they did at the time of the Black Plague. But because the disease usually doesn't become deadly until after the age at which most people have children, it is particularly difficult to weed out of the gene pool. Though hemochromatosis comes with evolutionary tradeoffs, surviving until reproduction is enough to ensure that the genes for hemochromatosis would be carried on. This is, as the book's title suggests, how the "sickest" survive.

❝ Today, we know that Aran suffered the effects of the most common genetic disorder in people of European descent—hemochromatosis, a disorder that may very well have helped his ancestors to survive the plague.

Today, Aran's health has been restored through bloodletting, one of the oldest medical practices on earth.

Today, we understand much more about the complex interrelationship of our bodies, iron, infection, and conditions like hemochromatosis and anemia.

Related Characters: Sharon Moalem (speaker), Aran Gordon

Related Themes:

Page Number: 21

Explanation and Analysis

At the end of the first chapter, Moalem summarizes the research that he has explored in his discussion of

hemochromatosis. By returning to the discussion of Aran Gordon, a long-distance runner who has hemochromatosis, he puts an individual face to the disease and illustrates how the research has helped to concretely improve the lives of those who are dealing with the disease. While Gordon was told that he would have five years to live if untreated, research in a variety of fields enabled him to treat the disease and live with it.

Moalem highlights the various aspects of that research and how they've combined to give Gordon a treatment plan. In understanding that the disease causes a buildup in iron but also limits the iron that other pathogens have access to, medical professionals are able to proscribe better treatment plans and even recognize how those treatments might help people with other diseases. Doctors have been able to reevaluate bloodletting, an old practice that was widely discredited after the 19th century, but which upon further investigation may have had some benefits (certainly for those with hemochromatosis, but also for those combatting other diseases).

Understanding the origins of hemochromatosis has also allowed scientists to recognize the benefits that anemia (low red blood cell count) may have, because anemia accomplishes some of the same benefits in preventing pathogens from using the body's iron. Thus, how doctors treat anemia has shifted as well. All of this illustrates how research in some fields can greatly impact and lead to advancements in others—Moalem argues that we need to be constantly curious about the past and search for answers in the present in order to shape our medical practices in the future.

Chapter 2 Quotes

❝ The Younger Dryas had arrived, and the world was changed.

Though humanity would survive, the short-term impact, especially for those populations that had moved north, was devastating. In less than a generation, virtually every learned method of survival—from the shelters they built to the hunting they practiced—was inadequate.

Related Characters: Sharon Moalem (speaker)

Related Themes: 

Page Number: 33

Explanation and Analysis

In the second chapter, Moalem focuses on the effects of the Younger Dryas—a period of rapid climate change that occurred around 12,000 years ago, in which temperatures dropped over 30 degrees. For humans who had migrated to Northern Europe, this proved disastrous, and Moalem illustrates how it forced people to adapt in multiple ways. First, like in the case study of hemochromatosis and the Black Plague, Moalem argues that any genetic advantage during this period of rapid change would be beneficial. He argues over the course of the chapter that diabetes enables people to survive in colder temperatures, and that this is why people with Type 1 diabetes occurs most frequently in people of Northern European descent. Thus, Moalem illustrates how the environment can be integral in shaping genes, resulting in adaptations that have lasted in humans' DNA for thousands of years.

A second adaptation, as Moalem hints at here, was a social one: humans experiencing this harsh weather were forced to structure society in a different way—not in a hunter-gatherer system, but instead by developing agriculture. However, this, too, resulted in some adaptations: Moalem brings up in a later chapter how farming led to the development of a mutation that enabled adults to break down lactose, because it was beneficial for farmers to be able to drink milk of the animals they fostered. This is another way in which the environment, in addition to cultural factors, led to the alteration of genes.

❝ So when the grape dumps water at the first sign of frost, it's actually protecting itself in two ways—first, by reducing water volume and second, by raising the sugar concentration of the water that remains. And that allows the grape to withstand colder temperature without freezing.

Related Characters: Sharon Moalem (speaker)

Related Themes:  

Page Number: 40

Explanation and Analysis

As Moalem explores the way in which diabetes might have provided an advantage to humans experiencing freezing temperatures, he turns to studies in the plant and animal kingdom. The first example he cites is that of ice wine, illustrating how grapes have developed two adaptations to cope with freezing temperatures: offloading water to prevent freezing, and increasing sugar concentration as a kind of antifreeze. Moalem then brings up a second example

of the wood frog, revealing how the frog does essentially the same thing. This illustrates how the environment (the colder temperatures, in this example) affects not only human adaptation, but how it's led to the development of adaptations in plants and animals as well.

Moalem then uses these studies to argue that diabetes is a similar adaptation because it floods sugar into the bloodstream and serves as humans' own natural antifreeze as well. He posits that people with diabetes were more suited to survive the previous ice age, the Younger Dryas, because of this condition. These parallel examples of the frog and the grapes also support the idea that research in seemingly disparate fields, like winemaking or animal biology, can help provide essential insight into our own evolutionary history—thus, Moalem implicitly argues for the necessity of interdisciplinary study.

> But what if a temporary diabetes-like condition occurred in a person who had significant brown fat living in an ice age environment? Food would probably be limited, so dietary blood-sugar load would already be low, and brown fat would convert most of that to heat, so the ice age "diabetic's" blood sugar, even with less insulin, might never reach dangerous levels. Modern-day diabetics, on the other hand, with little or no brown fat, and little or no expo- sure to constant cold, have no use—and thus no outlet—for the sugar that accumulates in their blood.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 47

Explanation and Analysis

As with the case study on hemochromatosis, Moalem concludes the chapter by summarizing the research that he has touched on over the course of the chapter. Diabetes floods the blood with sugar, lowering the freezing point of blood. In colder temperatures, sugar can also be converted to brown fat (without insulin), which can then be burned off directly as heat. All of these facts provide evidence for the idea that even though diabetes is a harmful and even potentially fatal disease, it possibly provided humans with an advantage during the Younger Dryas. This situational advantage made humans with diabetes more likely to survive and reproduce, and therefore more likely to pass the gene on—and this is why this disease has stuck around through generations of our ancestors.

Unlike hemochromatosis, however, this disease did not come about in response to another, more deadly disease. Instead, diabetes as a case study illustrates how large an impact our ancestors' environment can have on our genes. This is evidenced by the fact that Type 1 diabetes is particularly prevalent in people of Northern European descent—exactly the population which would have been hit the hardest by cold temperatures. But now, in modern day, people of Northern European descent who are no longer facing ice age-level temperatures in turn no longer have an advantage and are faced only with the problems that diabetes brings about.

Chapter 3 Quotes

> There is one notable exception to Jablonski and Chaplin's equation—and it's the exception that proves the rule. The Inuit—the indigenous people of the subarctic—are dark-skinned, despite the limited sunlight of their home. If you think something fishy's going on here, you're right. But the reason they don't need to evolve the lighter skin necessary to ensure sufficient vitamin D production is refreshingly simple. Their diet is full of fatty fish—which just happens to be one of the only foods in nature that is chock-full of vitamin D.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 56

Explanation and Analysis

The third chapter of *Survival of the Sickest* examines the relationship between the amount of sunlight a population gets and that population's skin color. This is due to the fact that different groups of people evolved so that the amount of melanin (pigment) they have in their skin strikes the right balance between absorbing enough sunlight and getting too much. Absorbing ultraviolet rays allows us to create vitamin D, but too much sunlight can destroy our stores of folic acid. Moalem cites research by anthropologist Nina G. Jablonski and geographic computer specialist George Chaplin to illustrate how the environment thus has a direct effect on our genes, and as a result our skin color. Those who live in sunny environments produce more melanin, which makes their skin darker and protects them from the light. In places with less sun, however, the opposite is true, so that those populations can get enough sunlight.

This quote acknowledges that the Inuit are exceptions to this idea, but they, too, provide evidence for the fact that the

environment has a major effect on genes and skin color. They receive little sun and yet still have dark skin; however, this is because their environment already provides them with enough vitamin D through fish. Therefore, they don't need light skin to absorb sunlight and produce vitamin D. It is clear, both in the populations that adhere to the rule and in the Inuit, that these environmental conditions help build the idea of race, both because they give the population common genes, and because those genes result in common physical characteristics (like skin color) among the population.

❝ This made clean water a real challenge, and some theories suggest that different civilizations came up with different solutions. In Europe, they used fermentation—and the resulting alcohol killed microbes, even when, as was often the case, it was mixed with water. On the other side of the world, people purified their water by boiling it and making tea. As a result, there was evolutionary pressure in Europe to have the ability to drink, break down, and detoxify alcohol, while the pressure in Asia was a lot less.

Related Characters: Sharon Moalem (speaker)

Related Themes: 

Page Number: 60

Explanation and Analysis

After discussing how a population's exposure to sun has an effect on the way the population's genes have evolved, Moalem goes on to illustrate how even geography and social conditions can affect our genes. In this example, Moalem notes how people of Asian descent have a genetic variation that causes their bodies to be less efficient at breaking down alcohol. He links this condition to the fact that European people used alcohol to clean water, whereas Asian people boiled water to clean it instead.

This case study emphasizes the idea that not only do outside environmental factors affect our genes, but that the social conditions that *we* develop can create evolutionary pressure in common geographic areas. The same is true in the next example Moalem brings up, which speaks about how the prevalence of dairy farming caused certain populations (namely Europeans) to develop less lactose intolerance. These case studies add another building block to our idea of race, illustrating how cultural differences that develop among common geographic populations can lead to the prevalence of certain genetic mutations among those populations and ethnic groups.

❝ Instead of worrying about whether or not there are distinct "races," let's concentrate on what we do know and use that to advance medical science. What we do know is that distinct populations do share distinct genetic heritages, which are almost certainly the result of different evolutionary pressures our various ancestors experienced as they settled and resettled across the globe.

Related Characters: Sharon Moalem (speaker)

Related Themes:  

Page Number: 62

Explanation and Analysis

During Moalem's ongoing discussion of how the environment can affect our genes and thus our ideas of race, he acknowledges that it is still difficult to define what race actually means. Throughout the chapter, he illustrates how the genes for skin color, for example, can evolve over time based on the environment in which a person lives; even though they are passed down, they can be adapted and changed. Yet even with this concession, he recognizes that people that share a geographic area also share genetic similarities because they have adapted to that environment.

Rather than focusing on what this means on a social level, Moalem emphasizes how research on those genetic differences can be helpful in the medical field. For example, people of African American descent who now live in colder areas are both in danger of not receiving enough vitamin D and having too much cholesterol in their bodies (because higher levels of melanin in their skin means they absorb less sunlight to convert cholesterol to vitamin D). But by understanding the evolutionary reasons for those adaptations, we can find better ways to treat those conditions. Rather than starting people a lifetime of a drug to lower cholesterol, those people might be better suited going to a tanning salon so that the ultraviolet rays can help convert that cholesterol to vitamin D. Moalem's priority, as he argues throughout the book, is to demonstrate how more information on our genetic makeup and origins can ultimately help us live longer, healthier lives.

Chapter 4 Quotes

On the other hand, as much as plants want animals to eat their fruit, they don't want animals to get much closer than that—when creatures start to nibble on their leaves or gnaw at their roots, things can get tricky. So plants have to be able to defend themselves. Just because they're generally immobile doesn't mean they're pushovers.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 78

Explanation and Analysis

This chapter explores the relationship between plant and animal evolution more generally, and in this quote Moalem illustrates some of the ways in which this happens. Plants develop fruit because they want animals to eat them: this gives their species a greater chance of surviving and reproducing, because the seeds are spread around in other areas. In turn, animals who learn that plants' fruits are good to eat are better able to survive because they have better food sources and are thus more likely to reproduce. The relationship is largely symbiotic, because each receives a benefit from the other and they each develop adaptations to take advantage of that relationship between plants and animals.

However, when animals begin to eat more than the plants' fruit, as Moalem points out here, the relationship becomes less symbiotic. Yet the plants also begin to develop other tools with which to combat the animals' eating habits. Moalem cites examples like thorns, chemicals like phytoestrogens that interfere with animals' reproductive systems, and other toxins. Thus, Moalem shows how the plant and animal kingdoms are deeply interconnected: when one evolves, the other quickly follows, spurring mutation and adaptation in a constant cycle.

The next time you're looking for some convenient birth control, you don't have to snack on a field of clover, of course. But if you take many forms of the famous "Pill," you're not doing something all that different. The gifted chemist Carl Djerassi based his development of the Pill on just this kind of botanical birth control. He wasn't using clover, though; he was using sweet potatoes—the Mexican yam to be exact.

Related Characters: Sharon Moalem (speaker), Carl Djerassi

Related Themes:

Page Number: 79

Explanation and Analysis

As Moalem describes the various ways in which plants prevent themselves from being eaten by animals, he goes into depth on one in particular: chemicals called phytoestrogens. Phytoestrogens wreak havoc on animals' reproductive systems as a defense mechanism to prevent them from having offspring and thus staving off animals in the long term. This serves as yet another way in which plants have adapted because of their relationship with animals, once again emphasizing the interconnectedness of these species.

Yet Moalem brings up phytoestrogens for another reason, because they led chemist Carl Djerassi to develop the first birth control pill. This serves as a primary example of how studying evolution can lead to developments in other fields. By observing how plants ward against animals using phytoestrogens, Djerassi was then able to use that compound to develop a medical innovation that would improve thousands of women's lives. This development serves as an argument for one of Moalem's running themes: the idea that research, particularly interdisciplinary research, is crucial in order to improve our lives and our health.

By releasing free radicals and raising the level of oxidants, fava bean consumption makes the blood cells of non-G6PD deficient people a less hospitable place for malarial parasites. With all the free radicals, some red blood cells tend to break down. And when someone with a mild or partial deficiency in G6PD eats fava beans, the parasite is in deep trouble.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 90

Explanation and Analysis

In this quote, Moalem breaks down the relationship between favism and malaria. He illustrates how favism, like hemochromatosis, can serve as an advantage when facing a deadlier disease, even if ultimately the effects of favism can be quite negative. Someone with favism (a G6PD deficiency) cannot eliminate free radicals in their bloodstream, thereby

making a person's red blood cells less "hospitable" for malarial parasites. It is particularly hard for favism not to be selected for, as Moalem explains, because one copy of the gene actually confers a great advantage in preventing malaria without the negative effects of the condition. Those with one copy are thus much more likely to survive and pass that gene on. This serves as another confirmation of Moalem's thesis: that sometimes, illness can be inherited because it is more advantageous than disadvantageous.

The case study of favism also highlights another of the themes in the chapter: the interconnectedness of the plant and animal kingdom. Moalem notes the oddity of the fact that people cultivate fava beans precisely in the regions where they are most likely to have favism. As the chapter goes on, Moalem describes the missing link: that these are also common sites for malaria-carrying mosquitoes. Though the beans are toxic to some people, for the majority, they confer a benefit in preventing malaria. Thus, despite the fact that they can be deadly, we continue to cultivate fava beans and use their free radicals to our own advantage.

Chapter 5 Quotes

❝ Former president Jimmy Carter has led a two-decade effort to spread understanding about the parasite's method of reproduction to every corner of the world, ensuring that its victims avoid water when looking for relief and that its potential victims avoid water that could be infected. According to the Carter Center, the worldwide incidence of Guinea worm infections had dropped from 3.5 million in 1986 to just 10,674 in 2005.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 96

Explanation and Analysis

As Moalem explores different kinds of parasites and host manipulation, he cites a remarkable statistic affirming the power of research and information. The Guinea worm uses "host manipulation" to reproduce: it burns its way out of the body with acid, and when humans try to seek relief by putting the burn in water, it signals the Guinea worm to release its larvae. Through former president Jimmy Carter's efforts to educate people about how Guinea worms reproduce, the rate of infection was reduced by more than 99 percent worldwide.

Throughout the book, Moalem emphasizes the importance of scientific research and the need for that research to cross fields. By studying how the Guinea worm has evolved to manipulate the actions of human beings, scientists can learn how to prevent us from being manipulated. But here, he takes that assertion one step further: not only do scientists and researchers need to learn through research, but providing that knowledge to people in general can help remedy the spread of infection. This is a major example of the way in which the spread of information can be even more effective medical tool or drug—it can result in tangible improvements in people's health.

❝ Most of these microbes are found in the digestive system, where they play crucial roles. These intestinal bacteria, or gut flora, help to create energy by breaking down food products we otherwise couldn't break down; they help to train our immune systems to identify and attack harmful organisms; they stimulate cell growth; and they even protect us against harmful bacteria.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 98

Explanation and Analysis

While Chapter 4 explores the animal kingdom's evolutionary relationship with plants, this chapter in part looks at our relationship to different bacteria—some of which can be very beneficial, even if bacteria often receive bad reputations as disease-carrying pathogens. Good bacteria called the gut flora have adapted to live inside us, and we in turn have come to rely on bacteria for crucial processes our digestive and immune systems. Thus, this relationship serves as another example of how our evolution is intertwined with the species around us. We have adapted to serve as a home for the bacteria while also using the bacteria's own adaptations and abilities to our advantage.

Gut flora's ability to ward off even more harmful bacteria is perhaps the most notable, because the bacteria directly save us from harmful microbes. They have a vested interest in making sure that we can survive and reproduce—and because they have developed abilities that are so useful to us, we, too, have a vested interest in helping them survive and reproduce inside our bodies.

Ewald believes that we can use this understanding to influence the evolution of parasites away from virulence. The basic theory is this—shut down the modes of transmission that don't require human participation and suddenly all the evolutionary pressure is directed at allowing the human host to get up and get out.

Related Characters: Sharon Moalem (speaker), Paul Ewald

Related Themes:

Page Number: 120

Explanation and Analysis

As Moalem explores the adaptive relationship between humans and various parasites and diseases, Moalem informs readers that viruses and other pathogens can evolve resistance to our defense systems. As we develop drugs, the pathogens in turn can adapt and become resistant to those drugs, leading us back to square one. This isn't exactly the same concept as adaptations in one species spurring another, but it does reinforce the connectivity between all life on Earth, and how some of the technology that we develop may not actually help us from an evolutionary standpoint.

Instead, Moalem focuses on how we can use our knowledge of the evolutionary imperatives (survival and reproduction) to guide diseases to be less deadly to us, as he explains in this quote. He gives the example of cholera, which can spread through still water or through human contact. When cholera can spread through water, it can be a lot more deadly because it does not require humans to transmit. But if countries use this knowledge to safeguard their water supplies, cholera becomes a lot less deadly because it needs humans to be mobile in order to spread the disease from person to person. This reinforces two of Moalem's themes: first, it shows how research and information is vital for us to understand the best methods for protecting ourselves and living healthier and safer lives. Second, it again highlights the idea that all species are interconnected, and that we can take action to shape the evolutionary path of the organisms and pathogens around us.

Chapter 6 Quotes

By introducing the harmless virus to our bodies, we stimulate our immune systems to produce antibodies specifically tailored to defend against that virus. Then, if we are exposed to the harmful version, our bodies are prepared to defend themselves immediately.

Related Characters: Sharon Moalem (speaker), Edward Jenner

Related Themes:

Page Number: 126

Explanation and Analysis

Moalem opens Chapter 6 by examining how our bodies create new immune responses when fighting a new disease. This is another example of how species can spur one another's evolution: fighting a specific virus or bacteria causes our bodies to adapt. We create antibodies for that pathogen that we can then carry for the rest of our lives, in order to fight off similar diseases. In the 18th century, a doctor named Edward Jenner even discovered how to manipulate our own immune response through a vaccine, taking the virus cowpox and using it to stimulate antibodies that could fight a related (but far more deadly) virus, smallpox. Moalem uses this to again highlight the necessity of research and how it can enable us to lead healthier lives.

Additionally, this anecdote serves as the introduction to the chapter because it hints at a topic that Moalem will explore later: how we create tailor-made antibodies for each pathogen that we encounter, because we don't have enough genes to make specific antibodies to fight every disease. Moalem foreshadows the idea that we are able to do so with the help of jumping genes, which respond to stresses in the environment or in our bodies to help us survive. Thus, Moalem hints at the idea that our genes are able to adapt to changing conditions around us, just as vaccines can.

McClintock believed that the jumps are a genomic response to internal or environmental stress that cells can't handle under their existing setup. Essentially, a challenge to survival triggers the organism to throw the mutation dice, hoping it will land on a change that will help. That's what she thought was going on with the corn plants she was studying—too much heat or too little water triggered the corn to gamble its survival on finding a mutation that could help it survive.

Related Characters: Sharon Moalem (speaker), Barbara McClintock

Related Themes:

Page Number: 138-139

Explanation and Analysis

Until this chapter, Moalem has illustrated how our genes are largely fixed—to the point where a plague in the 1300s or an ice age 12,000 years ago might have given advantages to people with certain conditions, so that those conditions have been passed down since then. Yet here, Moalem takes a different tack, suggesting that genes may not be as fixed as we might believe. While mutations were once thought of as completely random errors, McClintock's discovery of "jumping genes" argues that genes can spur their own adaptation—a much more rapid process than adaptations that have been accrued over generations.

Jumping genes, which can copy and paste or cut and paste themselves into other genes, allow our genomes to try to find advantageous traits while under stress. Even the way in which Moalem describes the corn in this quote implies that the corn is an active agent in its own evolution. Even though the process is still a "gamble," as Moalem states here, it is less random or rare than mistakes in the proofreading system. The gambles are intentional, and they are last-ditch attempts to survive untenable environments or conditions. All in all, the quote sets up a turning point in the book in which Moalem begins to argue how genes can be changed over the course of an individual organism's lifetime.

❝ According to Villarreal, this capacity of African primates to support the persistent infection of other viruses may have put our evolution on "fast forward" by allowing more rapid mutation through exposure to other retroviruses. It's possible that this capacity helped spur our evolution into humans.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 152

Explanation and Analysis

Moalem draws on research by Luis Villareal to illustrate how our evolutionary relationship with retroviruses has been very advantageous. Because retroviruses can shift our DNA, being able to support those retroviruses provides a great benefit to us as we use those viruses' ability to mutate. Because we share the susceptibility to retroviruses with African primates, this suggests that the presence of retroviruses in our bodies helped to spur our evolution into humans. Not only do viruses continue to spur our adaptation, but they also helped to spark our very humanity in the first place—showing the intertwined relationship between ourselves and viruses.

Additionally, because these viruses were thought to then become jumping genes, Moalem argues that those retroviruses continue to benefit us and help our mutations even in the present. Jumping genes, which can change our genes in times of stress, continue to allow us to mutate far more rapidly than we would have without them. This ability enables much more rapid adaptation and therefore give us a greater chance of survival in the face of new evolutionary challenges.

Chapter 7 Quotes

❝ Essentially, one or more of the compounds in the vitamin supplements fed to the expectant mothers reached down into the mouse embryos and flicked the *agouti* gene into the "off" position. When the baby mice were born, their DNA still contained the *agouti* gene, but it wasn't expressed—chemicals had attached to the gene and suppressed its instructions.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 158

Explanation and Analysis

This study, conducted at Duke University, serves as the first real breakthrough in the field of epigenetics, which holds that the expression of one's DNA can be altered by certain chemical compounds in a process called methylation. This experiment suggested that vitamin supplements fed to the experimental group were the sole reason why *agouti* mice's genes turned off and the babies were born brown and thin rather than fat and yellow.

This idea builds on Moalem's argument from the previous chapter, in which he showed how jumping genes can change an organism's genome in times of stress. These changes in phenotype (the expression of one's genes) are not necessarily due to stress, but they do argue for the idea that one's genes are not necessarily fixed and that our cells' building blocks may shift while we are developing as embryos and even throughout our lives. This has major implications on our health, as Moalem goes on to explore throughout the chapter, if we can understand the compounds that help us while avoiding those that can hurt us.

> According to the thrifty phenotype hypothesis, fetuses that experience poor nutrition develop "thrifty" metabolisms that are much more efficient at hoarding energy. When a baby with a thrifty phenotype was born 10,000 years ago during a time of relative famine, its conservationist metabolism helped it survive. When a baby with a thrifty metabolism is born in the twenty-first century surrounded by abundant food (that is also often nutritionally poor but calorie rich), it gets fat.

Related Characters: Sharon Moalem (speaker), David Barker

Related Themes:

Page Number: 163

Explanation and Analysis

Moalem provides research from David Barker to show how epigenetics affects human development and may provide the reason for the recent rise in obesity. He describes how fetuses whose mothers eat junk food will then have "thrifty" metabolisms, proving how the expression of their genes is changed simply by the diet of their mother and the lack of nutrition in that diet.

What is particularly interesting about this case study is that it seems to combine adaptations that developed thousands of years ago with responses to nutrition in the present moment. The fetus's metabolism is changed, believing that it is in a nutritionally poor environment, and provokes a response that adapted to conditions during a famine 10,000 years ago. Thus, this is an example of how our bodies are an amalgam of adaptations caused by the environment that our ancestors inhabited, as well as by the environment in which we live now.

Also inherent in this argument is the idea that obesity may be yet another condition that may have once been advantageous, because it served as an adaptation that helped in the case of food shortages—which is why it is still something that is passed on from parent to child. But now, with completely different conditions, that adaptation is no longer useful.

> Here's the first thing we don't know—we don't have anywhere near a complete understanding of which genes are turned off or turned down by which methyl donors. For example, methylation of a gene that influences hair color might lead to a harmless change—but the same process that triggered methylation of the hair color gene may also be suppressing a tumor suppressor.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 173

Explanation and Analysis

Throughout the chapter on epigenetics, Moalem warns that it is dangerous for us to try to manipulate our own genes with certain compounds at this moment, due to the fact that we don't fully know the consequences of compounds and may end up harming our bodies as well as helping them. This idea inherently reinforces Moalem's argument that our genome is adaptable during our lifetime on an individual level. Our genes are actually so mutable that we have to be careful about how we might change them.

This idea again emphasizes the need for further research on the subject and how that could be helpful. Understanding which compounds bring us benefits without other negative consequence, or which could provide necessary tradeoffs in the face of certain diseases and disorders, can certainly provide us with crucial information that could affect our health. This is why Moalem brings up the Human Epigenome Project at the end of the chapter, which is a project to help map how different compounds and environmental conditions affect our genes. By gathering and understanding this information, the project can ideally help us live longer, healthier lives.

Chapter 8 Quotes

> Many scientists believe cancer prevention is the "reason" cells have evolved with a limit on the number of times they can reproduce. The flip side to the Hayflick limit, of course—compromise, compromise—is aging. Once cells hit the limit, future reproductions don't really work and things start to break down.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Page Number: 189

Explanation and Analysis

When exploring the various reasons why aging might be preprogrammed into our DNA, Moalem returns to the central thesis of the book: that all adaptations are a compromise between short-term and long-term survival. Part of the reason aging occurs is because cells have a built-

in mechanism to lose DNA each time the DNA is replicated. We have superfluous DNA on our chromosomes that serves as a buffer against this information loss, but after 52 to 60 copies of that DNA, the buffer has been depleted and information is lost. This buffer, called the Hayflick limit, helps to prevent cancer cells from developing, as Moalem notes here. Yet again, he emphasizes the compromise of this adaptation: aging potentially helps prevent cancer, but it also begins to break down cells after a certain amount of time.

This highlights the fact that evolutionary tradeoffs are not simply found in people with disorders and diseases like hemochromatosis or diabetes (the case studies explored in the first two chapters). If aging serves as a tradeoff—wherein we receive the short-term benefit of staving off cancer despite the long-term harm of our bodies breaking down—then everyone is subject to the same evolutionary compromises.

❝ Biogenic obsolescence—that is to say, aging—might accomplish two similar ends. First, by clearing out older models, aging makes room for new models, which is exactly what creates the room for change—for evolution. Second, aging can protect the group by eliminating individuals that have become laden with parasites, preventing them from infecting the next generation. Sex and reproduction, in turn, are the way a species gets upgraded.

Related Characters: Sharon Moalem (speaker)

Related Themes:

Related Symbols:

Page Number: 191

Explanation and Analysis

After Moalem explains how aging may be preprogrammed into our DNA as a safeguard against cancer, he continues on to posit other evolutionary explanations for aging. He compares humans to the iPod, which, he notes, many people accused Apple of constructing with planned obsolescenc. This means that the battery would only last 18 months before it would break down and people would be forced to buy a new one—a principle that benefits the manufacturer rather than the consumer.

The iPod serves as an apt comparison for the way that aging might function in humans. Adaptation works as a way of getting "upgraded" because it allows for new helpful features in the face of current conditions. It is true, however, that the adaptations are primarily helpful to successive generations—not as much to the current generation. Thus, aging may not serve an individual, but it does serve the species as a whole. Again, it is a tradeoff because it causes individuals to die earlier than they might have otherwise, but it makes room for other individuals to allow the species to progress.

❝ That still doesn't explain the lack of evolutionary pressure against bipedalism and the accompanying reproductive risk caused by the change in pelvic shape. Unless—what if the water changed the equation somehow and made the process easier? If the water made the birthing process easier, then most of the evolutionary pressure would favor the advantages those aquatic apes gained from the shift to two feet.

Related Characters: Sharon Moalem (speaker), Alister Hardy, Elaine Morgan

Related Themes:

Page Number: 202

Explanation and Analysis

Moalem spends the second part of the final chapter discussing the evolutionary merit of the savannah hypothesis and the aquatic ape theory, drawing on the research by Elaine Morgan and Alister Hardy. They subscribe to the aquatic ape hypothesis, suggesting that humans developed as a response to living in and around water, which is why we have no hair and have fat on our skin (like other aquatic mammals) and why we have downward facing nostrils (which allow us to dive). This is in contrast to the widely-accepted savannah hypothesis, which holds that humans developed in response to the arid conditions of the African savannah.

Moalem then adds his own analysis to the discussion. Earlier, he introduced the idea that narrower pelvises (which we adapted to be able to walk on two legs) and large brains were somewhat inexplicable adaptations, because they made birth much more perilous to mothers. But here, he argues that statistical data on water births (which he goes on to cite) illustrates that water actually makes the birthing process easier. This provides additional hints for the aquatic ape hypothesis, because it implies that water mitigated the risks of the birthing process, allowing us to develop those larger brains and narrower pelvises. Moalem's research reinforces the idea that research on

disparate topics, like water births, can provide us with clues on our evolution.

Additionally, the fact that Moalem phrases his introduction to the topic in the form of a question here is notable. The question is somewhat a rhetorical one, as Moalem knows the answer to the puzzle of water births. But it serves as a reminder that asking questions and being curious is necessary to pursuing those questions in research, and it inspires readers to ask those questions as well.

Conclusion Quotes

❝ I hope that you'll come away from this book with an appreciation of three things. First, that life is in a constant state of creation. Evolution isn't over—it's all around you, changing as we go. Second, that nothing in our world exists in isolation. We—meaning humans and animals and plants and microbes and everything else—are all evolving together. And third, that our relationship with disease is often much more complex than we may have previously realized.

Related Characters: Sharon Moalem (speaker)

Related Themes: 

Page Number: 207

Explanation and Analysis

In Moalem's final paragraphs, he sums up all the primary themes of his book and its research. Each one of his case studies have served to prove one of these central three ideas. First, the fact that evolution is changing all around us is directly supported by the ideas that he touched on in the chapters on jumping genes and epigenetics: both of these principles illustrate how genes are in a constant state of change—even within one individual's lifetime.

The second idea, that nothing in our world exists in isolation, is proven by nearly every chapter. The various plants, viruses, bacteria, and other organisms that Moalem cites throughout the book have many functions that affect humans, from helping our digestive systems to staving off diseases to even making up parts of our genetic code. We and these other organisms are in that "constant state of evolution," and we continue to develop and progress based on one another's adaptations. Additionally, we are constantly evolving because of our environment, like changing our skin color to the amount of sun exposure we get or adapting to the availability of food or a new temperature.

And lastly, Moalem reiterates the primary goal of the book: to explain our complex relationship to disease. Even though diseases like hemochromatosis, diabetes, or favism contain inherent harm, they actually provided an advantage for the survival of generations past and present, and those conditions have therefore been passed down. True to the book's name, those that have survived are not always "the fittest"—in some cases, they are "the sickest."

SUMMARY AND ANALYSIS

The color-coded icons under each analysis entry make it easy to track where the themes occur most prominently throughout the work. Each icon corresponds to one of the themes explained in the Themes section of this LitChart.

INTRODUCTION

Sharon Moalem tells the reader that this book is about miracle of life and the medical wonders, myths, and mysteries it contains. He shares one such mystery of his own: when Moalem was 15, his 71-year-old grandfather was diagnosed with Alzheimer's disease. As a young man, it's incredibly painful for Moalem to watch someone he loves suffer, and he wants answers as to why this is happening. Another aspect of his grandfather's health further confuses Moalem: his grandfather has a lifelong love of donating blood, not only for the satisfaction of performing a good deed, but because he claims it alleviates his aches and pains. Puzzled by this and distraught over his grandfather's ever-diminishing memory, Moalem believes it's his responsibility to solve both mysteries.

Moalem opens with a personal anecdote that introduces disease as the primary concern of the book. His own feelings of pain, helplessness, confusion over his grandfather's Alzheimer's diagnosis show how devastating illness can be, especially when one doesn't understand the root cause of the problem. Young Moalem's decision to singlehandedly take on the challenge of solving his grandfather's medical mystery implicitly encourages readers to take a similar hands-on, self-motivated approach. By emulating young Moalem's attitude, people can learn more about the conditions that they and their loved ones face rather than defeatedly accepting ill health.

Moalem convinces his father to take him to a medical library, where he relentlessly searches for insight into his grandfather's health. He knows that his grandfather is giving up iron when he donates blood, so he pores over books about this element and stumbles upon his answer: a disease called hemochromatosis. This hereditary condition causes excess iron to build up in the body to the point that it can damage major organs. Giving blood is the most effective way to reduce the body's iron levels, so Moalem intuits that the reason his grandfather feels better when he donates blood is because it's treating his undiagnosed hemochromatosis.

Again, Moalem's self-driven pursuit for answers emphasizes the importance of scientific research (even into seemingly disparate topics) when trying to make sense of medical mysteries. The chance discovery that Moalem's grandfather's love of donating blood is actually rooted in a disease confirms this. Meanwhile, the fact that hemochromatosis is hereditary sets up another one of the book's most important, though counterintuitive, ideas: that often, even diseases we view as undesirable and debilitating are able to survive in the gene pool.

Moalem has a feeling that his grandfather's hemochromatosis and Alzheimer's are somehow connected—after all, if hemochromatosis can damage major organs like the liver, why couldn't it damage the brain? Unfortunately, no one takes 15-year-old Moalem seriously. But a few years later, Moalem chooses to major in biology in college, determined to continue pursuing the link between his grandfather's two diseases. After graduating, he even delays going to medical school to pursue a PhD in neurogenetics. Two years later, his research uncovers the answer he's been searching for: there is indeed a genetic association between hemochromatosis and Alzheimer's. Though Moalem's grandfather has already passed away at this point, Moalem feels hopeful that this discovery could help others.

Moalem's intuition that hemochromatosis and Alzheimer's must be related—and his years-long persistence in uncovering the link between the two—once again advocates for the importance of targeted and shrewd medical research into not only the root causes of diseases, but the connections among them. The fact that his hunch is ultimately proven right further emphasizes the importance of research for the betterment of humanity on a broad scale.

Moalem reveals that he, too, has hemochromatosis. When he gets diagnosed at 18, he wonders why so many people (30 percent of those with Western European ancestry) inherit the gene for this disorder. Why, he wonders, does evolution enable harmful traits like this to persist? This, Moalem says, is what *Survival of the Sickest* is about. Rather than just looking at symptoms and treatments, Moalem wants to uncover the evolutionary roots of diseases in the hopes that a deeper understanding will lead to helping people live longer and healthier lives—much like how Moalem himself has been able to manage his hemochromatosis.

The fact that both Moalem and his grandfather, along with 30 percent of people with Western European ancestry, have hemochromatosis is significant—there must be some underlying reason why a seemingly terrible disease has persisted in the gene pool over time. With this in mind, Moalem presents the thesis of the book: he aims to trace the evolutionary history of inherited diseases like hemochromatosis in order to better understand why they came about, why they were passed on, and how we can better treat them going forward.

First, Moalem says, this book will examine hereditary disorders and why they persist in the gene pool. Second, it will delve into how our ancestors' environments shaped our genes. Third, the book will show how the evolution of other organisms can give us insight into our own. Through this, Moalem hopes to impart a sense of reverence for the planet onto the reader, as well as to help them feel more in control of the future by giving them a more comprehensive understanding of the past. Before the reader continues on, Moalem encourages them to remember four things: that human life is interconnected with all other life, that the evolution of all organisms is interrelated, that genetic mutation isn't inherently bad, and that one's DNA isn't set in stone.

Here, Moalem offers a brief outline of the book's topics. In addition to showing how the diseases we inherit are rooted in our ancestry, Moalem will also show how humans (and our evolution) are connected to all of Earth's other life-forms. As such, he hopes to inspire curiosity and wonder in the reader, as well as to provide a more nuanced understanding of evolution and disease. Moalem also aims to debunk common misconceptions—like that genetic mutation is always bad or that one's genetic code is the be-all-end-all of one's health—in order to better inform the reader and help them take control of their own lives.

CHAPTER 1: IRONING IT OUT

In 1997, Aran Gordon, a top financial executive and marathon runner, began to train for the Marathon des Sables, a brutal 150-mile race across the Sahara Desert. As he trained, he experienced physical difficulty running: his joints hurt and his heart skipped a beat. He went to multiple doctors, but they were unable to determine what might be wrong, or they gave him incorrect diagnoses. After three years, they finally discovered the real problem: there were massive amounts of iron in his Aran's blood and liver. —he was "rusting to death."

Much like Moalem shared his and his grandfather's experiences in the introduction, here Moalem begins the main part of the book with a personal angle of the disease that he is about to discuss. He illustrates the fear and problems inherent in the doctors' lack of knowledge, both in diagnosing the diseases and in figuring out how to treat Aran. In this way, Moalem shows how, when the root cause of an illness is unknown, it can derail a person's life and stump even medical experts.

Hemochromatosis is a hereditary disease that disrupts the metabolization of iron in the body, causing it to build up in the blood, joints, and major organs. Unchecked, hemochromatosis can lead to liver failure, heart failure, and diabetes. It ultimately proves fatal if untreated. Hemochromatosis was thought to be incredibly rare until 1996, when the gene that caused the condition was isolated. Since then, scientists have discovered that the gene for hemochromatosis is the most common genetic variant in people of Western European descent.

Moalem sets up the idea that hemochromatosis is a very dangerous disease, but also that it is an incredibly common genetic mutation. Establishing the harm that it can cause will then allow Moalem to explore why it might have remained in the gene pool. He also provides a hint in letting readers know that the condition is common in people of Western European descent, as it suggests that it may have once provided this specific population with an advantage.

Moalem poses the question of why a deadly disease like hemochromatosis be part of so many people's genetic codes. He reminds readers of how natural selection works: if a genetic trait makes an organism stronger, that organism is more likely to survive, reproduce, and pass that trait on. If a trait makes an organism weaker, that organism is less likely to survive, reproduce, and pass that trait on. Over time, species "select" traits that make them stronger. Moalem then answers his first question with another question, asking the reader whether they would agree to take a drug they knew would kill them in 40 years if it was the only thing that would prevent them from dying tomorrow.

Moalem lays out the foundation of evolutionary theory proposed by Charles Darwin: that traits which give an organism an advantage will be "selected for" because those organisms are more likely to survive, reproduce, and pass those traits on to keep them in the gene pool. This idea is integral to the book, and it will be repeated over each chapter as Moalem illustrates how some adaptations that appear negative have actually proved beneficial in the past, because they allowed people to survive and reproduce in the short term.

Moalem shifts to exploring humanity's relationship with iron, which is an essential element for almost every function of our metabolism. Iron deficiencies are the most common cause of anemia, or low red blood cell count. Anemia can cause "fatigue, shortness of breath, and even heart failure." Iron is also important to other forms of life: oceans that are rich in iron develop reefs and other ecosystems, while oceans without it are essentially lifeless.

The necessity of iron for life-forms living in vastly different environments suggests that all species on Earth are fundamentally connected in their evolutionary adaptations. Given Moalem's previous question about short-term versus long-term survival, his observation that a person can have too little iron (anemia) as well as too much iron (hemochromatosis) suggests that there may be potential short-term advantages to having abnormal iron levels on either end of the spectrum—even if, in the long term, these conditions are dangerous.

Because iron is so important, the food industry currently supplements almost everything with iron. But Moalem warns that this may be too much of a good thing: bacteria, cancer cells, and other parasites also need iron, and they can use the iron in our blood and tissue to survive. In 1952, a microbial researcher named Eugene D. Weinberg proved that iron helps nearly all bacteria multiply freely.

Moalem shows how parasites, bacteria, and viruses have adapted based on our biology. Because our blood and tissue are rich in iron, harmful pathogens use this as a means of invading and growing stronger using our own resources. In this way, Moalem demonstrates that species tend to evolve and adapt in tandem despite the vast differences among them.

Because iron can have potentially lethal effects, we also have iron-related defense mechanisms. Iron is not found in key areas where infection can enter our bodies: the eyes, mouth, nose, ears, and genitals. These openings also have fluids with proteins called chelators which bind to iron molecules, preventing them from being used. Additionally, when we are beset by illness, our bodies lock our iron away from biological invaders.

Because parasites, bacteria, and viruses have adapted to start using the iron in human tissues, we have, in turn, developed defense mechanisms to try and combat their ability to access to our iron. This again illustrates how dependent the evolutions of various species are on one another, spurring adaptation in a kind of feedback loop.

Moalem takes another detour to the 14th century, as the bubonic plague swept across Europe. More than 25 million people were killed: between one-third and one-half of the continent's population. The bacterium that's thought to have caused the plague, *Yersinia pestis*, caused painful swelling in the lymph nodes until they burst through the skin. New research indicates that the more iron in a given population, the more vulnerable that population was to the plague. Healthy adult males were most at risk because they were the group with the least amount of iron deficiencies. They were twice as likely to die as women of the same age because menstruation, pregnancy, and breast-feeding all led to iron deficiencies, and children and the elderly were also prone to malnourishment.

Here, Moalem begins to tie hemochromatosis and our reliance on iron to our history. Though on its surface, research done on the Bubonic plague may not appear to relate to genetics or evolution, it actually provides insight as to why certain people might have had an advantage over others in surviving the plague. It is also a direct example of Moalem's previous point that humans have developed defense mechanisms and adaptations in response to bacteria's ability to take advantage of our iron.

Moalem then returns to hemochromatosis. Even though people with hemochromatosis have far more iron in their systems, it isn't distributed evenly in the body. While most cells end up with too much iron, white blood cells called macrophages have much less iron than others. Macrophages work like the law enforcement of the immune system, as they try to identify pathogens and destroy them.

Here Moalem isolates the key benefit of hemochromatosis: even though iron builds up in a harmful way, its depletion in one area of the body provides a benefit. This further illustrates his point that although diseases like hemochromatosis can cause serious health issues in the long term, they can inadvertently protect people from acute problems (like infectious disease) in the short term.

In a non-hemochromatic person, macrophages have plenty of iron, and infectious agents can use that iron to feed and multiply. But for those with hemochromatosis, whose macrophages do not have iron, the plague was unable to gain that strength, and therefore those people were able to combat the bacteria better and were more likely to survive. Even though hemochromatosis is ultimately harmful, being able to survive in the short term is more important because it allows people to reproduce.

Moalem combines the information he has presented on hemochromatosis and how bacteria and parasites interact with the iron in our blood, thus illustrating how hemochromatosis was actually selected for during the Black Plague because it gave those with the condition an advantage in being able to survive and reproduce.

Recent research suggests that hemochromatosis originated with the Vikings and may have actually evolved as a protective measure against iron deficiency. Some posit that Viking men may have offset the negative effects of hemochromatosis because their warrior culture resulted in frequent blood loss, which prevents the buildup of iron in the blood. As the Vikings colonized and settled on the European coastline, they passed on the condition to their offspring. Then, when the black plague began to sweep across Europe, those of Viking descent were much more likely to survive the plague, reproduce, and pass the mutation on to their children, which also gave them more resistance to subsequent outbreaks.

Moalem also examines the benefits of hemochromatosis in Vikings, illustrating how it could have held advantages even before the Black Plague because it guarded against anemia. Additionally, the negative aspects of hemochromatosis were even further offset by the unintentional bloodletting that naturally arose in the culture. Because they were then able to pass the trait on, and the trait was amplified by the Black Plague, Moalem illustrates how genetic conditions can be compounded by a variety of social and biological conditions.

This new understanding of hemochromatosis has prompted a change in perspective regarding two long-used medical treatments: bloodletting and iron dosing. Bloodletting is one of the oldest medical practices, derived from the thinking of the Greek physician Galen. He theorized that all illness resulted from an imbalance of the four "humors": blood, black bile, yellow bile, and phlegm. Thus, if someone had an illness, doctors balanced the fluids through fasting, purging, and bloodletting. Yet the excessive use of bloodletting in the 18th and 19th century was ultimately proven to be largely harmful. By the 20th century, most viewed the practice as a brutal example of prescientific medicine, and it was largely discontinued.

Moving on from bloodletting was considered to be a progressive development in medicinal practice, informed by new scientific discoveries. It was largely caused by the germ theory taking precedence over the theory of the four humors in understanding illness. This led to an important and novel understanding of how bloodletting was not helpful in every incidence of illness, as had been previously practiced.

Yet Moalem argues that the way bloodletting was broadly discredited may have been misguided. Bloodletting is actually the treatment of choice for hemochromatosis, as bleeding prevents iron buildup in the body's organs. It can also be used to combat heart disease, high blood pressure, and pulmonary edema. In moderation, bloodletting may have a beneficial effect because it reduces the amount of iron available for pathogens to feed on.

New understanding of hemochromatosis and the way that it can be helpful in combatting the Black Plague opened the door to understanding that bloodletting might be the proper treatment. In turn, this advancement in evolutionary understanding also led to the recognition that bloodletting might achieve the same beneficiary effect for other ailments. This allowed the medical community to reevaluate the dismissal of bloodletting and recognize that (just the like the diseases it was used to treat) it may, in fact, have some advantages.

Conversely, findings have called into question the practice of treating those with anemia with iron loading. A doctor named John Murray was working in a Somali refugee camp when he noticed that most of the Somali people had pervasive anemia—and despite the fact that they were exposed to a range of virulent pathogens, they were relatively uninfected. But when Murray started to treat some of the population with iron, their rate of infection skyrocketed. In another example, 35 years ago, doctors in New Zealand routinely injected Maori babies with iron supplements to prevent anemia. These children were then seven times more likely to suffer from potentially deadly infections as those who did not receive the injections.

Additionally, understanding how a lack of iron can actually be beneficial, in the way that Moalem is laying out here, can help people avoid mistakes like the one that John Murray and the doctors in New Zealand made. A lack of iron actually provides a similar benefit to hemochromatosis, because it prevents disease from gaining access to the body's iron. Together, these examples show that the more we understand about our own biological adaptations and how even seemingly disadvantageous traits can actually be helpful, the more successful we may be at keeping ourselves and others healthy.


Hemochromatosis and anemia aren't the only hereditary diseases that have helped combat other conditions. The second-most common genetic disease in Europe is cystic fibrosis, which causes people to die young, often from lung-related illnesses. But new research suggests that carrying a copy of the gene that causes the disease offers some protection from tuberculosis—which caused 20 percent of all deaths in Europe between 1600 and 1900.

Moalem brings up yet another disease in the chapter that can have benefits despite its long-term harm: cystic fibrosis. This is another example of one disease being beneficial against another more deadly disease, proving how even though tuberculosis isn't as much of a problem in today's society, our mechanism for combating it has been bred into our genes.

It took Aran Gordon three years to learn that he had hemochromatosis. He was told that untreated, he would have five years to live. Today, Moalem writes, we know that the genetic disorder may have helped his ancestors survive the plague. Today, Aran's health has been restored through bloodletting. Today, we understand much more about the relationship between our bodies, iron, and infection. Aran Gordon finished the Marathon des Sables for the second time in April 2006, a few months after he was supposed to have died.

Here, Moalem drives home his point by returning to the personal anecdote of Aran Gordon. Thanks to understanding about how hemochromatosis helped people survive the plague, the iron locking involved, and the renewed understanding of bloodletting, what once might have been a debilitating or fatal disease is now something that Gordon can live with. The ability to synthesize this research now allows people to live healthier, longer lives—and that, Moalem implies, is the ultimate goal.

CHAPTER 2: A SPOONFUL OF SUGAR HELPS THE TEMPERATURE GO DOWN

Diabetes is one of the most common chronic diseases—in 2007, approximately 171 million people had diabetes. For diabetics, the process through which insulin helps the body use glucose is broken, and sugar in the blood builds up to dangerously high levels. Unmanaged, this can lead to "rapid dehydration, coma, and death."

Moalem reinforces the idea of how some conditions can seem negative but may have been advantageous in the past—this time focusing on diabetes. Here, he lays out clearly how this condition is harmful to those who have it in the modern world.

There are two major types of diabetes: Type 1 is believed to be an autoimmune disease in which the body's natural defense system attacks the cells in the pancreas responsible for insulin production. In Type 2 diabetes, the level of insulin production is too low. Moalem writes that it is not fully known what causes diabetes, but genetics is definitely a major contributor. Type 2 diabetes exists across all population groups, but Type 1 diabetes is much more common in people of Northern European descent.

Like the chapter on hemochromatosis, Moalem begins to foreshadow some of the details that will become key to unlocking the puzzle of diabetes. Both Type 1 and Type 2 diabetes are thought to be at least partially inherited, and the fact that Type 2 diabetics are largely people of Northern European descent gives an initial clue to the fact that it may have been an advantage in colder environments.

Until about 50 years ago, most people believed that global climate change occurred very slowly. The accepted wisdom was that after the previous ice age, the Earth took a few hundred thousand years to warm up. In 1895, when astronomer Andrew Ellicott Douglass studied tree rings for clues about past climate change, he discovered that there was a century-long climate change that occurred around the 17th century which caused a significant drop in temperature. His findings were dismissed by the scientific community, however.

The development of understanding rapid climate change becomes Moalem's first example of the need for curiosity and the advantage of interdisciplinary research, like the implication of Ellicott's findings on global climate history. In learning more about how the environment has changed in previous centuries and millennia, evolutionary biologists can then use these conditions to understand adaptations that humans may have developed.

More evidence of rapid climate change accumulated, as a flower (*Dryas octopetala*) that is usually found in the Arctic was found in mud cores in Europe 12,000 years ago. This provided evidence for an ice age, which they named the Younger Dryas. By the 1950s and 60s, more evidence was discovered by boring into two-mile cores of ice in Greenland's glaciers—the equivalent of 110,000 years of climate history. The ice confirmed the existence of the Younger Dryas, a severe drop in temperature which occurred 12,000 years ago and which shockingly took only three years to end. They also showed that the stability of the climate in the last 11,000 years is an exception to the rule, not the norm.

Moalem draws a direct line between Andrew Ellicott Douglass's research and the discovery of the Younger Dryas. With this new understanding of rapid climate change, Moalem then goes on to illustrate how rapid changes in the environment can provide the conditions for any biological advantage to be immediately selected for. This research again emphasizes the benefit of interdisciplinary science, and how discoveries in one field can be immensely informative for another.

Just before the Younger Dryas, human migration had begun as people moved out of Africa and north into areas in Europe that had been uninhabitable during the previous ice age. But the warming trend ended abruptly, and in just a decade, average temperatures plunged 30 degrees. This likely caused thousands of humans to freeze or starve to death. But some humans survived, and Moalem asks whether some genetic trait might have provided a superior ability to withstand the cold. He also notes that humans likely also adapted socially, moving away from hunter-gatherer societies and instead developing agriculture.

While the chapter on hemochromatosis focused on one inherited disease that provided protection against another deadlier one, here Moalem shows how the environment of our ancestors can be another major factor in shaping our evolutionary history. Moalem hints that this rapid climate change, which caused mass death, could have made a condition like diabetes advantageous.

Moalem then explores the effect of cold on humans. While many famous people have had their heads cryogenically frozen in the hopes of one day being reanimated, human tissue doesn't react well to freezing, as the cold causes blood cells and capillaries to burst. The body does have some defenses against freezing: shivering creates heat, and blood becomes more constricted to the torso to keep vital organs warmer rather than the extremities.

Moalem here indicates another smaller adaptation that humans have developed globally in response to cold environments. Sacrificing the extremities for vital organs adds another dimension to the idea that every evolutionary adaptation is a tradeoff, and sometimes harmful traits are necessary if they prevent even more dire consequences.


Another adaptation is a specialized heat-generating tissue called brown fat. When blood sugar is delivered to a brown fat cell, it can be converted to heat on the spot, and doesn't require insulin to do so. Most adults don't have brown fat—to accumulate it, you need to live in Arctic temperatures for a few weeks and then remain there. One additional reaction to the cold that isn't fully understood is called cold diuresis: the increased need to pee when it's cold.

This adaptation that Moalem discusses provides yet another hint as to how he will tie his argument together. The ability to convert sugar into heat, without the need for insulin, would prove very advantageous for someone living in Arctic temperatures—and having diabetes would be make this ability particularly useful.


Moalem next turns to a subject in the plant world: ice wine. Ice wine was supposedly created by accident 400 years ago, when a German vintner's crop was hit by a sudden frost. The grapes were shrunken and yielded much less juice, but when he pressed them, they were incredibly sweet. The shrunken nature of the grapes was due to water loss, which plants evolved to do in order to protect themselves from freezing. The increased sugar concentration is for the same reason, as sugar is a "natural antifreeze."

Grapes' habit of offloading water provides a potential explanation for cold diuresis in humans, as humans do the same thing by urinating. And the fact that sugar helps to prevent the grapes from freezing provides yet another reason why it might be helpful to have extra sugar in the bloodstream in humans. These studies, even though they seem to be on a completely different topic than human evolutionary biology, provide key insights as to how diabetes might have been selected for.

One animal, the wood frog, has also uniquely adapted to the cold. Unlike hibernating mammals that go into a deep sleep in the winter, the wood frog buries itself and freezes solid. It has no heartbeat, breathing, or brain activity while it's frozen. But minutes after rising temperatures thaw the frog, it sparks into gear and gulps for air. Biochemist Ken Storey studied the frogs and discovered that when the frogs sense the temperature dropping, it moves water out of its blood and pools it in its abdomen. It also dumps glucose into its blood to lower its freezing point. Ice is sandwiched between the skin and muscles, putting them on ice—just as we use ice to transport organs for transplant.

Studies of wood frog, like the grapes in ice wine, provide additional clues as to how diabetics managed the cold better than other humans. Having more sugar in the bloodstream lowered the frogs' freezing point, which suggests that the same process could happen in the human body. Not only do these studies have implications for evolutionary biologists, but the frogs' ability could also provide new avenues for advancing organ transportation for transplants—again proving the benefit of interdisciplinary science.

Moalem ties the frogs to humans, noting that the people who have a propensity for diabetes (and thus for high levels of blood sugar) were descended from people who lived in Northern Europe. Any adaptation to manage the cold during the sudden onset of the Younger Dryas, he notes, would have been advantageous. Moalem also argues that they could have developed brown fat, which would allow them to burn off the excess sugar in their blood to generate heat.

Here, Moalem begins to tie his arguments together, noting how diabetes would have been an advantageous trait in people who lived in northern climates during the Younger Dryas, and therefore why that trait would have been passed down in people of Northern European descent. The disease is harmful today, but the fact that it provided a benefit 12,000 years ago ensured that the trait would be passed on.

There are other bits of evidence to support the theory: for instance, when rats are exposed to freezing temperatures, they become resistant to their own insulin. More diabetics are diagnosed in colder months than warmer months; a study of over 280,000 American veterans with diabetes showed that they had dramatically higher blood sugar levels in colder months. The difference in blood sugar levels was even more pronounced in those who lived in colder climates.

Moalem also illustrates how even changes in the environment today can shape how people's genes are expressed—colder climates can still bring out those same defense mechanisms that proved advantageous during the Younger Dryas.

Moalem reaffirms his thesis: that every evolutionary adaptation is a "compromise" between advantage in some circumstances and disadvantage in others. Someone with a diabetes-like condition living in an ice age environment would have limited food, and brown fat would convert excess sugar to heat. Modern-day diabetics, with little or no brown fat and little exposure to the cold, would have no use for the excess sugar. Moalem acknowledges that these connections aren't definitively confirmed, but that we should still pursue them rather than dismissing them.

Moalem again sums up the idea that we have evolved certain diseases because of the advantages that they once provided to our ancestors—this time, an advantage against an ice age environment. He also acknowledges that information on the subject is still developing, but he affirms the idea that research on this topic (and others that could relate to it) is necessary in order to find out more about our evolutionary past.

CHAPTER 3: THE CHOLESTEROL ALSO RISES

While the sun is necessary for all life on Earth, the sun is just as important to humans on an individual, biochemical level. Sunlight helps your body create vitamin D but also destroys your body's reserves of folic acid—both of which are essential to your health. Vitamin D ensures that we have sufficient levels of calcium and promotes bone growth. American milk is now fortified with vitamin D, but the vitamin can be made by the body itself. When exposed to the right kind of sunlight, ultraviolet B (UVB), we can convert cholesterol to vitamin D.

An essential part of the first two chapters of the book has been illustrating how evolutionary adaptations have built-in tradeoffs. Moalem shows here that this is true on a smaller scale as well: human evolution has had to find a balance between getting enough sunlight to produce vitamin D and not getting so much that the sun's UVB rays destroy the body's folic acid. Thus, not all adaptations necessarily result in diseases: rather, humans have evolved certain built-in tradeoffs that prevent *disease.*

While sunblock guards against sunburn and skin cancer, it also blocks the UVB rays we need for vitamin D. Conversely, researchers have discovered that tanning can help people with vitamin D deficiency, like people with Crohn's disease, a disorder that involves inflammation of the small intestine and impairs absorption of nutrients. On the other hand, folic acid is just as important to human life, and it is destroyed by too much UVB light. Folic acid is an integral part of cell growth, helping to replicate DNA when cells divide. It is particularly important during pregnancy, as too little folic acid can result in serious birth defects.

Although the medical community often cautions against excess sun exposure because of the risk of skin cancer, here Moalem shows that tanning can actually be advantageous for people with diseases that cause vitamin D deficiency. On the other hand, this could result in folic acid-related complications, particularly for pregnant women. Thus, Moalem again demonstrates that many of humans' biological mechanisms involve maintaining a delicate balance between different health problems on either end of a spectrum.

The skin both protects folic acid and serves as a key player in producing vitamin D. The wide range of human skin color is related to the amount of sun a population has been exposed to. It protects against sunburn and protects one's folic acid, because the more melanin in the skin (the darker it is), the less UVB light you absorb. Skin color can change, to some extent, based on response to sun exposure. When a person is exposed to the sun, melanin production is stimulated in order to protect from UVB rays.

Skin color serves as the key adaptation for how to maintain the balance between getting enough vitamin D and keeping enough folic acid. It is in this way that these adaptations start to build upon our idea of race. While Moalem ultimately recognizes that skin color is primarily a factor of geography, it also gives certain populations distinct common traits.

Skin color is directly related to the amount of sun exposure in a population. When the first humans were evolving in Africa, they had dark skin designed to block UVB absorption. But when some populations migrated north to places like Europe, they received too few UVB rays and couldn't produce vitamin D—therefore, they evolved to have lighter skin. Researchers posit that it would take 1,000 years for a population's skin color to change based on their climate.

Just as the environment may have played a key role in determining whether people developed diabetes during the Younger Dryas, the environment is another key factor here in determining vitamin D production and folic acid retention because of the way environment sparks an adaptation in a population's skin color.

There is one exception to this relationship between sun exposure and skin color: the Inuit, who are dark-skinned despite living in a place with little sunlight. But their diet is composed of fatty fish, which happens to be full of vitamin D. Therefore, they do not need lighter skin in order to create vitamin D.

The exception of the Inuit proves the general rule: if the Inuit, who live in the Arctic, do not need lighter skin because they already have enough vitamin D, it only serves as further proof that people with light skin have developed that way because they do not get enough vitamin D.


People with darker skin have an additional problem, however, because their skin blocks most UVB rays and therefore they may not produce enough vitamin D. But these populations have evolved a protein called apolipoprotein E (*ApoE4*) which increases free-flowing cholesterol in the blood to maximize vitamin D production. People throughout Northern Europe also carry this protein, because even with light skin, they receive so minimal sunlight with which to produce vitamin D. But though it allows people to create vitamin D, the cholesterol resulting from *ApoE4* puts people at greater risk for heart disease and stroke.

Here, Moalem makes the evolutionary tradeoff more explicit: people who do not get enough vitamin D increase their cholesterol production. But even while this allows them to mitigate their vitamin D deficiency, high cholesterol can lead to other problems. In addition, Moalem again emphasizes how environment can affect these adaptations and tradeoffs, because the amount of sunlight one gets (or that one can absorb) plays a key role in that overcompensation of cholesterol.


Moalem gives other examples of culture-specific gene development. People of Asian descent frequently have a genetic variation called *ALDH2*2* that makes them less effective at breaking down the by-products of alcohol. This causes them to appear and feel more drunk. This variation is rare in Europeans, however. Moalem explains that this is because as humans settled into cities and towns, they had to figure out how to clean their water. In Asia, people purified water by boiling it and making tea. In Europe, they used fermentation, and the resulting alcohol from that fermentation killed microbes even when it was mixed with water. Thus, there was evolutionary pressure in Europe to be able to break down alcohol, but not in Asia.

Temperature and climate aren't the only geographical factors that played a role in our ancestors' adaptations. Here, Moalem illustrates that the culture *of a population in a given geographical location can also have significant effects across generations. Different populations came to different solutions for cleaning water, which in turn affected their respective groups' genetic development and thus created common geographically-specific adaptations. This is another factor in our ideas of race: these genes developed in a population that already had similar traits, and their common culture added further similarities to their DNA.*

In additional to alcohol, this concept can also be found in the ability to digest milk. The majority of the world's adults cannot digest lactose. People who can continue to digest lactose after infancy are likely descended from farmers who drank animal milk, who evolved to retain the ability to break down lactose.

Being lactose intolerant is another example of how both culture and geography combined into a racially-specific gene. People of European descent are less likely to be lactose intolerant because dairy farming was more prominent there, unlike in Asia or Africa.

Moalem admits that even though these differences seem "racial," it is difficult to define what race means. Skin color isn't reliably based on genetics, as moving to a new environment would change a population's skin color. On the other hand, many Jewish people seem to share a distinct genetic heritage despite the fact that they can have very different appearances. Comparing the DNA of a large group of Jewish people called Cohanim (who trace their roots to Moses's brother Aaron), despite the fact that they came from all over the world, led researchers to discover genetic markers so specific that they almost certainly descended from just a few male individuals.

Moalem concedes that it's difficult to define what race is, as even though there are commonalities in the genes of given populations, it is difficult to know whether commonalities can be attributed to race. They're clearly not linked solely to appearance, as the example of the Jewish people illustrates. And even genes that constitute appearance can be altered based on geography. Thus, Moalem recognizes that there is nuance in the interplay of geography, genetics, and our ideas of race.

These studies are controversial, Moalem writes, and he says that while it's hard to define race, what researchers know is that distinct populations do share distinct genetic ancestry. This is most likely the result of the varied conditions that different groups of people experienced as they spread out across the world. As Moalem has already discussed, different circumstances that populations encountered (plagues, ice ages, and tropical diseases) all had an effect on how people evolved.

Even with Moalem's concession that race is a complicated issue, he asserts that much of what we think of as race are actually adaptations based on a common geography and culture—both of which largely remained the same for generations up until our recent period of globalization.

Moalem examines how even conditions in the last 500 years can affect traits in certain sub-groups of people. For instance, high blood pressure is particularly common in African Americans compared to the rest of the American population; their blood pressure is also very reactive to salt. Though Moalem again admits the theory is controversial, he posits that when Africans were taken to America against their will by slave traders, they were transported under horrible conditions and were usually not fed or given sufficient amounts of water. It's possible that those who naturally tended to retain more salt had a better chance of survival, as extra salt helped their bodies hold onto water and thus combat dehydration.

While the background of this adaptation is much more horrific and culturally motivated than the others Moalem has mentioned, the effects are similar to how the Younger Dryas affected people. In both cases, an immediate shift in environmental conditions and food availability made certain traits within the population immediately more advantageous, and therefore it made those people more likely to survive and reproduce. This effect, Moalem posits, continues to have ramifications for the descendants of those African slaves today.

Moalem returns to the adaptations of Africans in response to sun exposure: the evolution of darker skin to protect folic acid and increased cholesterol to produce vitamin D. But when populations with darker skin move to places like New England, they're twice as likely to be deficient in vitamin D and to have high cholesterol. This may be why African Americans who live in colder climates are more prone to rickets, prostate cancer, and heart disease.

Moalem returns to the compromise between vitamin D and folic acid, but he illustrates how the problem is exacerbated when people move out of the environments which provided them with the adaptation—essentially relinquishing their evolutionary advantage and making the downsides even more problematic.


The pharmaceutical industry has begun to tailor its drugs based on genetics, as new research has shown how genetic variations can affect our body chemistry and how we respond to drugs. Because of the consensus that normal hypertension drugs don't work as well on African Americans, there is a drug called BiDil for self-identified black patients who have heart failure.

Research on health conditions that arise from ancestral differences—particularly the relationship between vitamin D, skin color, and cholesterol—have, in turn, prompted scientists to create drugs that take these genetic differences into account. The fact that this had led to more effective medicine for African Americans further demonstrates the importance of understanding the root cause of a health condition.

Moalem says that one thing is clear: evidence suggests that when placed in the context of our current circumstances, the specific environmental adaptations that our ancestors passed onto us can significantly our health. We can use this information to tailor medical treatments—perhaps recommending tanning salons rather than lifetime prescriptions of drugs for excess cholesterol.

Rather than trying to compensate both for less vitamin D and for too much cholesterol, Moalem suggests a solution that will fix both issues at once. Thus, even though high cholesterol is an adaptation that has become problematic, understanding the condition's underlying causes by examining patterns of genetics and migration can lead to more effective treatments.

CHAPTER 4: HEY, BUD, CAN YOU DO ME A FAVA?

In ancient Greece, a variety of sources warned against eating fava beans, from Greek scholar Pythagoras to a cult called the Orphics (who believed the beans contained the souls of the dead). Moalem writes that these superstitions were not without merit. Favism is an inherited enzyme deficiency carried by 400 million people—the most common enzyme deficiency in the world. In extreme cases, people who have favism and eat fava beans experience "rapid, severe anemia that can often lead to death."

The introduction to this chapter is reminiscent of Moalem's discussion of bloodletting. While it is easy to dismiss these practices and beliefs as folklore of an ancient and less informed time, Moalem illustrates how they existed for a reason. Understanding the past, and how medicine or common knowledge has evolved over time, can provide evidence for some conditions in the present, as is the case with favism.

Scientists first recognized some truth behind the aversion to fava beans during the Korean War. American soldiers were prescribed drugs to combat malaria, including one called primaquine. About 10 percent of African American soldiers developed anemia while taking primaquine, and other soldiers (mostly of Mediterranean descent) experienced an even more severe version called hemolytic anemia.

Again, in noting that most of the soldiers who developed anemia were of African American and Mediterranean descent, Moalem foreshadows his eventual reveal of the common factors that lead to favism and anemia. Just as diabetes was beneficial for people in ice age conditions of Northern Europe, it's likely that there's an underlying adaptation behind why these particular groups develop anemia from primaquine.

Three years later, scientists discovered the cause of these side effects. The soldiers who reacted to the drug lacked an enzyme called G6PD, which clears out elements that are harmful to the cell. These elements include free radicals, which are molecules with unpaired electrons that can disrupt cellular chemistry. Primaquine is thought to stop the spread of malaria by preventing malaria-causing parasites from invading the body's red blood cells. But with a lack of G6PD to maintain the cell's defense systems, the cells become even more vulnerable. Hemolytic anemia can then lead to kidney failure, heart failure, and death.

Again, Moalem sets up the argument for why a disease like favism would be harmful, explaining some of the biology behind favism, anemia, and malaria. He illustrates why people have such a bad reaction to anti-malarial drugs, hinting at the idea that people who have favism don't need to take primaquine because they already have a certain degree of defense against malaria due to their red blood cell vulnerability. This drug only makes that condition deadlier, without the added benefits.

This lack of G6PD is known as favism, and it is named that way because when people who have favism eat fava beans, they undergo a similar reaction to the one that occurs after taking primaquine because of the free radicals in fava beans. The irony of favism is that the people who have favism are more likely to live in places where fava beans are cultivated: North Africa, Southern Europe, and around the Middle East (the countries that line the Mediterranean). Moalem again questions why humans would have evolved a mutation that causes problems specifically when eating a staple of their local diet.

In this case study, it is clear that like the other diseases, Moalem will ultimately prove how favism has an added benefit despite its potential harm. But there is an additional mystery that Moalem will also take on: favism's relationship with people or places that create fava beans. This enables Moalem to transition to his discussion on how plants, animals, and humans can impact one another's evolutions. Plants, he shows, have evolutionary purposes behind both their beneficial and toxic properties.

Moalem then shifts to the broader connection between evolution in the animal kingdom and evolution in the plant kingdom. He notes that plants that produce edible fruit evolve that way for their own benefit: animals learn to pick the fruit, eat it, and deposit the seeds somewhere else so that the plants spread and reproduce.

This is Moalem's first example of the symbiotic relationship between plants and the animals that eat them: animals who learn what parts of the plants are good to eat are more likely to survive, and the plants who develop fruit are able to move to other places and increase their species numbers.

Plants have also evolved defense mechanisms so that the fruit is the only thing the animals eat. These mechanisms include thorns, but also chemicals and toxins that they have developed. Clover, sweet potato, and soy all belong to a group of plants that contain chemicals called phytoestrogens. These chemicals mimic the effects of sex hormones like estrogen, and the compounds diminish animals' ability to reproduce. This ultimately proved useful to humans, however, as chemist Carl Djerassi based his development of the birth control pill on these hormones—specifically phytoestrogens produced by the Mexican yam.

Moalem's next example illustrates how evolutionary adaptations can work in a kind of feedback loop: because plants develop fruit, animals eat the fruit and also try to eat other parts of the plant. In turn, then, plants must evolve mechanisms to prevent animals from eating the parts that are essential to them. This example also illustrates how evolutionary research can have broader scientific implications, as discovering how phytoestrogens protect plants from animals enabled chemists to develop the birth control pill.

Plants also produce poisons to prevent predators from eating them. For instance, the cassava plant contains a precursor to cyanide, while the Indian vetch contains a neurotoxin that can cause paralysis. Plant toxins can also have milder effects, like interfering with digestions or burning lips. Raw habanero peppers have a chemical called capsaicin, which causes burning sensations in mammals but not in birds. This is because mammals' digestive systems destroy the peppers' seeds, while birds' digestive systems do not.

Moalem illustrates how the development of capsaicin is designed to be the most helpful in evolutionary terms, guarding against only the predators whose digestive systems are harmful to the pepper's seeds. Peppers' adaptation developed in a way to prevent mammals from eating the peppers, but not to prevent birds from eating them so that they continue to deposit the seeds in other places.

Humans will frequently still eat plants with toxins—between 5,000 and 10,000 every year—because we have also evolved mechanisms to manage those toxins. Tasting bitterness is one mechanism, as this ability allows us to detect toxins in plants and avoid eating them. However, not all compounds that are linked to bitterness are toxic—likely because most of the plants' chemical weapons are aimed at insects, bacteria, fungi, and herbivores.

Moalem illustrates how plant adaptation has even affected the evolution of humans, as we have evolved to detect and manage the toxins that plants produce as a part of their defense mechanisms. Again, this emphasizes the interconnectivity of all species and how each one can spur another's evolution.

In the past, humans have tried to increase plants' natural defenses in order to protect them from other predators like insects—sometimes with results that backfire. A potato was bred with more solanine (its natural poison), and it became so poisonous it was inedible. Celery defends itself with a toxin called psoralen, which causes sensitivity to sunlight in humans. It produces more psoralen when it feels under attack. For farmers who use pesticides, fewer insects attack the celery and it produces less psoralen. But organic farmers don't use these pesticides, and ironically, refraining from external poison actually results in more internal poison in the celery plant.

In these examples, Moalem illustrates some of the dangers in trying to manipulate genes of other organisms to our benefit, because those manipulations may have unintended consequences. In this way, humans can inadvertently influence the expression of evolutionary mechanisms in an organism like celery that may not have manifested otherwise, once again showing the intimate connection between different species.

Moalem returns to the connection between fava beans and favism. People who have favism and lack the G6PD enzyme cannot mop up free radicals, which results in anemia in more than 400 million people around the Mediterranean. However, this gives people an advantage over another common disease around Africa and the Mediterranean: malaria.

Here, as Moalem returns to favism, he also returns to his central thesis: favism is likely common (particularly around the Mediterranean) because it continues to prevent malaria, a disease that is even more deadly. In this way, it is similar to hemochromatosis (which protected against the bubonic plague) and diabetes (which helped primitive humans survive extreme cold).

Malaria infects almost 500 million people and kills more than 1 million people every year. Malaria causes joint pain, vomiting, and anemia. Ultimately, it can lead to coma and death, especially in children and pregnant women. It was initially thought that malaria was caused by unhealthy vapors emanating from still water (malaria is old Italian for "bad air"). This theory was incorrect, but it led to the development of air conditioning by Dr. John Gorrie, hoping to eliminate that "bad air."

The development of air conditioning serves as another example of how interdisciplinary research can be extremely beneficial—and even how incorrect theories on diseases can ultimately be helpful in sparking other innovation. Even though the cause of malaria is not actually air, this belief led to an essential modern innovation in the air conditioning.

In reality, malaria is caused by parasitic protozoa which are deposited in the human bloodstream through mosquitoes. The most dangerous protozoan is called *Plasmodium falciparum*. Scientist J.B.S. Haldane was one of the first people to understand that certain groups with anemia have better natural resistance to malaria. Today, many scientists believe that a G6PD deficiency (favism) provides even more resistance because the red blood cells are less hospitable to the protozoa, and because they are taken out of circulation more frequently, disrupting the parasite's life cycle.

Moalem provides the scientific explanation for why favism, and the resulting anemia, are beneficial in combatting malaria. This provides people with favism with a greater evolutionary advantage and a better assurance of survival, which is why people with favism are able to reproduce and pass on this enzyme deficiency.

Moalem then explores why the same populations with favism might have cultivated fava beans: he explains that favism is only passed on the X chromosome, and so many women only have one copy of the G6PD mutation. When someone with a partial or mild G6PD deficiency, or without the deficiency at all, eats fava beans, it makes the red blood cells less hospitable. Only women with two copies of the gene, or men with one copy, might have an extreme reaction to fava beans.

With this research, Moalem illustrates why favism is particularly advantageous: it is just as effective when one copy of the gene is passed on as when two copies of the gene is passed on. Therefore, most people receive the benefits of the deficiency through eating fava beans but do not experience the harmful by-products of the disease.

Humans have long been relying on herbal remedies, but the first antimalarial medicine came from George Cleghorn in the 19th century, who found a remedy in the bark of the cinchona tree. A century later, French chemists found the beneficial compound, quinine, and made a tonic from it to prevent malaria. However, over time, nearly every strain of malaria has become resistant to quinine. Fava beans, on the other hand, are still effective because they alter human body chemistry, not the protozoa's chemistry.

Moalem previously illustrated how plants and animals can influence one other's evolution. This holds true for humans and disease-causing pathogens as well, as even when humans try to develop vaccines or medicines to prevent disease, those pathogens can frequently evolve resistance to those efforts.

Many plant toxins can be harmful but also come with benefits: phytoestrogens can stop the growth of prostate cancer cells and may ease the effects of menopause. Capsaicin stimulates the release of endorphins, increases your metabolic rate, and can also serve as a natural painkiller. Psoralen in celery can cause skin damage but can also help psoriasis. Even common medications liked aspirin or taxol (an anti-cancer drug) are derived from plants. It's helpful, Moalem concludes, to recognize the benefit that plants can afford to us.

Again, Moalem emphasizes the evolutionary compromises in our relationship with plants. Like disease, even though plant toxins can be harmful, they can also be helpful. The key is learning more and understanding when it might be necessary to accept the potential harm in order to receive the benefits—the same principle by which the diseases Moalem references have come to be inherited in humans.

CHAPTER 5: OF MICROBES AND MEN

For thousands of years, the Guinea worm has plagued humans. The larvae of the worm can be found in still water and ponds, and when people drink the water, the larvae enter their digestive system, grow over time, and mate. Once the parasites are fully grown, they make their way to the skin, secreting acid to burn an exit tunnel for themselves. The burning sensation causes humans to cool themselves with water, and when the worm senses this, it emits a milky fluid full of thousands of larvae and the process starts over.

Here, Moalem gives a small case study of the Guinea worm, illustrating how the Guinea worm has adapted to reproduce just when humans are trying to seek relief from the Guinea worm's burns. This case study, and this chapter as a whole, serves as a wider exploration of how parasites and bacteria have evolved alongside humans and other organisms in order to survive and reproduce.

Former president Jimmy Carter has led a two-decade effort to inform people worldwide about how the Guinea worm is contracted and how it reproduces. His efforts have helped educated humans about water that could be infected and counseled them not to use water to relieve the burning sensation. This has caused infections to drop from 3.5 million in 1986 to 10,674 in 2005. By understanding how the Guinea worm has evolved, we can protect people from it.

Moalem argues here, however, that understanding this adapted behavior allows people to try and resist the urge to play into the Guinea worm's manipulation of its host. The increased knowledge alone helps in suppressing the Guinea worm's infection rate, which is one of the reasons that research in this area is so critical.

As humans evolve, infectious diseases evolve alongside us, and their "hardwired imperatives" are the same: survive and reproduce. Moalem emphasizes that not all bacteria and viruses are bad, however. About 1,000 different types of microbial creatures live in the human body, most of them in the digestive system. These gut flora help to create energy by breaking down food products for us, training our immune systems to identify and attack harmful organisms, and stimulating cell growth. This is why antibiotics can cause digestive issues, because they also kill helpful bacteria as well as harmful ones. The human body also frequently houses bacteria that can be harmful, but the gut flora can prevent those dangerous bacteria from growing to dangerous levels.

Unlike humans' relationship with the Guinea worm, and the rest of the case studies in this chapter, our relationship to the bacteria and viruses that have evolved inside our digestive system is actually a beneficial one. Like the evolutionary relationship between animals and plants that was explored in the previous chapter, this relationship shows how interspecies connectivity and adaptation can be very helpful, as we serve as a home for these "gut flora," while they in turn help us digest food or kill other, more harmful organisms.

Not all relationships between organisms and their hosts are so symbiotic (mutually beneficial). The Guinea worm, for example, is a pure parasite. And when its victims feel the urge to seek out water, the infected person is experiencing "host manipulation," which occurs when a parasite provokes its host to behave in a way that helps the parasite to survive and reproduce.

Here, Moalem defines the key idea of this chapter: host manipulation. This concept is another way in which species have adapted to each other's evolutionary development, and in these cases parasitic species can use a host's adaptations to its own advantage—often to the host's detriment.

Moalem then examines other examples of host manipulation in nature. In Central America, there lives a kind of spider that spins orb-shaped webs. A particular species of wasp then stings the spider, paralyzing it, and lays eggs on its abdomen. The spider continues as normal, but when the egg hatches into a wasp larva, it makes holes in the spider's abdomen and the larva feeds on its blood. When the larva is ready to cocoon, it injects the spider with chemicals, and the spider completely changes its behavior. Instead of building circular webs, it builds a special web to protect the larva's cocoon. When it is finished, it sits in the center of the web, and the wasp kills the motionless spider and builds a cocoon inside the webs before hatching a week later.

The relationship of the Central American wasp and spider exhibits another, more direct method of host manipulation, in which the wasp literally overrides the spider's ability to think for itself. The example illuminates how this adaptation likely came about: the ability to use the spider's web-building skills for its own advantage gave the wasp additional protection during its cocoon phase and thus made it more likely to survive. Even though researchers may not be sure how the wasp larva accomplishes this feat, it proves undeniably advantageous.

Host manipulation generally involves an important step in the parasite's reproduction. Adult flukes, a kind of worm which live in sheep, need to find a way to get into the body of another sheep so that the species doesn't die out when the original host sheep dies. The eggs of the fluke are discarded with the sheep's dung. A snail then eats the eggs, and when they hatch, they are secreted by the snail as slime. Ants feed on the slime, and the flukes inhabit the ant. Then, the fluke manipulates the ant's brain: every night it causes the ant to climb to the tip of a blade of grass, waiting to be eaten by a passing sheep.

It also follows that host manipulation would generally involve a step in reproduction, because the imperative to survive and reproduce is key in spurring adaptation. Like the example of the spider and the wasp, this example of the flukes proves how dependent the flukes are on a multitude of species in order to reproduce, and hence why they might have adapted to be able to manipulate the behavior of an organism like an ant to ensure their own survival.

Viruses and bacteria also engage in host manipulation. For instance, the rabies virus colonizes the salivary glands of its host, making it difficult to swallow and causing foaming at the mouth. The virus also chemically induces the animal to be more aggressive and agitated, leading it to bite. When the anima's mouths is foaming with rabies-filled saliva, its bites are infectious. In all of these cases, the host isn't acting in a completely new way—rather, the parasite has evolved to influence its host to help the parasite survive and reproduce. However, we can learn to shift the evolution of the parasite so that it's less harmful to us.

Moalem takes a more commonly known example of disease, like that of rabies, to further emphasize how many diseases engage in host manipulation like parasites do. Bacteria and viruses have also evolved to take advantage of their hosts—a concept Moalem has already illustrated in the chapter on hemochromatosis, showing how illnesses take advantage of the iron in our immune response.

T. gondii is a parasite that can infect any mammal but can only reproduce in cats. The spore cells of *T. gondii*, called oocytes, can last a year outside a host. They can infect an animal when they are eaten or when animals eat the flesh of an infected animal. Once an animal is infected, *T. gondii* cells insert themselves inside brain and muscle cells. *T. gondii* infects as much as half the world's human population, but it is generally benign in humans. In mice, however, the parasite causes them to become fat and lethargic and lose their fear of predators—it even draws them to the scent of cat urine, which gets *T. gondii* back to cats.

Moalem examines yet another example of host manipulation in mice, once again illustrating how evolution can even be species-specific. T. gondii *doesn't affect humans because it would be unlikely for their cells to pass from a human to a cat—yet it has a much more significant effect on mice because mice can be eaten by cats. Thus, these adaptations are again shown to be in service of* T. gondii*'s own ability to survive and reproduce.*

Moalem examines another form of host manipulation: sneezing. Most people think of sneezes as symptoms. But when a person is already infected with the cold virus, it is actually a form of host manipulation: the cold virus learns to trigger the sneezing reflex in order to help spread the virus to other people.

This example illustrates how, like the Guinea worm, understanding can help us prevent the spread of diseases. In recognizing that sneezing helps the cold virus pass from person to person, we can practice behaviors (like covering our nose) that prevent this spread.

Pinworms also use host manipulation. Pinworm infection is one of the most common infections contracted by children. Pinworms grow to maturity in the large intestine and then make their way out to deposit microscopic eggs on the skin. They also deposit allergens to cause itching. When children scratch their skin, eggs get under their fingernails, and the children deposit those eggs to anything they touch—including into their mouths, where the process starts again.

In this example, like the examples of the Guinea worm or sneezing, understanding how pinworms are transmitted can help inform people on how to treat or prevent them. For example, simple measures like proper handwashing and preventing children from scratching themselves or putting their fingers in their mouths can help a great deal in reducing the infection's spread.

Cholera uses more passive methods. Cholera is a waterborne disease that causes severe diarrhea. Diarrhea is how the disease reenters the water supply and ensures its ability to find new hosts. Malaria also manipulates human hosts by incapacitating them—when someone with malaria is incapacitated, they are a helpless target for mosquitoes. Mosquitoes that bite infected humans then pick up those malaria-carrying protozoa and are able to infects others.

Here, Moalem introduces the idea that understanding how we are a part of the transmission process can help us put evolutionary pressure on diseases to be less deadly.

Diseases affect human behaviors in other ways, outside of host manipulation. This includes instinctual behavior: for example, disgust at sights and smells prompt us to avoid things that are full of harmful bacteria, like animal waste or spoiled food. It also includes learned behavior like covering one's nose and mouth when sneezing or washing one's hands before a meal.

Again, just as diseases and pathogens have evolved to take advantage of our behaviors, so too have we developed mechanisms and even social customs to help stave off those diseases, like the ones that Moalem describes here.

There are additional behaviors that may have developed to put the survival of a species over the survival of individuals: for instance, sick primates, beetles, and birds wander away from their kin to protect them from infection. Additionally, some species like lobsters have evolved to avoid their brethren when they become infected (even before showing signs of infection). This may also be the biological reason for xenophobia, as we instinctually perceive outsiders as threats to our own health and survival—even if that instinct is no longer practical.

Moalem next touches on some instincts that further emphasize surviving and reproducing on a species level rather than on an individual level. These are additional instincts that seem harmful to an individual but may help the species as a whole. Additionally, Moalem's point about xenophobia is another important issue to be aware of: by understanding the instinct behind these impulses, we can overcome discriminatory social behaviors.


Just as we have been evolving to survive disease, organisms that cause disease have been evolving alongside us. Penicillin was first used to treat staph infection in 1942. Eight years later, 40 percent of staph infections were penicillin-resistant. We then developed methicillin to treat those strains in 1959. Two years later, the first methicillin-resistant staph (MRSA) was reported. Treatment then switched to use vancomycin, and the first case of vancomycin-resistant staph infection (VRSA) was reported in 1996.

Moalem reiterates the central idea of the chapter: that even when we try to combat disease, it is easy for them to adapt to the biological weapons that we throw at them because they adapt very quickly. What we instead must do, as Moalem goes on to argue, is to find ways to put evolutionary pressure on the diseases to evolve to be less, not more, deadly.

Even if these organisms can evolve quickly, we can use their biology to direct their evolution to be less virulent (less harmful to their hosts). Paul Ewald, a pioneer of evolutionary biology, examined how microbes can move from one host to another. He found that they do so in three basic ways: close proximity through air or physical contact (like the cold or STDs); through an intermediate organism (like malaria); or through contaminated food or water (like cholera). Ewald asserted that diseases that travel through physical contact face pressure against virulence: they rely on hosts to carry them around, and therefore their hosts must be healthy enough to be mobile. But when infectious agents don't need hosts to be mobile, they are often deadlier.

Moalem illustrates the practicality behind understanding these interspecies relationships. By examining how viruses and bacteria interact with humans to transmit diseases, we can then find ways to protect ourselves not by treating them temporarily, and in the process making them more virulent (as with staph infections), but instead forcing them to evolve to be less deadly (as with cholera).


However, Ewald believes that understanding transmission methods can help us influence the evolution of parasites away from virulence. He takes cholera as an example: cholera can spread through humans or through water. If sewage flows easily into rivers that people wash in or drink from, then the cholera strain would evolve toward virulence because it can multiply freely without humans and rely on its access to the water supply for transmission. But if a country develops ways to protect its water supply, the bacteria should evolve to be less virulent because it will rely on humans to spread.

Through Ewald's research on evolutionary biology and disease transmission, and by understanding how cholera interacts with humans, he was able to come up with practical ways in which to make the disease less deadly to humans. This illustrates the necessity of interdisciplinary research and how an increased understanding of those topics can make our world tangibly healthier for humans.

Ewald's theory isn't always applicable: some parasites are capable of surviving outside a host for a long time, like anthrax. But by understanding how organisms have evolved alongside us, we can potentially prevent parasites like the Guinea worm from spreading and reproducing or change the course of diseases like cholera and malaria.

Moalem recognizes that Ewald's research won't help us with every disease. But by highlighting how research has helped us treat cholera or the Guinea worm, Moalem makes an implicit argument for the necessity of further research to help us combat other diseases.

CHAPTER 6: JUMP INTO THE GENE POOL

At the end of the 18th century, a doctor in Gloucestershire, England named Edward Jenner discovered a pattern: milkmaids who caught cowpox seemed resistant to smallpox. He scraped a cowpox sore from a milkmaid and purposefully infected teenage boys, who as a result were protected from smallpox. This became the first vaccine, and the word actually comes from the Latin name for cowpox, *vaccinia*.

While the previous chapter illustrated how microbes and other pathogens have learned to evolve adaptations that help them survive and reproduce, this chapter focuses on what humans can do to do the same. Vaccines illustrate how we can use evolutionary information from viruses (i.e., seeking out viruses that will produce antibodies to more harmful diseases) that can then help us survive deadlier diseases.

Today, we know more about how vaccination works: modern vaccines introduce a harmless version of the virus into our bodies, stimulating our immune system to produce antibodies tailored to defend against the virus. But for a long time, scientists didn't understand how our bodies created antibodies to fight against every microbial attacker because we couldn't have enough genes dedicated to each one—until they recognized that genes could change.

This chapter also introduces the idea that we can develop some adaptations much more rapidly than previously thought. Moalem describes how for a long time, we didn't fully understand our own immune response, highlighting the ongoing need for research.

When a sperm and egg cell combine to form a zygote cell, all of the DNA needed to build a human being is already in place—the instructions are carried in 3 billion pairs of nucleotides, which amount to fewer than 30,000 genes. These genes are organized into 23 chromosomes, which carry the same type of instructions in each person but with individualized content (say, for hair color or eye color). Every cell in the body contains the same DNA, except for sperm and egg cells—which contain only one set of 23 chromosomes rather than two sets.

Moalem provides background information on DNA and how we are born with all the genetic information we will ever have. At first, it seems that this emphasizes the fact that DNA is rigid and relatively unchangeable outside of small, random mutations. But given Moalem's previous point that genes are changeable, it's likely that our genetic code is actually a lot more mutable than we were once thought.

Interestingly, less than 3 percent of a person's DNA contains instructions for building cells; the other 97 percent isn't active in building anything. Scientists initially called this genetic material "junk DNA," believing that it didn't help us in any way and had simply stayed in the gene pool for millions of years. But more recently, scientists have discovered that this genetic information—now called "noncoding DNA"—may be incredibly important in to the evolutionary process. What may be even more surprising is that researchers now believe that as much as a third of our DNA has developed from viruses.

Over the course of the chapter, Moalem illustrates how scientists' ideas of "junk DNA" have shifted, again emphasizing the need for research in a multitude of fields. He implies that by understanding the evolution and adaptation of viruses, researchers can then recognize how that adaptation has, in turn, helped humans evolve.

For a long time, the scientific community believed that genetic changes were the product of accidental mutation—errors in copying DNA information from one cell to another that got through our genetic proofreading system. Mutations can also occur when organisms are exposed to radiation or chemicals. Sometimes, a random mutation will give the organism an advantage, which in turn makes its survival and reproduction more likely. This is when natural selection steps in: the mutation increases in successive generations, causing evolution.

Moalem introduces the fact that DNA is relatively unchangeable and that evolution is prompted only by small, random mutation. After all, much of his book has emphasized how the DNA of our ancestors, as much as 10,000 years ago, is still shaping our genome today—giving some credibility to the idea that "biology is destiny." Yet he articulates this idea as a jumping off point only to show how thinking and research on the topic has progressed and that this belief is actually antiquated.

More recently, scientists recognized that it would be unlikely for mutations to occur only randomly, because the ability to react to environmental changes and pass on adaptations would be selected for. Additionally, geneticists originally believed that every gene had a single purpose, which would suggest having more than 100,000 genes—but in reality, we only have about 25,000. Thus, genes must interact and shuffle to produce the proteins necessary for human life. Scientists now conceive of genes as "an intricate network of information" that can react to changing circumstances. If one gene fails, another gene can "pick up the slack." Thus, it is unlikely that small random mutations have led to our evolution, because other genes would simply compensate.

Here, Moalem provides a series of points to argue why it would be advantageous for genes to be more adaptable. Even though not all mutations are good, the mere ability *to spur those mutations for a chance of adapting more quickly in the face of environmental pressure would be very helpful in enabling our survival. Additionally, he gives some evidence that genes are already capable of adapting to new circumstances because they are able to respond to changes in the environment— or, as Moalem has noted before, of developing antibodies for new pathogens.*

Jean-Baptiste Lamarck, according to popular accounts, was the chief proponent of a theory called inherited acquired traits. The theory holds that traits acquired by a parent during their lifetime could be passed on to their offspring—like giraffes' necks stretching further and further with each generation to reach leaves on higher branches. According to history, Charles Darwin then proved Lamarck's theory incorrect with his theory of natural selection. Moalem writes that little of this story is true: Lamarck promoted inherited acquired traits, but he also believed in natural selection—and Darwin believed in both as well. The irony is that the theory of inherited acquired traits isn't completely wrong.

The theory of inherited acquired traits is often contrasted with Darwin's theory of natural selection, but Moalem makes a point of illustrating the ways in which the theory may not have been so off—genes might be more mutable than Darwin's theory supposes.

Barbara McClintock was a revolutionary thinker who was largely ignored by her peers. She received her Ph.D. in 1927 at age 25, and she focused the next 50 years of her career on research on corn genetics. McClintock discovered that in certain circumstances, particularly when the corn was stressed, whole sequences of DNA moved from one place to another and triggered significant changes in the genome. These were often caused by changes in the environment, and the "jumping genes" relocated to certain parts of the genome more often than to other parts. It seemed as though the corn was mutating intentionally rather than randomly.

McClintock's research provides the first tangible example of how an organism's genes can adapt at a much more rapid pace than previously thought. Not only that, but they can adapt during an organism's lifetime. This proves how organisms can be immediately impacted on a genetic level by changes in their environment—a concept vastly different from the idea that a change in environment can make certain adaptations more advantageous and passed down due to that fact. This implies, as indicated by the use of the words "active" and "intentional," that these adaptations are not passively selected for but are actively mutated.

Barbara McClintock's findings were largely faced with skepticism until 1983, at age 81, when she received the Nobel Prize. Her discoveries opened the door to the possibility of intentional mutation and much faster evolution. Scientists are still only beginning to understand how these jumping genes (transposons) work—sometimes they copy themselves and insert new material elsewhere, or sometimes they cut themselves out of their starting place and insert somewhere else. One study showed the enormity of the effect they can have: a jumping gene in one line of fruit flies gave them the ability to resist starvation, withstand high temperature, and have a 35 percent longer life expectancy.

The example of the fleas suggests that not only are jumping genes able to respond to environmental pressure (for example, a lack of food), but that these genes can also be passed down from one generation to the next. This gives credence to the inherited acquired traits theory for which Lamarck has historically been lambasted, and it also provides some evidence for the idea that adaptation can occur at a much more rapid rate than previously believed.

McClintock believed that these responses were caused by internal or environmental stress, spurring jumping genes to take a chance on mutating in hopes that they would get a mutation that might help. When that occurs, the proofreading mechanism is suppressed and adaptations are allowed. Today, scientists believe this notion that the genome is not as rigid as once thought, and that mutation is not simply random.

Moalem sums up McClintock's findings of jumping genes, suggesting that genes are not necessarily set in stone even after an organism is born, and that the immediate environment of an organism can have an effect on its genes and spur it to advantageous mutation.

In the 1980s and 1990s, researchers studied other organisms that exhibited the same jumping genes: *E. coli*, which appeared to target specific areas of its genome where mutations were likely to be advantageous—a process researchers called "hypermutation." When *E. coli* was placed in an environment with only lactose (which it could not digest), studies showed increased mutation in the bacteria's genome, and not just in an attempt to overcome lactose intolerance.

The example of E. coli *demonstrates that organisms are not simply spurring mutations that might help them overcome a particular environmental stress; rather, the jumping genes are shifting in a way that might allow them to develop* any *helpful mutation, providing evidence for the idea that jumping genes can lead to any number of adaptations. Additionally, the study of the* E. coli *illustrates how environmental factors are important in spurring those adaptations.*

Moalem transitions to how jumping genes can play into human evolution. In the 19th century, biologist August Weissman divided the body's cells into two categories: germ cells (egg and sperm cells) and somatic cells (all other kinds of cells). Weissman's theory, now known as the Weissman barrier, holds that information in somatic cells is never passed on to germ cells. Thus, a mutation in one's red blood cells would not be passed on to one's children—only a mutation in the germ line would be passed on. But new research suggests that this might not necessarily the case.

Again, Moalem introduces long-held scientific concepts so that he can illustrate how research and accepted science have progressed. Since the 19th century, conventional wisdom dictated that mutations that occurred during a person's life would not then be inherited by that person's offspring. However, as with the discovery of jumping genes, it's likely that there may be exceptions to the Weissman barrier theory.

Jumping genes are very active in the early stages of brain development, and Moalem posits that this may help create the variety and individuality that make every brain unique. This activity is only found in the brain because it benefits from individuality—the heart, by contrast, does not. The immune system also welcomes diversity, and scientists from Johns Hopkins have found that jumping genes may help us produce antibodies to develop protection against invaders. However, even if we develop antibodies, we can't pass them on to our children because of the Weissman barrier. Babies are born with a small number of antibodies, which is why breast milk (which contains some of the mother's antibodies) is important for babies.

The fact that jumping genes have helped us develop the individuality in our brains is significant, as it again suggests that our DNA (and even our intelligence) is not totally set in stone. Further, the diversity that jumping genes create in our immune system is evidence for why we can adapt so many antibodies, a puzzle that Moalem brought up at the beginning of the chapter.

There is now evidence that one-quarter of active (coding) human genes have incorporated DNA from jumping genes. The more we understand about how they work, "the more they may reveal about how our immune systems protect us against disease." Moalem also notes that as much as half of the "junk DNA" that was previously believed to be unhelpful is actually made up of jumping genes.

The fact that so much of our noncoding DNA is made up of jumping genes illustrates how important it may have been to evolution. Jumping genes would presumably have conferred an advantage to humans that adapted them because those humans were more likely to develop helpful mutations, and they were therefore better equipped to survive and reproduce.

Additionally, the jumping genes discovered in human DNA look a lot like virus DNA. A virus is essentially a small portion of genetic code that can't reproduce on its own—instead, viruses reproduce by infecting a host and using the hosts' cellular machinery to replicate. Retroviruses are a subset of viruses that are made of RNA (which usually acts as a messenger, copying instructions from DNA to create specific proteins). Retroviruses are able to reverse the process of DNA being copied to RNA, and they can write themselves into a person's DNA.

Retroviruses reinforce one of the ideas from Moalem's earlier chapters: that we are evolving alongside *viruses, not independent of them. More than that, viruses may be helping us to evolve from the inside, not only spurring our evolution from the outside, because jumping genes might have once been viral DNA and now enables us to adapt more rapidly.*

Retroviruses can thus write themselves into the DNA of cells in the germ line of an organism, and that organism's offspring is then born with the virus encoded in its DNA. If the virus is harmful, it is unlikely that offspring will survive. But if the virus is not harmful, the offspring can survive and reproduce, and the virus becomes a permanent part of the gene pool. Scientists know that at least 8 percent of the human genome is composed of helpful retroviruses. Viruses can help us because they are "master mutators" which can evolve incredibly fast and help us adapt.

Moalem demonstrates how viruses—and jumping genes—not only provide us with acquired mutations but can then enable us to pass on those mutations. Viruses have a vested interest in our survival, because that is how those viruses then continue to be passed on. Thus, this interspecies adaptation is mutually beneficial, because it might allow us to overcome all kinds of different environmental obstacles.

Moalem reiterates that jumping genes are probably descended from viruses, and these genes have helped us evolve into complex organisms much faster than we could have otherwise. Humans and African primates also share an interesting genetic trait: our genomes have been modified by a retrovirus in a way that makes it easier for us to be infected by other retroviruses. This capacity to support infection may have enabled us to evolve at a much faster rate, as exposure to other retroviruses could have facilitated more rapid mutation.

Again, Moalem emphasizes how having viruses and jumping genes as a part of our DNA has actually been incredibly beneficial to us—even suggesting that their involvement in our genome is what allowed us to evolve into humans in the first place. Thus, while Moalem has demonstrated how viruses can be harmful, they can clearly also help us adapt and survive.

CHAPTER 7: METHYL MADNESS: ROAD TO THE FINAL PHENOTYPE

As of 2007, one-third of American children (25 million kids) are overweight or obese. In the last 30 years, the percentage of obese 2- to 5-year-olds has doubled, and the percentage of obese 6- to 11-year-olds has tripled. This is partially due to the rising popularity of fast food, television, and video games—but it may not tell the whole story. There is emerging evidence that the dietary habits of women in the early stages of pregnancy may impact the metabolism of their children.

Moalem continues investigating the idea that DNA is not necessarily fixed and can be impacted during early stages of development. Here, Moalem suggests that although obesity is strongly correlated with environmental factors, there may also be a genetic component.

This is not to suggest that children inherit the weight problem of their parents. Rather, research in the new field of epigenetics suggests that certain chemical compounds can suppress the expression of specific genes—these compounds act like a "genetic light switch." Epigenetics is concerned with uncovering how children can inherit new traits despite their DNA remaining the same.

Epigenetics, like the concept of jumping genes, proves that one's genes are not necessarily fixed—or at least, that they do not tell the whole story. Even if someone has a gene, compounds can be added that prevent it from being expressed, which can result in stark changes to our bodies.

The first big breakthrough in epigenetics came in 2003, in a study at Duke University. Researchers bred mice with the *agouti* gene, which is characterized by obesity and a yellow coat. For generations, the mice were bred normally and had the same genetic information. Then, researchers separated pregnant *agouti* mice into two groups. In the control group, they gave the mice a regular diet, and their babies were also fat and yellow. In the experimental group, they fed the mice a variety of vitamin supplements. Their babies, by contrast, were thin and had a dark coat—but their genes had not changed.

This first experiment at Duke University provides proof for the theory of epigenetics. The only difference between the two groups of mice was the addition of vitamin supplements during pregnancy, and yet they had completely different appearances and even different states of health throughout their life—suggesting that DNA is not always fixed. This hints at the wide-ranging impact that the study of epigenetics could have on our future.

These groundbreaking results proved that one or more of the compounds in the vitamins "turned off" the *agouti* gene without changing the genes themselves—a process called methylation. One of the leaders of the study explained that maternal nutrition has long been considered important, but that this study illustrates exactly how maternal nutrition can impact how genes are expressed in the mother's offspring. Epigenetics erased the idea that genetics are set in stone. This wasn't completely surprising, as identical twins (who have the same DNA) are often very similar but don't always get the same diseases, nor do they have the same fingerprints.

The field of epigenetics has wide-ranging practical applications, though Moalem provides multiple caveats throughout the chapter explaining that we still don't fully understand which compounds turn on and off which genes. Yet by doing this kind of research, we may ultimately be able to identify the substances which help us, allowing us to live healthier and longer lives.

Researchers have also noted the ability of certain species to adapt to conditions based on the mother's experiences during pregnancy. For instance, depending on the time of year a mother vole will give birth, baby voles are born with a thick or thin coat. The offspring of the freshwater flea *Daphnia* will have a larger helmet and spines if the mother is in an environment crowded with predators. One species of lizard is born with either a large body and long tail or a small body and short tail, depending on whether the mother smelled a lizard-eating snake while pregnant.

The case studies of these animals prove how some animals have already adapted to use epigenetics naturally. Input from their surroundings during pregnancy directly leads them to have offspring with more advantageous conditions. This is quite different from environmental adaptations that have been passed down for thousands of years, as epigenetic adaptations can occur in a single generation.

These epigenetic adaptations are also present in humans and may be partially responsible for the increase in childhood obesity. A British medical professor named David Barker proposed that when mothers eat junk foods, which are low in nutrients, the embryo may receive signals that it will be born into a harsh, food-scarce environment. This can cause them to develop "thrifty" metabolisms that are more efficient at hoarding energy. Ten thousand years ago, this helped a baby survive, but in today's age, a child with a slower metabolism that is surrounded by calorie-rich, nutritionally-poor food will become overweight.

Epigenetics helps explain the rising rate of obesity, as Barker emphasizes the importance of maternal nutrition in the early stages of pregnancy. Yet this case study also reminds readers of Moalem's overarching thesis about diseases that were once advantageous when humans lived in extreme conditions. These "thrifty" metabolisms helped our ancestors overcome lack of food and enabled their survival. Now, however, that adaptation is a liability as the Western diet has shifted to food that is nutrient-poor but calorie-rich.

There is new intriguing evidence that fathers and grandmothers can pass epigenetic information onto their offspring as well. Men who smoked before puberty had sons who were significantly fatter by the time they were nine. The toxins from smoking indicated a difficult environment, resulting in an epigenetic change in their sperm. The same issue was not found in daughters, suggesting that these epigenetic markers are passed on the Y chromosome. In the case of grandmothers, when a human female is born, she already has the complete set of eggs she will have for life. Thus, our mother's eggs developed in the womb of our grandmother and may have been affected by epigenetic signals in our grandmother's environment as well.

This case study emphasizes that it is not only the diet of mothers that should be of concern—chemical signals can equally shape a father's sperm and affect his children as well. Epigenetic signals from grandmothers can similarly shape their daughters' eggs, thereby affecting their grandchildren's methylation patterns. Both of these cases demonstrate how a wide variety of sources and chemicals can change a child's genetic expression.

The researchers who studied the *agouti* mice believed that early nutrition can affect all genes, including the germ line. Therefore, traits that a parent or grandparent acquires can be inherited by future generations, which follows the theory attributed to Lamarck. Some researchers in epigenetics even call themselves "neo-Lamarckians."

Moalem returns to Lamarck to argue again that inherited acquired traits may not have been so incorrect, because changes in the germ line can then be passed on. Thus, the DNA of generations of offspring can be significantly affected by certain epigenetic signals during one organism's development.

Epigenetic changes can occur throughout life as well. Researchers studied baby rats that were given to different sets of mothers: one group that was standoffish, and one group that was nurturing. They found that babies who were given to the nurturing group grew up to be confident and relaxed, but babies that were ignored by their mothers grew to be nervous and stressed. This was not only due to "nurture" (i.e., the mothers' behavior), however. Babies that were groomed by their mothers showed a decrease in methyl markers around the genes involved in brain development because the mothers' attention triggered methyl markers that would have otherwise impeded the babies' developing brains. In this case, parental care changed how the babies' genes were expressed. Researchers believe it's likely that the same could happen in humans.

Here, Moalem illustrates two additional concepts about epigenetics that demonstrate the wide variety of conditions under which epigenetics can come into play. First, this example looks at rats after they have been born, rather than the other examples, all of which examine fetal development. Additionally, in this example, the methyl markers were stimulated not by any external chemical compound, but seemingly from the rats' own internal response to the mothers' care. This reinforces the idea that a wide variety of factors can change one's genes, even while developing at a very young age.

Methylation is not inherently good or bad—it depends on the gene being turned on or off. In some cases, methylation can suppress important genes, like in the story of identical twin girls, Elizabeth and Eleanor. The two were treated identically until their early twenties, when they moved apart. In 2000, Eleanor was diagnosed with breast cancer, while Elizabeth had the disease. After studying their genes, researchers showed how their methylation patterns diverged when they moved apart, leading only Eleanor to develop cancer.

The case of Elizabeth and Eleanor illustrates that epigenetic factors can continue to affect us throughout our lives, not just in early development. The fact that methylation can cause something as harmful as cancer highlights the importance of more research on epigenetics, isolating compounds that can negatively affect us in order to prevent this kind of reaction.

There is more evidence to support the idea that methylation is tied to cancer: there is a significant connection between breast cancer recurrence and the amount of methylation of a gene called *PITX2*. This information allows doctors to tailor patients' treatments based on their genes. Methylation of certain cancer-suppressing genes can also be an early warning sign, allowing doctors to measure one's risk.

The isolation of the PITX2 *gene, and the consequences that it can have for cancer treatment, again emphasize the importance of interdisciplinary science: geneticists and doctors can use their mutual knowledge to improve treatment outcomes for patients.*

Epigenetics is still an emerging field, and there is much about it that researchers still don't understand yet—including which genes are turned off by which methyl donors. It is important not to try to alter our genes with certain methyl donors, because we don't know what other genes may be affected by them. The first drug that tried to deliberately affect methylation patterns was called azacytidine, and it inhibited the methylation patterns of certain genes to try to prevent MDS—a collection of blood disorders. But six months after the drug was approved, the drugs were turning off as many genes as they were turning on.

Moalem concedes that there is danger in trying to use our knowledge of epigenetics to alter our genes, even for worthy causes like preventing disorders and diseases like cancer. But this only emphasizes the need for further research so that we can better understand how methylation interacts without genes—and so we can ultimately use that information to live healthier lives.

Moalem gives another example, illustrating how little we understand of epigenetics. In the months after 9/11, there was a dramatic spike in late-term miscarriages in California—but only in male fetuses. Moalem explains that we can only speculate as to why this might have happened. Males are more demanding on the mother's body during pregnancy and less likely to survive if malnourished. Perhaps, he writes, we have evolved a kind of system that is triggered in times of crisis: lots of females and a few strong males give a population better chance for survival than the other way around. There is also evidence that in times after conflict, more men are born, and that women who predicted that they would live into old age were more likely to have male babies.

Here, it is possible that we have adapted a response that is on its surface negative, in terms of triggering miscarriages—particularly because it appears to go directly against the natural imperative of survival and reproduction. But this response may ultimately have developed because it allowed for greater survival of the species as a whole. The final piece of evidence Moalem references also indicates that even something as simple as mindset can affect epigenetics.

The first big epigenetic breakthroughs were published as the Human Genome Project was completed, which mapped out the 3 billion nucleotide pairs that make up our DNA. But epigenetics proves that this road map is only a starting point, because epigenetics tells us "which roads are open and which roads are closed." Thus, the Human Epigenome Project identified the chemical changes and relationships that determine how DNA will function, as well as uncovering how environment can impact human health.

The Human Epigenome Project reveals the need for more research: it is not enough to map out the human genome because, as Moalem has illustrated throughout this chapter, our biological code is not completely set in stone, and the way those genes are expressed can allow for a great deal of adaptation.

CHAPTER 8: THAT'S LIFE: WHY YOU AND YOUR IPOD MUST DIE

At 12 years old, Seth Cook is the oldest living American with a rare genetic disorder called progeria, in which children age at a rate of 10 times the speed of people without it. By the time a baby with progeria is about a year and a half old, their skin starts to wrinkle, their hair starts to fall out, and they develop cardiovascular problems and degenerative diseases. Most people who have progeria die in their teens.

Given the other diseases that Moalem has referenced, the reader can reasonably assume that despite progeria's obviously harmful effects, the aging process may actually help us survive in the short term despite hurting us in the long term.

In April 2003, researchers isolated the genetic mutation that causes progeria: a defect in a protein called lamin A that provides structural support for cells. With the mutation, cells deteriorate much more rapidly. In 2006, another team of researchers connected lamin A to normal human aging. The implications of this are significant, as it provides some clue as to why aging occurs. Scientists continue to debate what causes aging: whether it is wear and tear over the years or a product of evolution. Progeria suggests that aging is preprogrammed.

The fact that aging may be preprogrammed into all of our genome suggests that every person is subject to the kind of evolutionary tradeoffs that Moalem describes, not simply those with hemochromatosis or diabetes. Thus, we are all subject to evolutionary adaptations that give us some protection earlier in our lives, even if they are detrimental later.

In the 1960s, Scientist Leonard Hayflick discovered in that cells can only divide a fixed number of times (52 to 60 times) before the cell division becomes an issue (known as the Hayflick limit). Every time a cell reproduces it loses DNA; in order to prevent the loss of important information, chromosomes have extra inconsequential DNA at their tips (called telomeres) so that they do not lose essential information. After that fixed number of times, cells start to lose more important DNA. But this limit serves an evolutionary purpose: it guards against cancer.

Aging serves as another example of a condition that is preprogrammed into our genes which offers us a short-term benefit because it serves as a safeguard against cancer, but it becomes more of a liability the older we get. Aging thus illustrates how we can develop a defense system even against conditions within our own bodies.

Cancer is a family of diseases characterized by uncontrollable cell division and growth. There are many lines of defense in the body against cancer, including the Hayflick limit. However, cancer cells have developed an enzyme called telomerase, which can lengthen the telomeres at the ends of chromosomes, so that there's less loss of genetic information and cells can reproduce forever.

Even though cancer is not exactly another living thing, it, too, has learned to adapt against our own DNA regulation systems much in the way that viruses, bacteria, and other invaders have found their own ways to adapt to our defenses.

There are other evolutionary explanations for aging mechanisms: the Hayflick limit doesn't explain why different animals have vastly different life expectancies. Moalem notes that in mammals, there's a close correlation between size and life expectancy in different species. This is likely because a species with a greater risk of being eaten or greater environmental threats faces evolutionary pressure begin reproducing at an earlier age so that future generations mature faster. A shorter lifespan also allows species to evolve faster, because there is a shorter length of time between generations.

Moalem demonstrates other ways in which aging, and the shorter lifespan that comes with it, can actually confer an evolutionary advantage upon certain species. In smaller species, it provides a greater chance for reproduction before being eaten by a predator and enables quicker adaptation. Thus, even though it seems like a disadvantage, it can actually help the species as a whole survive.

Moalem writes that programmed aging confers an evolutionary benefit on the species, like a biological version of planned obsolescence. He compares humans to **iPods**, which some people accused Apple of designing with planned obsolescence, so that the batteries would only last about 18 months. Similarly, by clearing out older models of humans, aging can make room for new models. Aging can also protect the group by removing individuals who are more likely to have diseases. Reproduction, by contrast, is how species are upgraded.

Moalem's comparison of humans to iPods illustrates how aging can be both beneficial and damaging. It is damaging on an individual level, because each individual has a shorter lifespan. It is beneficial on a species level, however, because each successive generation can improve on the last and live a healthier or longer life.

The prospect of programmed aging opens a door to possibilities like learning how to inhibit telomerase in cancer cells so that they cannot reproduce indefinitely—or to rebuild lamin A so that aging in people with progeria (or even people without it) might be reversed.

The importance of research is again emphasized, as learning about progeria or how cancer cells function can benefit the study of the other. Research allows us to develop ways to both counter these diseases and perhaps to lengthen the lives of people on a larger scale.

Moalem next explores how humans have evolved to give birth in the way that they do. Childbirth in humans is riskier, longer, and more painful than in our genetic cousins. This is due primarily to two factors: humans have large brains, and humans are bipedal. The fact that we have evolved to walk on two feet has made the pelvis more narrow, and the fact that we have evolved to have bigger brains makes it more difficult to squeeze through a mother's pelvis. Because the human birth canal isn't one constant shape, fetuses also have to twist their way through it and usually face away from the mother, which makes it difficult to give birth without assistance.

Moalem illustrates how the way in which humans give birth also comes with an evolutionary compromise that our ancestors adapted over time. Because having a large brain and being able to walk on two feet conferred so much of an evolutionary advantage to humans, these developments overcame the relative additional risk of making it harder for women to give birth.

Moalem then examines our evolution into humans as a whole: where once we were furry and walked on all fours, we gradually lost our hair and walked upright. The conventional theory on how this happened is called the "savannah hypothesis," which holds that prehumans moved out of the forest and into the savannah, perhaps because of environmental change. They had to find a new way to get food, leading them to start hunting. This led our ancestors to walk upright so they could scan the horizon for food, and cover long distances between food and water. They also developed tools and cooperation to do so, leading to bigger brains—and because the savannah was hot, they lost their hair.

The savannah hypothesis is another example of the way in which our genetics have been shaped by our environment. When humans moved out of the forest, instead of simply finding food to eat, they started to develop hunting. This, in turn, spurred their evolution to walk upright, develop larger brains, and lose their hair.

Writer Elaine Morgan became interested in evolution in the 1970s. When she read books on the savannah hypothesis, she became skeptical that only male humans would spur evolutionary adaptation. Morgan wrote a non-scientific book called *The Descent of Woman* in 1972 which refuted the savannah hypothesis. She simply argued that humans would not have walked upright in order to cover distances faster, as most things that walk on four legs can outrun us. There also aren't any other hairless animals in the savannah, debunking the idea that we lost our hair because of the heat.

The savannah hypothesis is still widely accepted by anthropologists. The controversy over Morgan's books, then, is likely fueled by the fact that they're not fully backed by research—this indicates that more research is required if the scientific community is to be swayed away from the savannah hypothesis.

Morgan came across the work of marine biologist Alister Hardy, who proposed a theory called the "aquatic ape" hypothesis, suggesting that a band of woodland apes became isolated on an island and adapted to the water. He noted that like marine animals, humans have no hair, and we have fat attached to our skin (unlike other land mammals). He proposed the only reason for humans to share these traits with hippos, sea lions, and whales would have been "an aquatic or semiaquatic past."

The aquatic ape theory, like the savannah hypothesis, also demonstrates how the environment serves as the determining factor in our evolution. In either case, our genes have clearly been greatly affected by the environment of our ancestors.

Very few people took Hardy seriously until Elaine Morgan, who built a compelling case on top of his theory. She theorized that for a long time, our prehuman ancestors spent time in and around the water, which helped them survive both on land and water. The water helped them evolve toward bipedalism, as standing upright enabled them to swim farther out and still breathe, and the water helped to support their upper bodies. It explains why we lost our fur, why we have fat, and why we have down-facing nostrils, which allowed us to dive.

Elaine Morgan even builds on the proposals of Alister Hardy, illustrating even more ways in which an aquatic environment would have changed the development of our ability to walk upright and why we might have developed noses with downward-facing nostrils. The theory again highlights the importance that the environment can play into our development.

Moalem returns to the idea of birth, to add his own contribution to the aquatic ape hypothesis. He examines water births, noting that for a long time, people believed water birthing was dangerous, with risks of infection and drowning. But according to an Italian study published in 2005, there is no increase in the rate of infection in mothers or newborns. Babies don't breathe until they feel air on their face, mitigating the fear of drowning and also protecting them from inhaling fecal matter or "birthing residue" that can cause an infection in their lungs during conventional deliveries.

Moalem ties the idea of birth, which he introduced earlier in the chapter, into the discussion of evolution. He illustrates how the environment in the aquatic ape hypothesis might also have been a factor in the way in which humans evolved to give birth. As he demonstrates here, it is just as safe (if not safer) to give birth in water, and thus it provides some clues that water might have played some part in our development.

Additionally, first-time mothers delivering in water have much shorter first stages of labor and need fewer episiotomies. The process may also be less painful: only 5 percent of women asked for an epidural in water births, compared to 66 percent of women giving birth conventionally. These results offer another suggestion that the aquatic ape theory might be correct, particularly because babies reflexively hold their breath and make movements that propel them through the water—a surprising instinct for an animal if it did not evolve around the water.

Even information about a field as different as water births can possibly provide clues into our evolutionary past. Thus, the research on water births that Moalem cites here serves as another example of the importance of interdisciplinary research and how it can help develop science in a variety of fields.

Moalem explains that his book is all about questions: the first being "Why?" and the second being "What can we do with that?" Moalem suggests that this curiosity has already led us to develop new ways to combat infection by limiting bacterial access to iron, or to open up new avenues of research through animals like the wood frog, or help us put pressure on infectious agents to evolve away from virulence. He explains that if we don't ask questions, we'll never find out what we could have discovered.

Moalem returns to the idea that asking questions and promoting curiosity can lead to new avenues of research and new helpful discoveries. As he has argued throughout the book, only by understanding where we have come from can we understand how evolution is affecting us today and what we might be able to do with that knowledge going forward.

CONCLUSION

Moalem concludes that he hopes readers come away with an appreciation of three things: that life is constantly being created and recreated, that everything is interrelated, and that humans have a surprisingly complex relationship with disease. He notes that we should appreciate our health and life itself. Moalem emphasizes that we should have reverence for how beautiful and intricate life on Earth is. He finishes by saying that the more we learn about this complex development of life, the more it looks like a miracle: "the miracle of evolution."

Moalem ends his book by summarizing some of its key ideas: first, that we are constantly evolving and adapting, spurred by the imperatives of surviving and reproducing. Second, that our genes are shaped by the world around us, including the environment and other organisms. And third, that disease can play a surprising role in our evolution—and only by understanding its tradeoffs can we learn more about how to shape our health in the future.

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