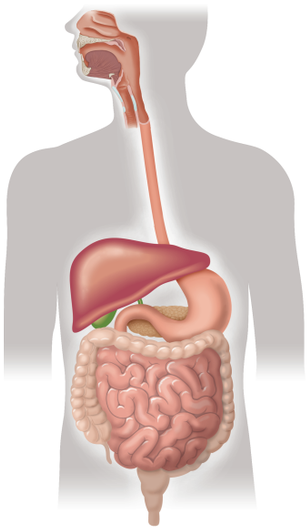
We should now introduce ideas from Darwinian biology into medicine



22

Darwinian Medicine

Two hundred years ago, the practice of medicine was dangerous to the health of the patient. Physicians had very few tools to treat contagious disease. The septic conditions of surgery ensured that those who could not afford new instruments and clean bedding had a high likelihood of dying. Physicians also deliberately bled their patients, based on archaic and ill-founded notions about human physiology.

Some time after 1900, things changed. Going to the doctor actually increased your chances of survival. A revolution in medicine was under way, a revolution that has had cumulative benefits for human survival.

This revolution was brought about by the application of modern science, especially modern biology, to the problems of medicine. Microbiology, genetics, immunology, neurobiology, and organic chemistry are just some of the basic sciences that have helped to build an effective medicine. Much of modern biology has contributed to the development of a newly benign and efficacious medicine.

But some biological fields have contributed little to contemporary medicine, specifically the fields that derive from Darwinian thought. Evolutionary biology and ecology are generally excluded from the practice and teaching of medicine, with only a handful of exceptions. When medical school faculty and practicing physicians do use Darwinian ideas, they are more often based on outmoded evolutionary or ecological ideas from the nineteenth century, or simply illogical.

But some modern-day evolutionary biologists and ecologists, such as **George C. Williams, Randolph Nesse,** and Paul Ewald, have rejected this medical tradition. Instead, they take it as their business to introduce modern Darwinian analysis into medicine. Whether dealing with human deformity, contagious disease, aging, or brain disorders, modern Darwinians are making a strong case that their fields should contribute to the improvement of contemporary medicine. ❖

HUMAN IMPERFECTION

22.1 Some of our medical problems arise from our evolutionary history

Many medical problems arise from basic features of the human body. Death by drowning, for example, happens because we cannot efficiently extract oxygen from water. Such deaths do not require a pathogen, extreme age, or psychiatric delusion. They happen because of built-in limits to the human form, imperfections. There are two kinds of human imperfection: universal and idiosyncratic. The first kind of imperfection comes from evolutionary history. We evolved as land-dwelling animals with skeletons on the insides of our bodies. We cannot fly using our own limbs. We cannot make food from the sunlight that hits our skin. We are limited, or imperfect, in ways that are shared by all members of our species.

Idiosyncratic human imperfection is due to variation within our species. Some individuals are born with metabolic defects. Hemophiliacs, for example, have poor blood-clotting function. Minor injuries can cause them to bleed to death. (We will consider this type of imperfection in the next module.)

In many ways, physicians are practicing evolutionary biologists and ecologists, although they usually do not know it. A lot of the problems that they deal with arise from our evolutionary history and our ecology.

One problem with our evolutionary history is that we evolved over hundreds of millions of years from an ancestral aquatic chordate. Although we have some fossils of possible ancestors from about 500 million years ago, there is a modern-day species that is apparently much like them: *Amphioxus*. *Amphioxus* has very simple anatomy. Water flows in through the mouth, supplying food particles that are collected by the gills. The **pharynx** functions as the front end of the digestive tract. There are no specialized organs for respiration (see Figure 22.1A).

But humans cannot just push materials through the pharynx, willy-nilly. We deal with multiple kinds of materials: solid, liquid, and air. And we have very different destinations for these substances: air to the lungs, solids and liquids to the stomach.

We have adaptations for processing these substances differently. We chew solids and then swallow. While we swallow, a membrane called the **epiglottis** closes off the entry to our lungs, the **trachea**. We have nostrils that enable us to take in air even when we are chewing our food and are polite enough to keep our mouths shut (all this is shown in Figure 22.1B).

But it often happens that some food gets lodged in the trachea. Then we cough, to clear the obstruction. Sometimes

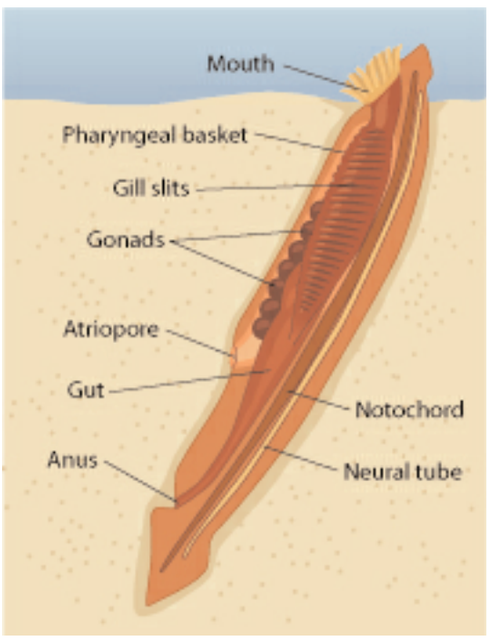


FIGURE 22.1A **Anatomy of *Amphioxus***

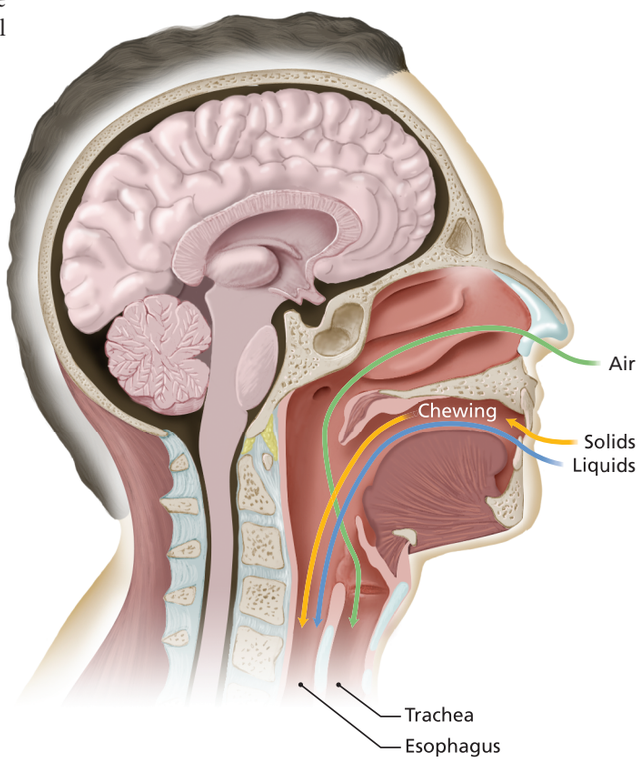
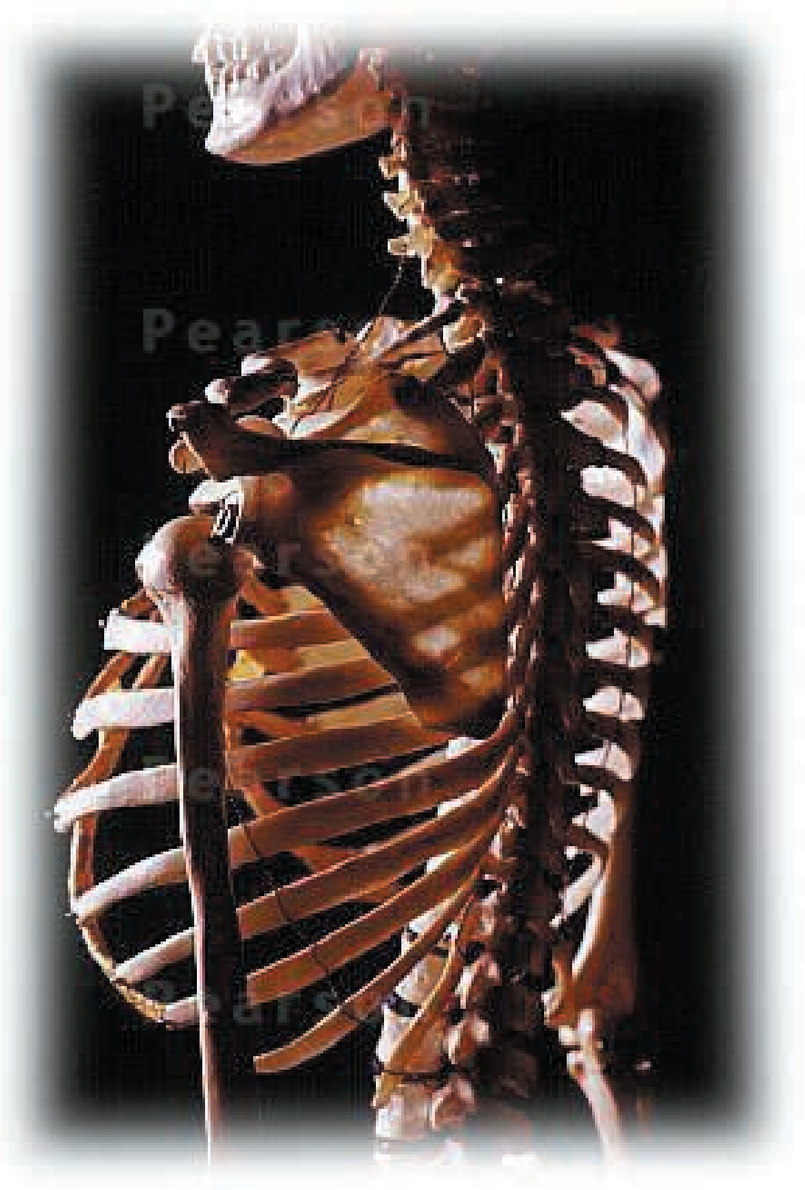


FIGURE 22.1B **Cross Section of a Human Head, Showing Our Pharyngeal Anatomy**

coughing does not work. If there is complete obstruction of the trachea, we **choke** to death. This is death by evolutionary history. We could have had respiration separated from food ingestion. Insects, for example, breathe using passageways distributed over the body, with many openings. They cannot choke. They can have their breathing blocked when their body surface is fouled. They can have their guts obstructed by small pieces of rock and other hard materials. But these two problems have nothing to do with each other. In mammals, with our evolutionary ancestry as a small aquatic animal, too many passages meet at the pharynx: nasal passages, mouth, esophagous, and trachea. So we choke. It should be noted that horses can drink and breathe at the same time. Horses are apparently ahead of us, evolutionarily.

Our pharyngeal structure is just one example of a universal human imperfection. Another is the spine. Most mammals are quadrupeds. The body is hung on the spine, with additional support coming from the pectoral and pelvic "girdles." The spine is only rarely stacked vertically, even in other primates. But humans are upright bipeds, forcing the spine to play a major structural role in keeping us vertical. Vertebrae are little suited to this anatomical task, so humans have chronic problems with posture, vertebral degeneration, and back pain. If you are too young to have experienced these medical problems, you are almost certain to do so as you get older.

A significant part of the future of medicine will consist of remedies for problems that have been bequeathed to us by our evolutionary history.



22.2 Genetic diseases are extreme forms of human imperfection generated by rare genotypes

The foremost examples of idiosyncratic human imperfection are the genetic diseases. Some individuals get genetic diseases. Most do not. **Genetic diseases** are disorders that occur in virtually all individuals that bear a particular genotype at a single locus. These diseases were already introduced in Chapter 4, because they are usually targets of purifying selection.

Although these diseases are not common, they absorb a substantial amount of medical resources and attention. Patients with disorders like cystic fibrosis and Tay-Sachs disease spend a large fraction of their lives receiving medical treatment. In the case of cystic fibrosis, this medical care has greatly extended patients' lives.

In the case of **phenylketonuria** (**PKU**), immediate medical care of the afflicted can largely treat the underlying condition. Specifically, dietary changes that eliminate **phenylalanine** from the patient's food prevent toxic buildup of phenylalanine. Even though PKU is a genetic disease with severe consequences when untreated, it has a simple, effective treatment. This particular medical disorder brings out a very general point about medicine: Medical problems have their roots in biochemistry, anatomy, and other features of the human organism. The cause of a disease, whether genetic or environmental, does not absolutely prevent or allow effective treatment.

Whatever their prospects for treatment, the underlying origins of genetic diseases are interesting for medical practice and evolutionary understanding. There are two main theories explaining these origins.

The first theory is that genetic diseases are produced by recurrent mutations of no benefit. These mutations frequently may be recessive, in which case the genotype that produces the disease is homozygous for a pathological mutant gene. But some disorders are caused by dominant alleles. Huntington's disease has this pattern of inheritance. For highly deleterious dominant alleles, such as those that cause childhood progeria—a disorder that is always fatal before reproductive maturity—only newly occurring mutations cause disease. Purifying selection eliminates these dominant alleles before the start of the next generation. Figure 22.2A shows the genetic and selection mechanisms that shape the incidence of genetic diseases caused by deleterious alleles.

The second main theory is that some genetic diseases have deleterious effects in homozygous combinations of alleles,

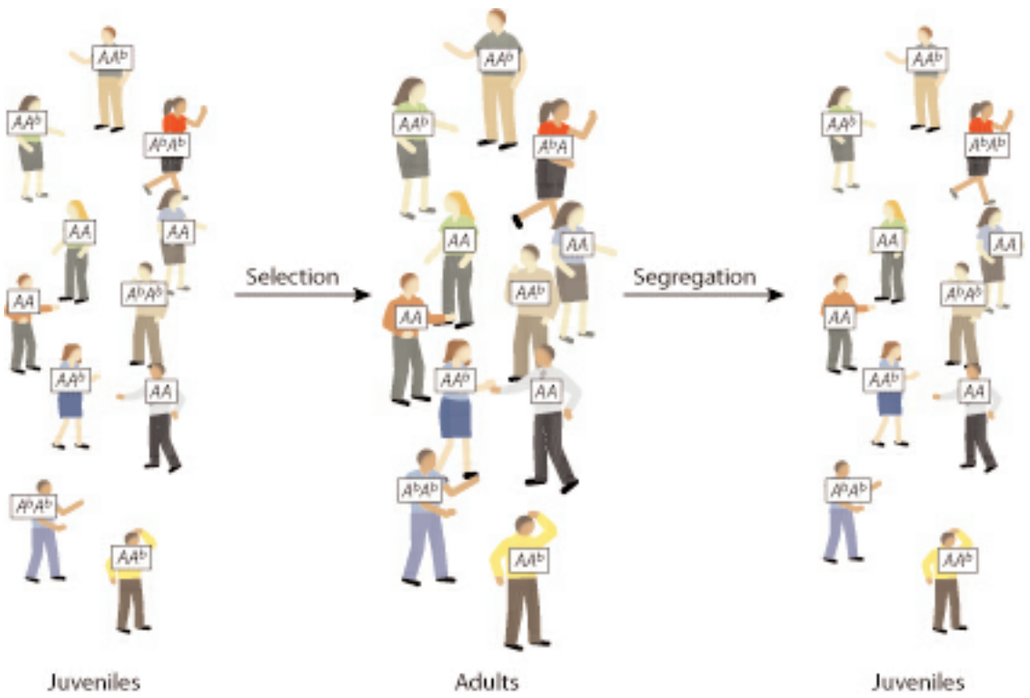


FIGURE 22.2A Genetic Diseases Caused by Recurrent Mutation Mutation adds individuals with alleles that cause genetic disorders, while selection removes individuals with these genetic disorders. Because mutations recur, selection never eliminates the genetic disease from the population.

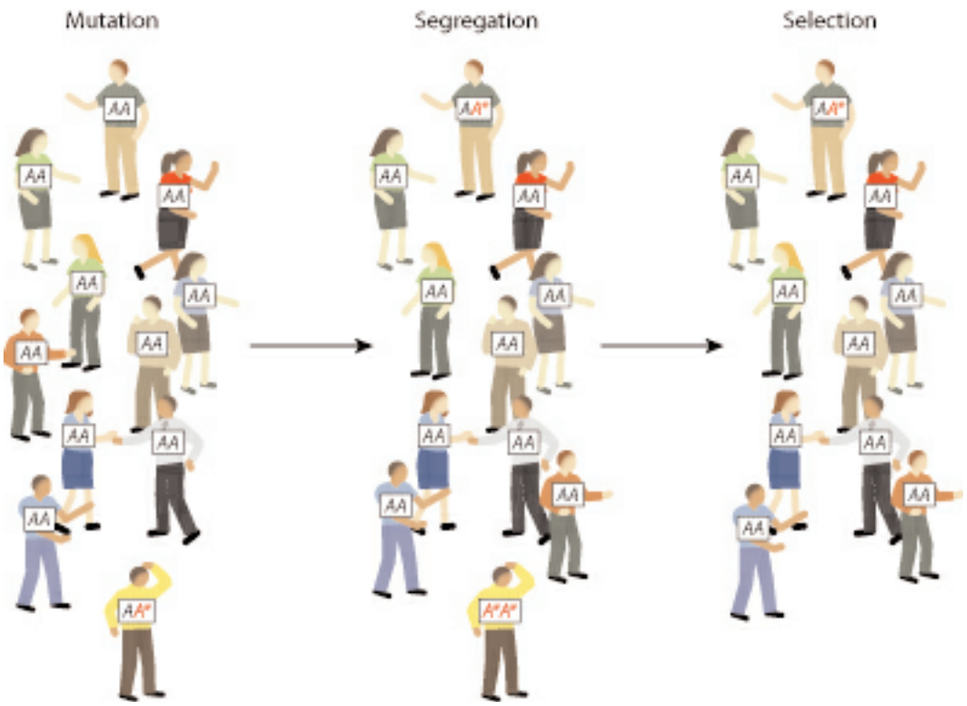


FIGURE 22.2B Genetic Diseases Caused by Selection The disease is caused by homozygosity for an allele (A*) that is beneficial in heterozygotes. Selection eliminates many of the homozygotes, but the heterozygotes generate more homozygotes with the genetic disease by segregation.

but are beneficial in heterozygous form. The type specimen for such disorders is sickle-cell anemia, a biological phenomenon that is an example of heterozygote advantage, as described in Chapter 4. In regions with active malaria outbreaks, the allele that causes red blood cell sickling appears to reduce the rate of malarial infection. The heterozygote is the genotype with greatest fitness, because it is resistant to malaria, but its level of sickling is minor. Figure 22.2B shows how this kind of genetic disease is evolutionarily maintained in human populations.

Evolution of Medical Disorders

It is counterintuitive for genetic diseases to exist at all. Natural selection is intuitively expected to prevent bad things with genetic causes. The problem is that while natural selection acts on individuals and their reproduction, its effect on single individuals is not always benign. Only its average effect on the individuals in a population is benign. Natural selection, as shown in Chapter 4, tends to increase the average individual fitness over the whole population. It may achieve this end by moving gene frequencies to values at which some individuals suffer medical harm.

Evolution is not a process guaranteeing benefits to all individuals. Natural selection does not take care of us. Individuals who have severe sickle-cell anemia are produced by natural selection in areas with malaria.

In addition, mutation will always occur. We have no prospect of forever eliminating mutations. Although many mutations have little effect on the human phenotype, other mutations have catastrophic effects. These mutations will produce genetic diseases.

22.3 From an evolutionary perspective, germline engineering is not usually a good idea

The specter of genetic diseases raises the equally dramatic possibility of using molecular technology to engineer the genes that are passed to offspring. **Germline engineering** can be defined as altering the genetic information passed from one generation to the next. In its simplest, most powerful, form, germline engineering might take all individuals who carry a genetic disease allele and eliminate that allele. How this might be done will depend on molecular technology. The technological details are not of concern here. Let us suppose that we have the technology to eliminate gametes bearing particular alleles. Figure 22.3A shows how germline engineering might work.

But we have a more important problem to solve. Is this a good idea? If we could engineer the germline of the human species, should we? Many religions and political ideologies specifically proscribe such acts. The Roman Catholic Church is profoundly opposed to tampering with our hereditary nature. European Greens have a political ideology that similarly is opposed to such interventions. But then there are religions and political movements, like the eugenicists of the 1930s and the present-day extropians, who very much favor such interventions. Therefore, it is not adequate to evaluate germline engineering by simply asserting that it's wrong. For some people, it is profoundly right.

Evolutionary biology and ecology supply useful information for this debate, but not because they can tell us what is right or wrong. There is no concept of the "natural" that can be imported into medical practice from Darwinian biology to tell us what is right or wrong. Indeed, the very idea of "nature" is almost the opposite of the implications of Darwinian biology, which reveals vast amounts of genetic variation within species. There is no specific human nature to conserve.

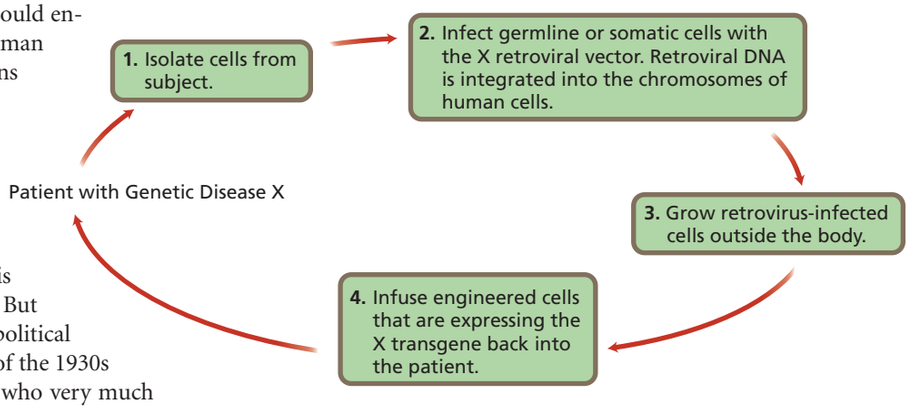
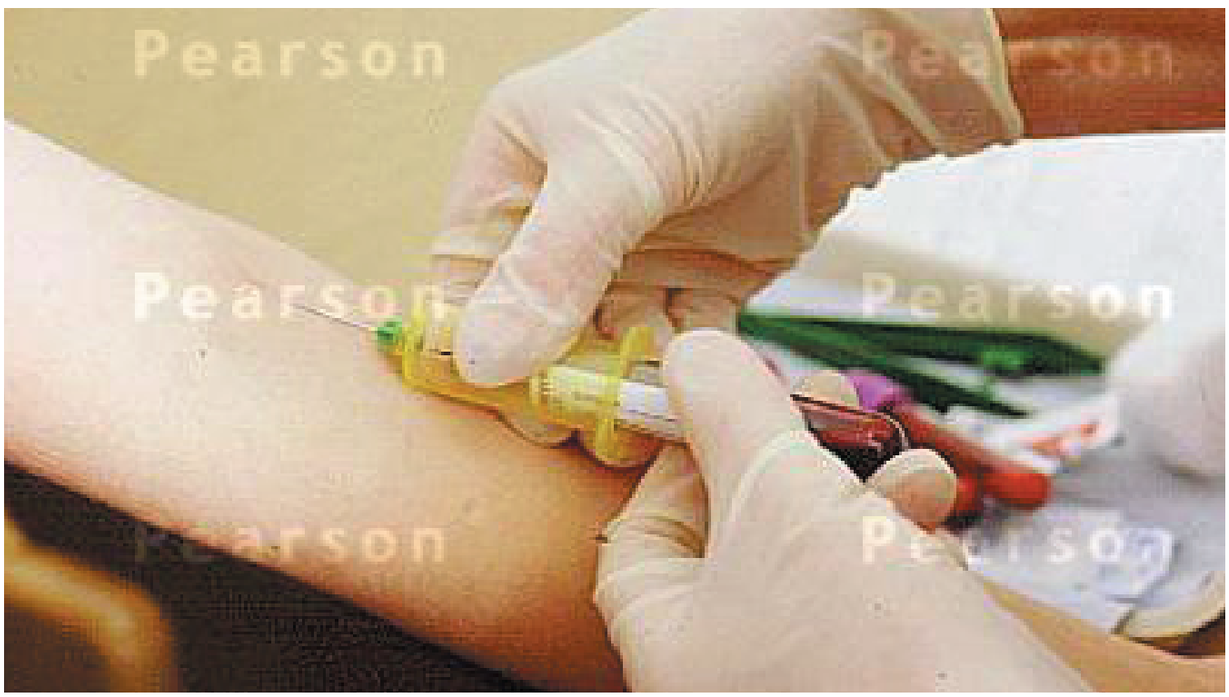


FIGURE 22.3A How Genetic Engineering Works



Darwinian biology can contribute two important matters of fact, which need to be considered in any germline engineering project. The first of these is that changing the germline constrains our descendants to our present level of knowledge. Suppose that germline engineers find a genetic substitution that reduces immunological problems like allergies and autoimmune diseases. This genetic change is unlikely to completely solve these problems, so we would hope to have better molecular genetic solutions for immune diseases in the future. The problem is that past rounds of germline engineering will have to be undone in future germline engineering. Even if this can be done at all, which is open to doubt, it adds a step that might go wrong.

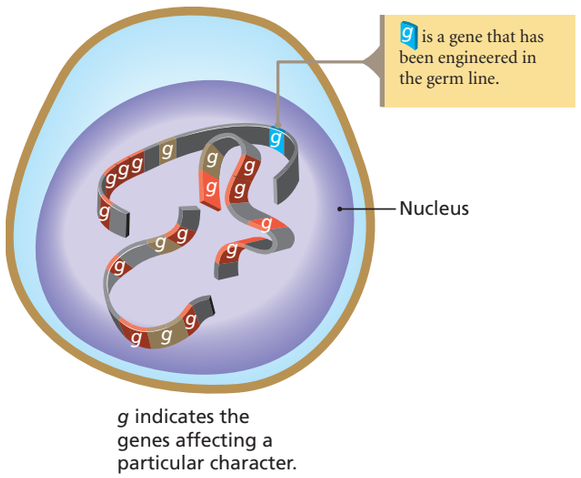
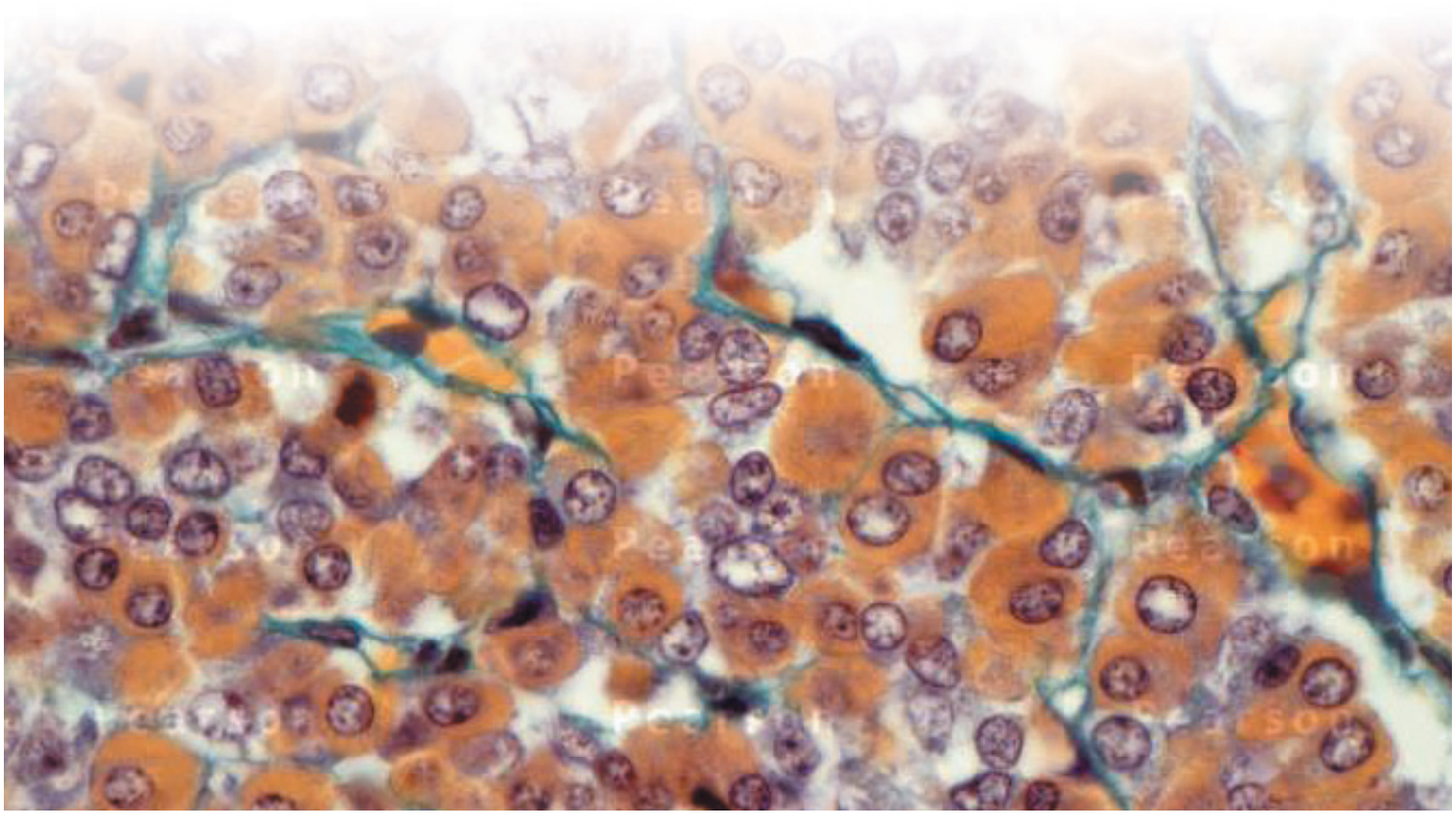


FIGURE 22.3B Many genes are likely to be unaffected by a single manipulation of the germline, and many of the unaffected genes will affect the medical problem.

The second important fact about germline engineering is that it is an engineering solution, based on molecular genetic knowledge. Natural evolution in real ecological settings, on the other hand, is an open-ended process incorporating alleles with beneficial effects that depend on the particular environment, whether we understand these beneficial effects or not. Germline engineering is likely to manipulate a small number of DNA sequences at a time, while natural evolution may act on hundreds of loci simultaneously. This contrast is illustrated in Figure 22.3B. In this sense, natural evolution has an inherent superiority in the volume of genetic information that it can sift.

There may be a few cases in which none of these technical problems will limit the success of germline engineering. One such case would be the removal of overwhelmingly deleterious alleles. But the evolutionary and ecological issues indicate that germline engineering may be subject to major problems and limitations, leaving aside any ethical or religious argument against its use. ❖



22.4 Somatic engineering is less problematic than germline engineering

The term *genetic engineering* usually does not refer to germline engineering. Instead, it refers to molecular reengineering of somatic cells. For example, the artificial incorporation of a normal copy of a gene that is missing in the patient is used to produce a protein that is vital to metabolism *in that patient*.

Considerable progress has been made with **somatic engineering** to treat **adenosine deaminase (ADA) deficiency**, shown in Figure 22.4A. Lack of the ADA enzyme causes some incidental abnormalities, but its most important effect is to undermine immune response. Patients with this disorder are less resistant to viral, bacterial, and other infections, which greatly shortens their lives. Somatic gene therapy for this disorder has been successful in some cases. One method is to take cells from the patient's immune system and culture them under glass in the laboratory. The cultured cells are infected with a virus bearing the normal *ADA* gene. Once the cultured cells have been infected with this virus and have successfully incorporated the *ADA* gene into the cellular genome, the cultured cells are reintroduced to the patient's body, as shown in Figure 22.4A. This procedure has been done clinically with success, and the treated patients have retained immune function since the somatic introduction of the *ADA* gene.

Although this type of therapy changes the DNA of patient cells, it is not evolutionarily different from providing insulin by injection to control hereditary diabetes. In either case, a molecular intervention saves a life; but it does not alter the gametes of the patient, thus leaving their children unchanged genetically. But this does not mean that such somatic therapy has no effect on evolution.

The profound point for evolutionary biology is that patients with genetic diseases get to have children at all. Because they do get to live long enough to have children, any genetic deficiency that predisposes them to their disease will be transmitted by them to the next generation, if they reproduce. Patently, such medical intervention will change the genetic future of the human species. For some individuals, this is a hot ethical issue. They are opposed to such effects on the genetic future of the species. The Nazis, for example, were opposed to saving the lives of people *they* regarded as hereditarily unfit—such as mentally retarded children, homosexuals, gypsies, and Jews. Being systematic about their concern, the

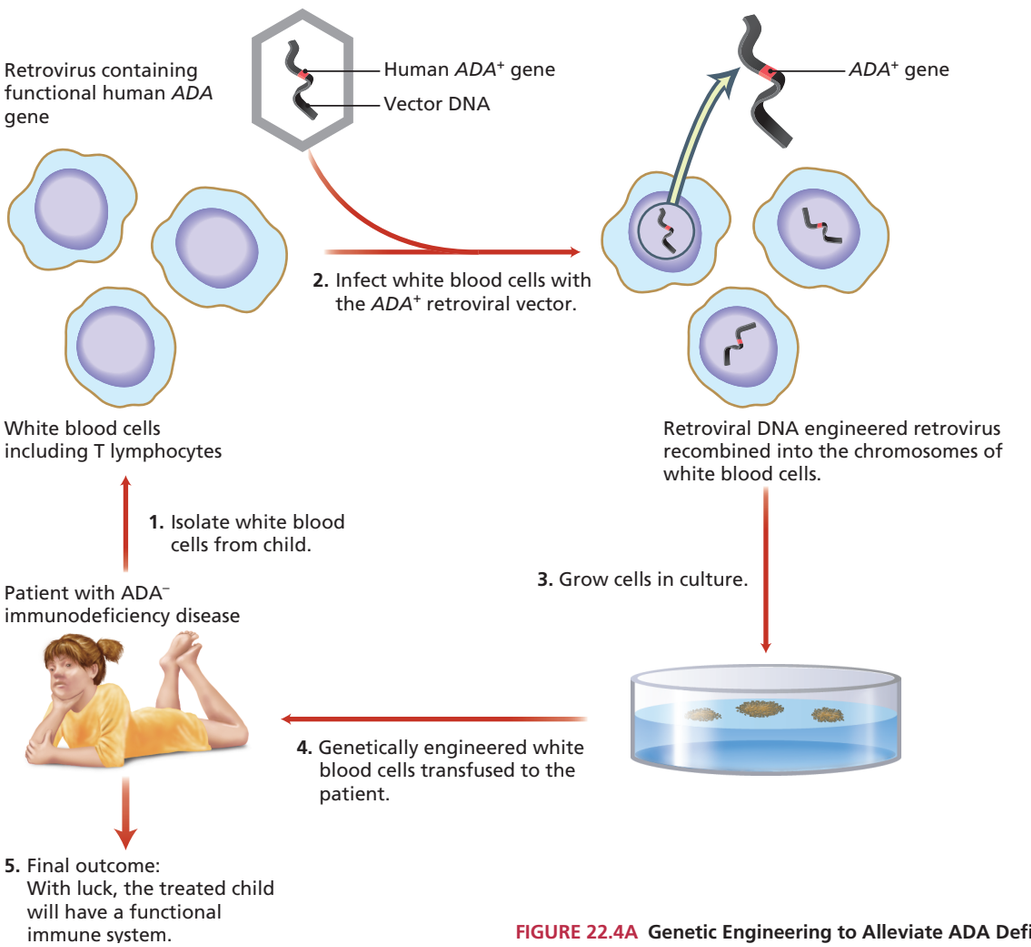


FIGURE 22.4A Genetic Engineering to Alleviate ADA Deficiency

Nazis killed members of these groups. Other groups, such as the Roman Catholic Church, are opposed to tampering with our genetic future, regardless of the imperfections that are transmitted to the next generation.

To put this controversy into better focus, recall that a vast range of medical problems are influenced by genetic vulnerability—from nearsightedness to cardiovascular disease to cancer. All of these problems have some genetic component. Medical interventions from optometry to open-heart surgery help people survive; people who might otherwise never have had children instead have children who inherit a greater genetic susceptibility to these diseases. Virtually every human alive today carries genes that might incline their children to one medical disorder or another. Purifying the human species by eliminating the medically unfit, or merely denying medical care, is not feasible. Even if we wanted to create a genetically purified human species—and many of us do not want to—the project is illusory. Almost all of us would have to be killed or sterilized. This would then leave the genetically ideal survivors with a small population size, resulting in inbreeding. Over time, deleterious mutations would arise and accumulate in the tiny population of "supermen," making further rounds of eugenic cleansing necessary. There is no escaping genetic imperfection in humans.

Contagious Disease

22.5 Human diseases are shaped by long-term evolution and global ecology

The treatment of contagious disease was one of the great successes of twentieth-century medicine, especially thanks to antibiotics and **vaccines**. It is easy to think of such figures as Pasteur, Fleming, and Florey as heroes because of their discoveries concerning the biology and prevention of contagious disease. Their work has saved millions of lives. But contagious disease is also singularly important as a Darwinian arena, where evolution, ecology, and medicine meet in the determination of the survival or death of medical patients.

Although it is natural to focus on acute contagious diseases, recent medical research has shown that many chronic diseases are caused by unsuspected pathogens. Just one example of this is that many stomach ulcers are now known to be produced by infection with the bacterium *Helicobacter pylori*—contrary to prior medical dogma, which did not imagine that a contagious disease was involved in ulcers. **Paul Ewald** has proposed that numerous chronic diseases, such as Alzheimer's disease, are products of our ecology rather than our genetics. Time will tell.

In many cases, the relationship between parasites and their hosts is one that is ripe for coevolution, as described in Chapter 14. The most important reason to expect coevolution is the dependence of the parasite on the host for the completion of its life cycle, and the possible death of the host from the parasitic infection. Together, these life-or-death possibilities will make natural selection intense.

Humans have coevolved with a number of diseases. One of the best examples of such coevolution is the **smallpox** virus. In seventeenth-century Europe and elsewhere well into the twentieth century, smallpox was a common cause of death. In addition, smallpox caused scarring and, in some cases, blindness, providing the victim survived. But the smallpox virus had no alternative host to humans. This high degree of specialization made it possible to eradicate the disease through the use of vaccines. The only remaining threat of a smallpox outbreak comes from germ warfare stockpiles. Figure 22.5A shows a smallpox victim.

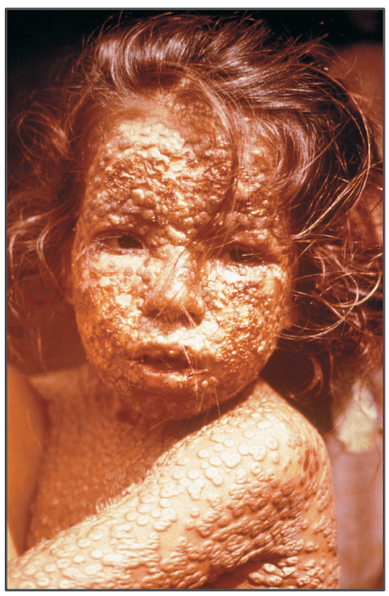
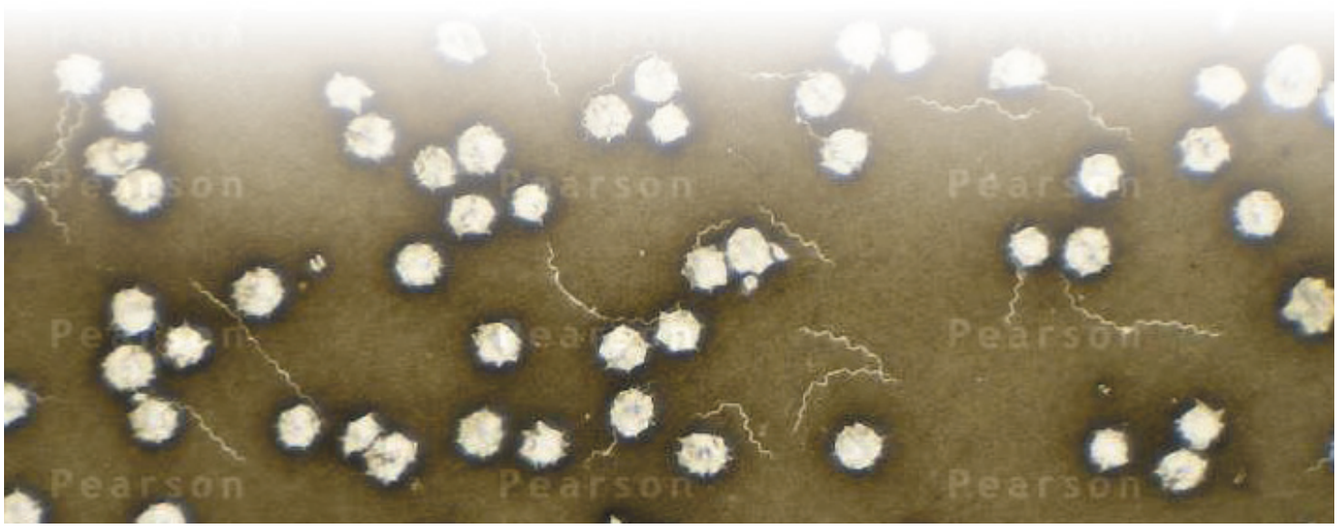


FIGURE 22.5A A Patient Suffering from Smallpox



The prospects for medicine over the next few decades are not likely to involve further human evolution. A few decades is only one human generation, and relatively little genetic change will take place within one generation—unless more than 90 percent of the human population is killed off in that generation. This scenario would require thermonuclear war. For the purpose of developing medicine on a Darwinian basis, it is a reasonable assumption that humans will not be evolving significantly in the immediate future.

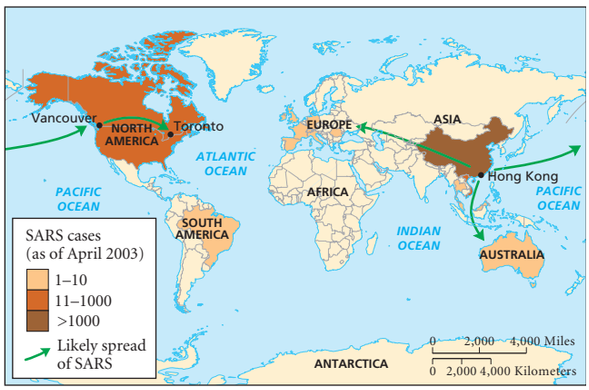


FIGURE 22.5B **The Global Spread of SARS**

On the other hand, many of our pathogens undergo hundreds or thousands of generations per calendar year. This gives them tremendous potential to evolve. At the evolutionary level, our diseases are moving targets—while we virtually sit still. This is an evolutionary asymmetry full of frightening possibilities, some of which, as we shall see, have been realized.

In addition to being evolutionarily inert, for most medical purposes, humans are distributed globally. With modern transportation, diseases that originate in one part of the world can quickly spread. Rural China, for example, is a major source of influenza epidemics that take only months to cause extensive school absenteeism in Wisconsin, thousands of miles away. Our global accessibility makes humans an excellent host organism for pathogens. The **severe acute respiratory syndrome** (**SARS**) outbreak is a perfect illustration of this pattern. Figure 22.5B shows the geographical course of SARS infection.

Coupled with easy access geographically, humans are numerous. With a population in the billions, we present many potential targets of infection. We are also a large organism, compared to most animals. We supply a lot of tissue for infection, making us a lush target for new pathogens.

22.6 Some of our body's responses to contagious disease are beneficial: Vomiting is good for you

A main theme of Darwinian medicine applied to contagious disease is the complexity of disease symptoms. For example, we get a cold and our noses run, our temperatures rise, and our throats hurt. A naïve way of looking at these cold symptoms is to interpret them as the effects of the cold viruses replicating in our bodies. And this is probably true of many disease symptoms: They are effects of pathogen replication.

But not all disease symptoms fit this pattern. Some symptoms are *defensive*, produced by the host to ward off the pathogen, or at least reduce its impact on the host. Fever is the classic example of a disease symptom that is a defense. Ironically, modern medicine does the best that it can to reduce fever. Yet the evidence is clear that the body elevates its temperature itself. Desert iguanas that regulate their body temperature by the amount of sun exposure seek more sunlight when they are infected. And such defenses work. If the iguanas are denied access to sunlight when they are infected, their disease becomes more severe. Many experiments with mammals give similar results: Reduction in fever by drugs tends to increase the severity of infections. Aspirin and acetaminophen have both been implicated in laboratory experiments. They reduce fever, and in so doing they often prolong infections, worsen other disease symptoms, and even increase death rates.

Does this mean that no one should ever bring their fever down? No—very high fevers can cause brain damage and even bring on death. Very high fevers should be treated as medical emergencies. But the pharmaceutical reduction of moderate fever may prolong minor illnesses.

Together with fever, the body has a wide range of disease defenses. Of particular importance are the defenses that actively expel pathogens: tearing, sneezing, coughing, vomiting, diarrhea, and copious urination (Figure 22.6A). Again, these include defensive symptoms that have been aggressively reduced by modern medicine, even though such medical treatment may have prolonged infections. This effect has

FIGURE 22.6A How the Body Defends Itself against Pathogens

been demonstrated quite well for diarrhea. Treatment with drugs that suppress diarrhea can prolong intestinal infections by bacteria.

But diarrhea brings up an additional category of symptom: *manipulative* symptoms. Some pathogens use the body's defense mechanisms to foster their infection of new hosts. **Cholera** is caused by the bacterium *Vibrio cholerae*, which infects the human body by ingestion (Figure 22.6B). Once it gets to the intestines, *Vibrio* faces competition from our normal bacterial colonists, such as *Escherichia coli*. To solve this problem, the pathogen induces acute diarrhea, flushing the *E. coli* out of our intestines. Once this has been accomplished, *Vibrio* has an intestinal environment better suited to its replication. Continued diarrhea also helps spread the pathogen to new hosts, particularly by infecting water supplies. In this case, early suppression of diarrhea might reduce the intensity of infection.

These examples show that there are no simple rules in the treatment of disease. A treatment that helps control one disease symptom might make another disease symptom worse. The most reliable generalization is that diseases involve complex interactions between pathogens and host. Treatment of contagious disease therefore requires some sophistication. Part of that sophistication must include knowledge of the evolutionary history and ecological circumstances that define a particular disease. ❖

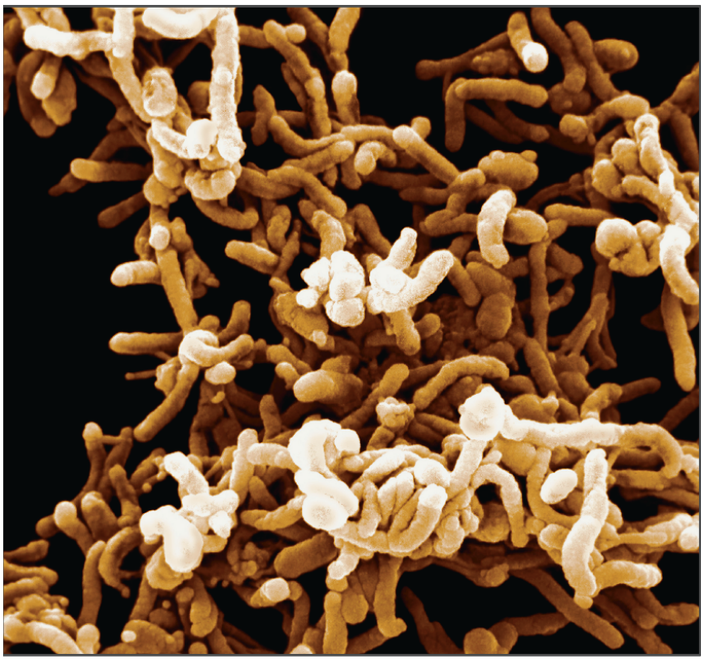


FIGURE 22.6B **Cholera Bacterium**

22.7 The evolution of pathogen virulence depends on the ecology of infection

Contagious disease is one of the most intimate couplings of evolution and ecology, and of course one of the most important. Perhaps no single phenomenon reveals this better than the relationship between the pattern of disease transmission and the lethality of infection.

Human diseases vary widely in their lethality, and that variation is of enormous interest to us. The **HIV** and **Ebola** viruses kill most of those whom they infect—HIV in years, Ebola in days. Cold rhinoviruses and many gut bacteria rarely kill humans. What is responsible for this disparity in the consequences of infection, the **virulence** of a pathogen?

One of the major factors is the ecology of disease transmission. Of particular importance is the likelihood that a particular pathogen will soon find a new host. And that in turn is shaped by a seemingly innocuous factor—whether the pathogen is transmitted directly from host-to-host contact. The pattern of lethality among different types of pathogen is shown in Figure 22.7A, taken from Paul Ewald's book, *Evolution of Infectious Disease*. Pathogens that are transmitted only from host to host are much less likely to kill their hosts relative to pathogens that have some intermediate phase that does not involve human infection, in their life cycle. Such intermediate phases usually involve organisms called **disease vectors**, which the pathogen can infect and which bear the pathogen from host to host.

Famous examples of such a vector-based pathogen are the species of the genus *Plasmodium* that cause **malaria**. Their life cycles are summarized in Figure 22.7B. Malaria newly infects millions of people each year. It is the number one killer among vector-borne human diseases, in total number of deaths. An interesting aspect of malarial transmission is that it does not require its human host to be well enough to go out and mingle with others. The mosquitoes that are its primary transmitters come to the afflicted, suck their blood, and move on to infect individuals free of infection by biting them. Unlike medical doctors, the disease vector makes house calls.

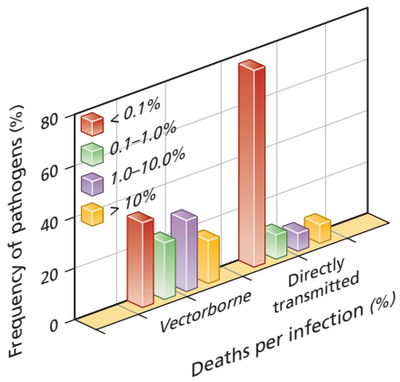


FIGURE 22.7A Mortality rates from untreated infections due to arthropod vectors vs. mortality rates with direct transfer from person to person.

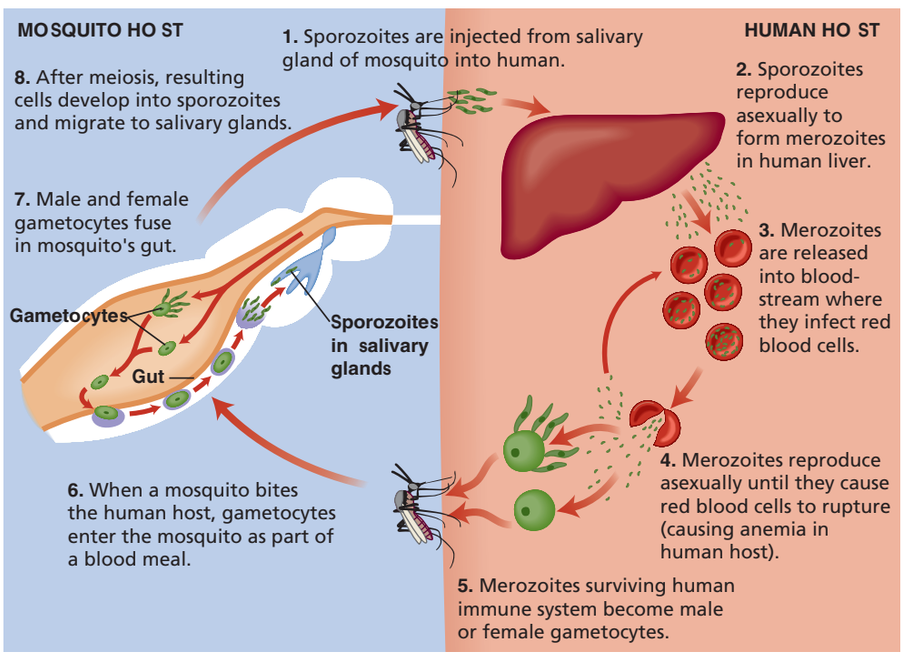


FIGURE 22.7B **Life Cycle of the Malaria Parasite, *Plasmodium***

Compare this pattern with the common cold, typically caused by the benign rhinoviruses. People with colds spend very few days in isolation, returning to workplaces and schools in short order. In such settings, their sneezes, coughs, and nasal drippings falling onto pencils, paper, and furniture handily transmit the infection to new hosts. If those afflicted with colds were instead so debilitated that they could not return to public life readily, the infection might not make it to a new host due to a lack of opportunity to infect a new host.

These patterns reveal that pathogens that have more access to new hosts may evolve lethality. For human purposes, this suggests that when human behavior changes, pathogens may change their lethality by evolution. The upsurge in promiscuity among Western populations since World War II has provided a natural opportunity for more lethal venereal pathogens to infect new hosts quickly. The spread of HIV through the West since 1970 is perhaps a predictable consequence of more promiscuous human sexual behavior. ❖

22.8 Resistance to antibiotics has evolved in bacteria, requiring the development of new antibiotics

Some aspects of present-day medicine can be understood using Darwinian ideas. But other aspects of medicine require active management using Darwinian principles. Perhaps no single area of medical practice requires evolutionary and ecological thinking more than the use of antibiotics.

Antibiotics were one of the most important medical discoveries of the twentieth century. **Antibiotics** are compounds that kill bacteria, often with very few side effects for the patients who use them. First developed in the period around World War II, antibiotics played an important role in that war, saving many lives that would have otherwise been lost and allowing the speedy return of soldiers to battle. For a time, it seemed as if antibiotics and **antivirals** would usher in a new era of medicine, in which contagious disease would be largely vanquished. This era of boundless optimism did not last long. By the 1960s, reports of bacterial strains resistant to antibiotics became common. Gonorrhea cultured from prostitutes commonly showed resistance to antibiotic treatment, requiring extended medication with one or more antibiotics.

The cause of **antibiotic resistance** in bacteria was not hard to determine: The bacteria had evolved genetically. A particularly common mechanism for the evolution of antibiotic resistance was the acquisition of plasmids bearing genes that thwarted the action of antibiotic medicines. These plasmids spread contagiously not only within bacterial species, but between bacterial species.

Some of the new bacterial strains have proven remarkably difficult to eliminate using antibiotics. Particularly in hospitals, in which new hosts are readily available, local outbreaks of bacterial infection have killed dozens of patients. Among those most susceptible to dying of antibiotic-resistant bacterial infections are the elderly and the newborn, two groups that are likely to be in hospitals. Doctors who examine a series of hospital patients in quick succession probably further foster the spread of potentially deadly infections among vulnerable groups.

Several features of modern medicine foster the evolution of bacterial resistance to antibiotics (Figure 22.8A).

1. The U.S. Food and Drug Administration makes it difficult to get approval for new antibiotics. Yet evolutionary first principles suggest that the use of a limited repertoire of antibiotics will make it easier for bacteria to evolve resistance.
2. Most physicians try just one antibiotic at a time, with a short period of medication. This gives bacteria the opportunity to adapt to one antibiotic at a time. The use of multiple antibiotics at one time is likely to allow fewer bacteria the opportunity to survive antibiotic treatment.
3. Collecting patients together in hospitals, and to a lesser extent clinics, maximizes the opportunities for exchange of resistant bacteria between patients. This practice also fosters the exchange of antibiotic-resistant plasmids between unrelated bacterial strains.
4. Most important, antibiotics are often mis-prescribed for viral and other diseases, especially at the insistence of patients who do not understand the biology involved.

With the widespread consumption of antibiotics, the human population is virtually an incubator for the evolution of bacteria that cannot be eliminated using known antibiotics.

As if the foregoing points were not sufficient cause for concern, two more problems highlight the likelihood that many bacteria will soon evolve resistance to antibiotics. First, though Western countries confine the use of antibiotics to patients under a doctor's care, many developing countries

1. Lack of new antibiotics

Turning off the pipeline of antibiotic development by stringent government regulation ensures that bacteria face a limited repertoire of antibiotics.

2. Using one antibiotic at a time

If a bacterium is particularly nasty, the only way to overcome its resistance may be to attack it with multiple antibiotics at the same time. But standard medical procedures dictate one medication at a time.

3. The hospital environment

Collecting sick and compromised patients together in one building gives bacteria excellent opportunities for infecting new hosts. Effective quarantine of infected patients is crucial, but rarely achieved.

4. Incorrect prescription

Sick patients commonly badger their physicians for antibiotics when they have viral infections, or no infection at all. Their use of antibiotics imposes selection on their bacteria for resisting the mis-prescribed antibiotic, with bad consequences when a bacterial infection does occur.

FIGURE 22.8A How We Sabotage Antibiotics

have virtually unregulated use of antibiotics, without a doctor's prescription. Because antibiotics are expensive by the standards of these countries, many do not take a full course of antibiotics. This makes such casual antibiotic use almost ideal for the evolution of antibiotic resistance in bacteria. Secondly, and almost unbelievably, Western farmers use feed that contains antibiotics. They do so because agricultural animals grow faster when they are routinely fed antibiotics. However, such use is again not calibrated to ensure the complete elimination of bacteria, allowing bacteria to undergo selection for antibiotic resistance.

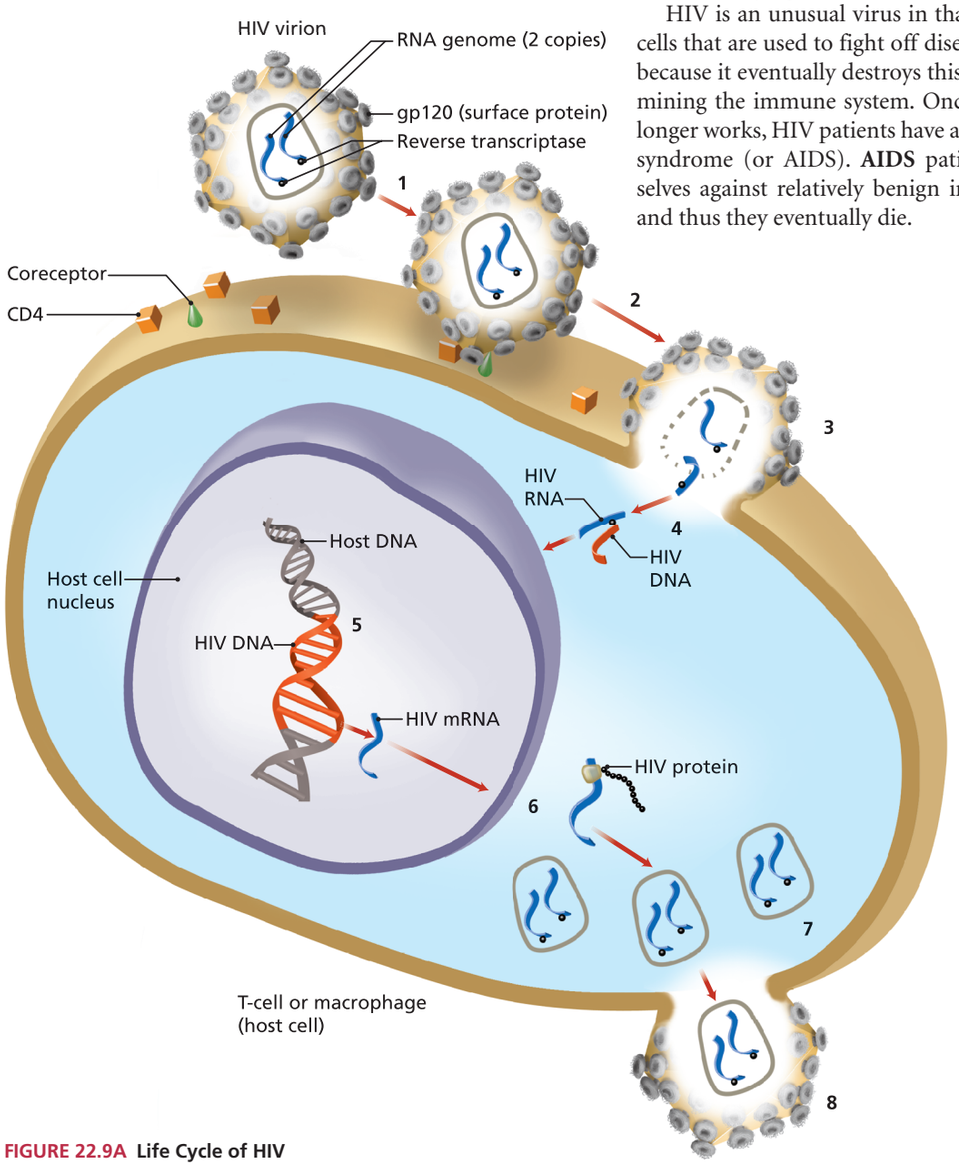
These features of our medical ecology combine to undermine one of the most important weapons available to the medical profession. Antibiotics are still generally useful in the treatment of bacterial infection. How much longer this will continue depends on the reform of pharmaceutical development, medical practice around the world, and even agriculture. ❖

22.9 HIV illustrates the importance of rapid virus evolution in medicine

The human immunodeficiency virus (HIV) is probably the deadliest pathogen to have attacked the human species. HIV infection seems to eventually kill 95–99 percent of its victims, regardless of treatment. It has already killed somewhere between 10 and 20 million people, with a total of about 40 million infections so far. Given the lack of an effective vaccine for the foreseeable future, as well as no cure, these numbers are bound to grow. In sub-Saharan Africa, where the incidence of infection exceeds 10 percent of the total population, HIV is bringing about a demographic revolution—and a humanitarian disaster. In the worst-case scenario, HIV could eventually wipe out all members of our species, excepting only a tiny fraction of highly resistant individuals. This would leave our species with only some thousands of survivors—an impact comparable to that of thermonuclear war. How did our species acquire such a scourge? How does HIV work? And what can be done about it?

Other primates have immunodeficiency viruses like HIV, although they do not suffer lethal consequences from infection with these viruses. Humans probably acquired HIV strains from other primates; and other primates may have been infected with human HIV. Among the possible mechanisms of transmission between primate species are human consumption of "bushmeat," the flesh of other primates, and bites from flying insects like mosquitoes.

HIV is an unusual virus in that it infects the white blood cells that are used to fight off disease. HIV is a deadly disease because it eventually destroys this entire class of cells, undermining the immune system. Once their immune system no longer works, HIV patients have acquired immuno deficiency syndrome (or AIDS). **AIDS** patients cannot defend themselves against relatively benign infections, like tuberculosis, and thus they eventually die.



1. HIV's extracellular, or virion stage
2. HIV's gp120 protein binds to CD4 and coreceptor on host cell
3. HIV's RNA genome and reverse transcriptase enter host cell
4. Reverse transcriptase synthesizes HIV DNA from HIV's RNA template
5. HIV DNA integrates into host genome and is transcribed to HIV mRNA
6. HIV mRNA is translated to HIV protein by host cell's ribosomes
7. New generation of virions assembles inside host cell
8. New virions bud from host cell's membrane

FIGURE 22.9A Life Cycle of HIV

Medications such as AZT can be used to control HIV infections. The problem is that the virus quickly becomes resistant to such medication and resumes proliferation. The use of multiple medications against HIV has shown promise in forestalling progression to AIDS, but it is likely that this medication strategy will eventually cease to work as well, because of HIV evolution. Why is HIV so resistant to antiviral drugs? Figure 22.9A shows the life cycle of this virus. HIV is an **RNA virus**: It uses RNA to encode its genes. When it enters a host cell, HIV makes a DNA copy of its RNA, using reverse transcriptase. This DNA is then incorporated into the host cell's genome, where it is transcribed to make many copies of the virus RNA. This complicated life cycle gives RNA viruses very high mutation rates. The virus also produces many descendants. The combination of a high mutation rate and abundant offspring gives HIV enormous evolutionary potential. It is probably one of the fastest-evolving things on the planet. It is likely that HIV will evolve gene sequence changes that will evade virtually any antiviral compound that we throw at it. This is a supremely dangerous pathogen: We can't stop it, and it kills off cells vital to our survival.

But there are two additional levels to the ecological and evolutionary story of HIV. The ecology of HIV infection varies. In some geographical areas, like sub-Saharan Africa, it has spread widely. In some particular groups found in other geographical areas, it has spread widely: intravenous (IV) drug abusers, homosexual men, and prostitutes. Among these groups HIV appears to be particularly virulent, quickly spreading and quickly killing its hosts. But among other groups, like heterosexuals in Western countries who do not use IV drugs or sell their bodies for sex, the virus has spread slowly. It appears to be less virulent among such groups. This fits evolutionary theory. The groups with virulent HIV appear to have more opportunities for virulence to evolve, because transmission is more common. Paul Ewald has predicted that HIV should evolve toward more benign infection in the groups that do not transmit it as often. If so, the widespread abandonment of promiscuity and IV drug abuse could "domesticate" HIV. This would forestall our virtual extinction.

But what if people, being people, do not inhibit themselves? What is the prognosis for the HIV epidemic? There is some evidence that a tiny number of people are naturally resistant to HIV infection, despite repeated exposure. They resist progression to AIDS. In the worst-case scenario, the rest of us will die and these individuals will be the relicts of the species. ❖

AGING

22.10 Evolution and genetics offer new hope for the medical treatment of the elderly

In the West, the twentieth century saw the practice of medicine advance from success to success across a broad front. Newborns survive more often. Except for HIV, contagious diseases have mostly been fended off by a combination of vaccines, antibiotics, and hygiene. Accident victims now receive outstanding emergency care. Heroic surgery rescues victims of heart disease and cancer from certain death.

But the treatment of the elderly has improved little. It is true that when the elderly get a particular disease, such as cancer, medicine has more tools to treat the disease. But the elderly have poor survival rates after medical treatment. And nothing is done about the fact that they have been greatly debilitated by aging: from sagging skin to wasting muscles, from diminished memories to chronic pain.

Unlike virtually every other medical specialty in the twentieth century, even psychiatry, **geriatrics** has not made much progress. One might blame medical practitioners, except that in this case geriatrics has not been slow to build on the successes of its relevant biological discipline, **gerontology**. Over most of the last century, such successes have been almost wholly absent. Geriatrics has not worked, because gerontology did not make progress with the biology of aging. At least until recently.

As outlined in Chapter 7 on life histories, we now have a fairly successful theory for aging: Aging evolves because of a decline in the force of natural selection during adulthood. This theory is nicely developed mathematically, and it works in laboratory experiments, so far principally with insects.

Since 1950, gerontologists instead pursued theories of aging based on molecular and cell biology, theories based solely on physiological mechanisms of aging. But they had little success. Each of their theories, from somatic mutation to error catastrophe to limited cell replication, has failed as a way to explain aging in general. The intrusion of evolutionary biology into the field has not been universally welcomed, but it has had some influence. More and more of the work in gerontology is guided by evolutionary considerations.

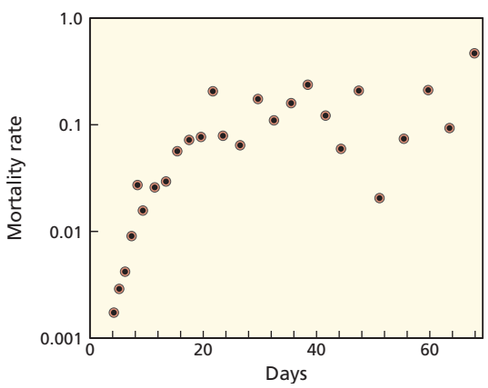


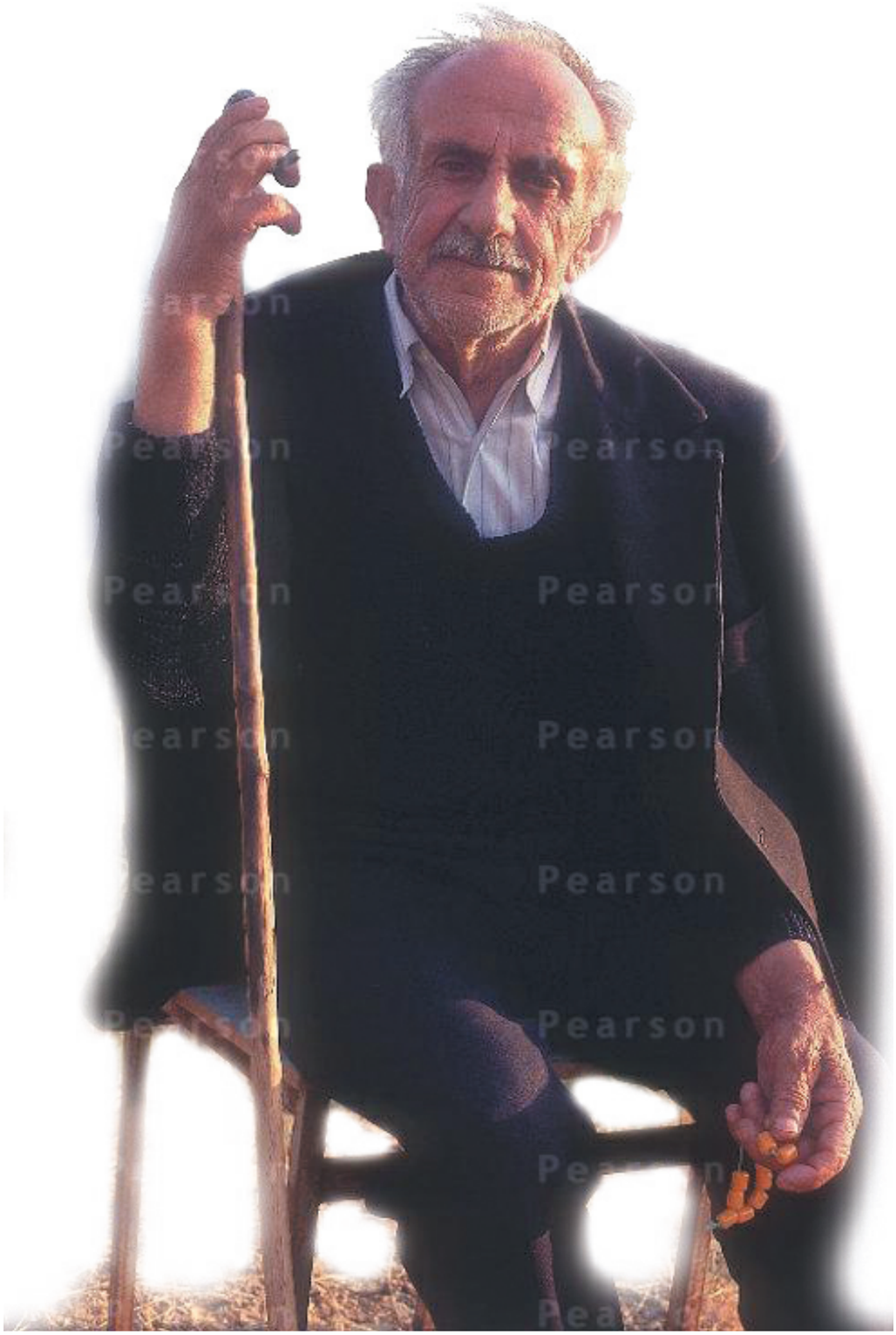
FIGURE 22.10A Aging in *C. elegans*

The area of gerontology that has been most influenced by evolutionary ideas is the genetics of aging. Since 1980, with the demonstration that genetic change could be used deliberately to postpone aging in fruit flies, more and more geneticists have found ways to create organisms that live longer genetically.

The first substantial successes came with the genetics of aging in the nematode worm, *Caenorhabditis elegans* (Figure 22.10A). Starting with **age-1**, nematode geneticists have found a multiplicity of genes that give increased life span when mutated. Many of these genes are part of the pathway that regulates an immature stage called the **dauer**. The dauer worm delays reproductive maturation. A controversy has recently arisen concerning the metabolism of genetically longer-lived worms. In some studies, all mutant alleles that increase life span also have reduced metabolic rates. In *Drosophila* research, it was shown a long time ago that reduced metabolic rate in a small cold-blooded animal can give increased lifespan. Reduced metabolic rate appears to "stretch" life. On the other hand, the longer-lived flies (see Chapter 7) have no reduction in metabolic rate, and their total metabolic work per lifetime is greatly increased.

However the details work out, evolutionary and genetic research on aging is now supplying the field of gerontology with the scientific foundations that it used to lack. This should have two effects:

1. It is now possible to go through the field of gerontology with evolutionary theory as a guide, winnowing out the failed science and, at the same time, pursuing the attractive scientific leads with some hope of making progress. Gerontology can now be as successful as such biomedical fields as immunology, oncology, and the like, at least in principle.
2. It is now reasonable to consider reformulating geriatrics. In the past, geriatricians have been fairly circumspect. Holding out hope of changing the human aging process to this point has been the hallmark of the charlatan, because geriatrics had found no tools with which to ameliorate the aging process itself. Now this possibility is at least worth discussing, because altering the aging process genetically and dietarily has become routine within a newly successful gerontology. ❖



22.11 Humans live so long due to patterns of selection

The starting point for Darwinian geriatrics must be the fact that humans are very long-lived organisms. This is partly because vertebrates are generally long-lived, compared with insects, nematodes, and other small invertebrate animals. There is nothing special about a vertebrate living for years, as opposed to the weeks and months that most animals live even when kept under excellent conditions. But humans can live for more than a few years. We can live for more than a century.

Part of the explanation for our longevity is related to size. Larger vertebrates tend to live longer. But that is not a complete explanation. We are also longer-lived for a large vertebrate. Some illustrative longevity data are shown in Table 22.11A.

What could explain greater human longevity? Old-style gerontologists were fond of explaining superior human longevity as a result of superior "homeostasis" or "canalization"—confusing and ambiguous concepts that derive from physiology. But none of these theories ever worked, so we can safely dismiss them.

More data might be revealing. Table 22.11B shows some **maximum longevity** patterns associated with different ecologies. Certain patterns are striking. Organisms that have shells live much longer than similar organisms that lack

TABLE 22.11A Longevities of Some Large Mammals

Species	Common Name	Maximum Longevity
Balaena mysticetus	Bowhead whale	211 years
Homo sapiens	Human	122 years
Elephas indicus	Elephant	70 years
Rhinoceros unicornis	Rhinoceros	50 years
Hylobates lar	Gibbon	32 years
Papio papio	Baboon	27 years

TABLE 22.11B More Comparisons of Longevity among Species

A. Flying versus Nonflying Vertebrates

Taxonomic Group	Common Name	Maximum Longevity
Order Chiroptera	Bats	Up to 24 years, many over 10 years
Class Aves	Flying birds	Up to 68 years, many over 30 years
Class Aves	Non-flying birds	27–28 years
Order Rodenta	Rats, mice, and so forth	3–8 years

B. Reptiles

Taxonomic Group	Common Name	Maximum Longevity
Alligator sinensis	Alligator	52 years
	Snakes	Mostly more than 20 years
Genus *Testudo*	Tortoise	Several species more than 100 years

C. Invertebrates

Taxonomic Group	Common Name	Maximum Longevity
Coelenterata	Coelenterates	90 years (died by accident)
Schistosoma	Schistosomes	25–28 years
Lumbricus terrestris	Earthworm	5–6 years
Homarus	Lobster	50 years
Blaps gigas	Beetle	>10 years
Megalonaias gigantea	Bivalve	53–54 years
Octopus vulgaris	Octopus	3–4 years

them. Turtles, for example, often have maximum life spans of more than 70 years. Other reptiles have life spans averaging less than 20 years. Bivalves, like oysters, clams, and mussels, have life spans averaging more than 10 years, while other mollusks have life spans averaging less than 5 years. What is it about having shells that matters for aging?

A pattern that is perhaps even more obvious is the contrast between flying vertebrates and other vertebrates. Birds that have roughly the same size as rodents live far longer. Small rodents live just a few years, less than 10 maximum. Birds of the same size can live 40 to 60 years. Even within the birds, the flightless ostrich and emu have shorter life spans than all but a few flying bird species. Within the mammals, the flying bats have average life spans of 15–20 years, longer than rodents of comparable size.

The straightforward way to explain these patterns is the effect of organismal biology and ecology on the force of natural selection. Species that fly or have thick shells will tend to be preyed upon less often compared to species without these adaptations. So their natural ecology will usually be one in which they tend to live and reproduce to later ages. That difference in their ecology will in turn lead to a prolongation in the force of natural selection, following a pattern similar to that imposed on the fruit flies in the experiments on the evolution of aging. And, as those experiments showed, such a prolongation of the force of natural selection will tend to result in the evolution of postponed aging. This is how evolutionary biologists explain why flying and armored species tend to live longer.

But what of humans? Humans have a general-purpose mortality reducer—the human brain. With the human brain we are better able to avoid predators and accidents, thanks in part to prudence and in part to our tools. This must have had an effect analogous to that of flight or shells: Our survival and reproduction at later ages were enhanced, strengthening the force of natural selection at later ages. Strengthened natural selection then led to the evolution of a human body that could better withstand the ravages of time. We live longer because we are smarter. ❖

22.12 Postponement of human aging will be achieved by combining evolutionary and other biotechnologies

Despite the slow progression of human aging, the desire to postpone, slow, or reverse the process has been perennial. So long as medicine was generally impotent, the repeated failure of attempts to postpone human aging was not a notable blemish on the practice of medicine. Now that medicine has become generally effective, its failure to control the process of aging is prominent.

There have been two main responses to this situation. The medical establishment has generally eschewed the goal of postponing or slowing human aging, often with the implication that it is an impossible project. Recent successes in the postponement of aging in laboratory animals, however, suggest that this defeatism with respect to the postponement of human aging is outmoded.

The other response to the lack of medical interventions for aging has been to decry the medical establishment as conspirators intent on preventing the treatment of aging, perhaps because so much of medical practice derives from diseases that are associated with aging. What this criticism fails to address is the sheer difficulty of controlling aging. Many genes are involved, and finding even a few of them in simple organisms, like nematodes and fruit flies, has been difficult.

A rational compromise between these two views might be the following perspective from Darwinian medicine. Aging is a complex set of pathologies that are caused by a pervasive failure of adaptation at later ages. This pervasive failure in turn is due to a falling force of natural selection. Although this force of natural selection can be increased at later ages in simple animals, this is not a practical, or ethical, program for changing human aging. Therefore, any medical or biotechnological approach to postponing human aging will be difficult.

Difficult, but probably not impossible. The key is that many of the genes found in fruit flies and nematodes are represented in modified form in humans. If we can learn enough about manipulating the genes that control aging in simple lab animals, then we have the possibility of using such knowledge to develop antiaging medications and procedures that will work in humans.

This strategy cannot be based on the assumption that antiaging tricks that work in, say, fruit flies will always work in humans. But evolutionary homology connects many of the genes in fruit flies to genes in humans. Such homology has been exploited experimentally in studies of development in fruit flies and humans. A major contributor to our scientific understanding of human development has been the study of the genetics and molecular biology of development in fruit flies, as described in the accompanying box. There is every reason to hope that a similar carryover can be achieved in research on aging, some of the time.

Figure 22.12A sketches a variety of research pathways that might lead to the medical postponement of aging in humans. Some of these pathways start with fruit flies, some with nematodes, and some with humans. The postponement of human aging requires that we use the full range of biological disciplines, from evolutionary biology to genetics to molecular biology. Because postponed aging has already been achieved in fruit flies and nematodes, we know that it is not impossible in human. But it will not be easy. ❖

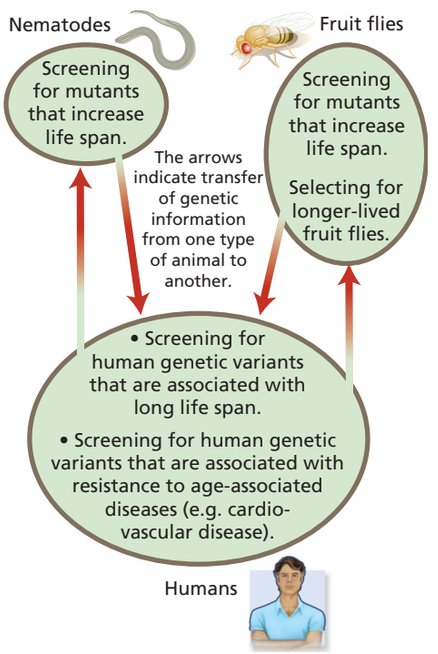


FIGURE 22.12A Biotechnological Postponement of Aging

From *Drosophila* to Mammal—Developmental Biology

Among the successes of recent cell biology has been the use of discoveries in fruit-fly research to understand mammalian development. Among the bizarre types of mutation in fruit flies are the homeotic mutations, which turn fly antennae into legs or duplicate the entire thorax, among other amazing effects. These effects occur because homeotic genes orchestrate the positional information underlying fruit-fly development.

But there's more. Mammals have genes with similar DNA sequences to those of fly homeotic genes, as do many other animals. It turns out that the homologous mammalian genes play a similar homeotic role, controlling the use of positional information in mammalian development. The fruit-fly work set the stage for a major step forward in our understanding of mammalian development. A similar boost for geriatrics might come from studies of the genetics, evolution, and physiology of aging in fruit flies and nematodes.

BRAIN DISORDERS

Not all "mental illness" is pathological 22.13

It is brains that produce behavior. Therefore, aberrations in that behavior may reflect an underlying **brain disorder**. As with the symptoms of contagious disease, not all of the symptoms that concern psychiatrists are manifestations of brain disorder. Behavior that radically reduces fitness is likely to reflect an underlying brain disorder. But behavior that does not reduce fitness, however odd, may not be due to a brain disorder. Such behavior might even enhance fitness, in some cases.

Psychiatry tends to focus on behavior that is deviant from social norms. It is common for families to bring their deviant members to the attention of health-care professionals. In many cases the deviant behavior is a symptom of a significant brain disorder. But there are also cases of deviant behavior that do not lead to an impairment of fitness, and these cases are not medical problems from the standpoint of Darwinian medicine.

Phobias and other **anxiety** disorders are extremely common in human populations. People are afraid of snakes, heights, confinement in small spaces, crowds, and so on. Often they are troubled by their fears and anxieties, and seek out medical doctors to give them prescriptions for tranquilizers. All too often they then become addicted to these tranquilizers. Many people also use alcohol and tobacco to reduce their anxieties, and so become alcoholics and victims of lung cancer.

Yet anxiety and fear are basic brain functions that serve to keep us out of trouble. Anxiety and fear mobilize the autonomic nervous system in ways that foster "fight or flight": increased heart rate, rapid breathing, increased blood flow to the muscles, and so on. When severe, these symptoms are considered "panic attacks" by medical doctors. But what if fleeing is an appropriate reaction to danger, whether the danger comes from a snake or a vengeful enemy?

Anxiety and fear are mobilizing emotions that serve important functions. Individuals who suffer extremely high levels of these emotions may have a significant disorder. But in many cases these disorders may involve normal Darwinian brain functions that people find distressing. They could be analogs of diarrhea and fever, which can save lives but are not pleasant.

One way to view anxiety disorders is as part of a spectrum. Some individuals undoubtedly suffer too little anxiety. This causes them behavior problems that may result in their early death or injury. Other individuals are virtually paralyzed by fear, which prevents them from going outside to shop, socialize, or date. People at both of these extremes may suffer from some reduction in Darwinian fitness, as a result.

Most of the human population suffers from anxiety, but not so much as to reduce Darwinian fitness. Almost everyone would be fearful or anxious if kidnapped. Likewise, they would be fearful if a mugger pointed a gun at them. The fear would mobilize them to flee or fight, based on their body's physiology, even if they do not do either. In our ancestral environment, contact with poisonous snakes or large predators probably had the same effect. Fear and anxiety are adaptations to a dangerous world, not psychopathologies. Only at their extremes of predominance or absence are they problems of psychiatry, from a Darwinian perspective. And it is notable that the complete absence of anxiety and fear might be the greatest problem of all. This analysis is shown graphically in Figure 22.13A. ❖

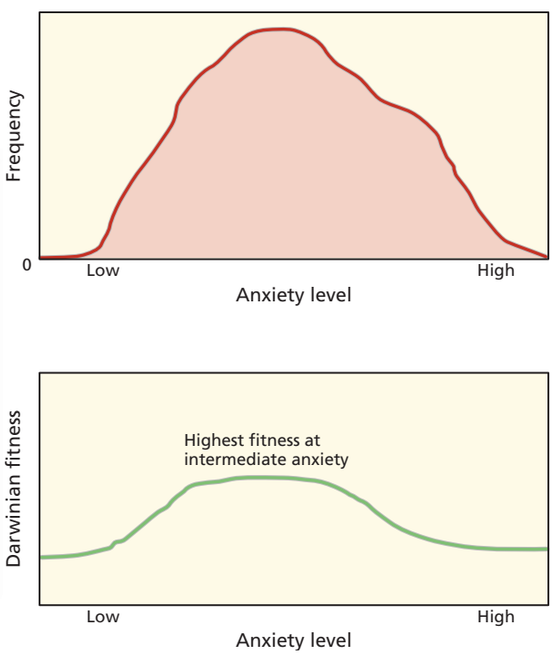


FIGURE 22.13A A Hypothetical Spectrum of Anxiety and Its Possible Consequences for Darwinian Fitness

22.14 Schizophrenia is an example of a Darwinian brain disorder

Schizophrenia is characterized by delusions, hallucinations, and other failures to differentiate reality from other subjective experiences. Everyone experiences **hallucinations** and **delusions** during dreams. But we know that they are dreams, and we discount their relevance to our everyday lives. Schizophrenics have difficulty testing the reality of their hallucinations and delusions. The diagnostic medical criteria for schizophrenia are given in this module.

Along with this disconnection from reality, schizophrenics may experience paranoia, intense fear or anxiety, and depression. Their IQs tend to be reduced. Unmedicated schizophrenics have great difficulty keeping a job, sustaining a marriage, or retaining friends.

It is difficult to build a reasonable case for natural selection specifically favoring the maintenance of schizophrenia. Schizophrenics have reduced survival rates and reduced mating frequencies. They are often kept in psychiatric institutions, or they live on the streets as homeless vagrants. Medicated schizophrenics have remission of 30–70 percent of their symptoms and may function at a job or in a family. But sufferers often do not comply with medical treatment.

There is one historically important theory based on the idea of schizophrenia as a functional condition. This is the "schizophrenic shaman" theory of anthropology. It proposes that schizophrenics may have functioned as tribal shamans, using their hallucinations and delusions to guide the tribe spiritually. It is conceivable that schizophrenics could have played this role. But that leaves unaddressed the question of how these schizophrenics would have found a mate and produced children. Perhaps their shaman status helped them to obtain a mate? A further problem with this theory is that shamanism is often based on drug-induced hallucinations, using peyote for example, which suggests that psychiatrically normal people can be shamans.

The alternative evolutionary theory is that schizophrenia is a pathological condition that is not favored by natural selection. If so, how can it attain frequencies as high as 1 percent in human populations? Part of the problem may be lesions to sensitive areas of the brain. If mechanical trauma occurs during fetal development or birth, it might later generate schizophrenia. Or infections, chronic and acute, could cause such lesions. Ewald has proposed multiple pathogens as causes of schizophrenia, from *Toxoplasma gondii* to Borna disease virus. There is also evidence that schizophrenia is inherited. This suggests that the disorder might also arise from rare genotypes at many loci, singly or in combination. If so, it could be maintained by recurrent mutation, like cystic fibrosis and other genetic diseases. It has been suggested that recessive genes might be responsible for schizophrenia, genes that might have some beneficial effect in heterozygotes. If so, it is unlikely to be a behavioral benefit, because unlike some other brain disorders, no such benefit has been found among schizophrenics or their near relatives. (Such cases are discussed later in the chapter.) It is remotely possible that a gene for schizophrenia might have some beneficial effect on a totally unrelated medical problem, like heart disease, perhaps in heterozygotes. There is a little evidence for greater reproductive success among the near relatives of schizophrenics. For now, the most reasonable assumption is that schizophrenia is a deleterious disorder maintained in populations by developmental misfortune, disease lesions, recurrent deleterious mutations, or a combination of all these agents.

Diagnostic Criteria for Schizophrenia

A. Characteristic Symptoms: Two or more of the following
1. Delusions
2. Hallucinations
3. Disorganized speech
4. Catatonic behavior
5. Flat affect; lack of speech

B. Social or Occupational Dysfunction
Reduced functioning in one or more major areas:
1. Work
2. Interpersonal relations
3. Self-Care
4. Academics (when appropriate)

C. Duration
Continuous signs of the disturbance must persist for at least 6 months

D. Exclusions
1. Affect disorders have been ruled out as a cause of aberrant behavior.
2. Substance abuse has been ruled out as a cause of aberrant behavior.
3. Another medical condition, such as a brain tumor, has been ruled out.

E. History of a Major Developmental Disorder
If autism or a similar disorder has been previously diagnosed, diagnosis of schizophrenia requires prominent delusions or hallucinations for at least a month.

From Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), *4th ed. (Washington, DC: American Psychiatric Association, 1994), 285–86. Not to be used for medical diagnosis.*

Explanation of some of the terminology:

Delusions—incorrect and persistent conclusions about the material or social environment

Hallucinations—sensory experiences that do not correspond to externally observable events

Catatonia—lack of responsiveness, lack of awareness of surroundings

Flat affect—lack of joy or distress in circumstances where they are appropriate

Self-care—getting adequate hygiene, nutrition, sleep

Affect disorders—see below

Autism—a pervasive failure of normal social and intellectual development in children not due to gross brain abnormality

22.15 It is unclear whether all affect disorders are actively sustained by natural selection

Most people get depressed. When they lose a job, a family member, or a significant other, many people go through a period of feeling little enthusiasm, disrupted sleep, changed eating habits, and difficulty concentrating. If this condition lasts for a few days, it is entirely normal. If it lasts for six months, then it is clinical depression. At least 10 percent of a human population will experience a clinical depression once in their lives. In some countries, this percentage is even higher. The diagnostic criteria for **depression** are given in this module.

A few people get high without drugs or alcohol. They experience great surges of energy during which they cannot sleep, cannot stop talking, are obsessed with sex, and spend money unwisely. This is **mania**. Many people experience a mild version of this pattern when they fall in love, graduate from college, or suddenly receive a large quantity of money. But for most of us, this "natural high" lasts no more than a few days. In manic depressives, the high may last for weeks, even months. Only 1 percent of a population, or less, experiences sustained mania. When mania ends, it is often followed by clinical depression, though there are rare manics who are never depressed. The diagnostic criteria for mania are also given in this module.

Clinical depression and sustained mania are **affect** disorders, the term *affect* referring to sustained positive or negative emotion. Affect is virtually a human universal. Affect disorders are very common, especially depression without a preceding period of mania.

Individuals who never experience mania, but do suffer from depression, are grouped separately from those who experience mania. Depression is analogous in many ways to anxiety disorders: Both are unpleasant experiences that interfere with functioning when they are extreme and sustained. But most people experience negative affect and anxiety. Doctors try to medicate either condition when their patients complain of suffering. But depression after the death of a child seems about as functional as phobia toward snakes or heights. If parents felt little sense of loss when a child dies, then they would be less likely to avoid circumstances that could kill or harm their other children. Depression, like anxiety, is an adaptive brain function that may reach an extreme in some patients. Being happy is not a Darwinian imperative. The Darwinian imperative is to propagate your genes. Depression can be thought of as an instance of signaling within the brain that gears behavior toward fitness enhancement. It may be hypertrophied in some individuals, in the same way that some of us are very tall or very short. But it is not necessarily a brain disorder.

Manic depression is quite different. Manic depressives have a 20–25 percent increase in their death rates, mostly from suicide, but also from substance abuse and other dangerous behaviors. Furthermore, manic depression is strongly inherited, with a heritability that exceeds 50 percent. If one identical twin is manic depressive, the other twin is also manic depressive about 70 percent of the time. Why are 1 percent of humans subject to this disorder? It could be that manic depression is another brain disorder, like schizophrenia, maintained by mutation and brain damage. But there is evidence for this condition, unlike schizophrenia, of some beneficial effects. Both manic depressives and their close relatives show a tendency toward verbal creativity. Among great English poets, more than 50 percent probably had manic depression. There is no such association with disorders involving schizophrenia or anxiety. In some obscure way, manic depression is associated with an enhanced brain function. This makes it plausible that natural selection might maintain genes that foster manic depression. But in no way does it establish this conclusion.

Diagnosis of a Major Depressive Episode

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, delusions, or hallucinations.

1. Depressed mood most of the day, nearly every day, as determined from either subjective reports or observation of behavior. May also manifest as irritability.
2. Markedly diminished interest in most normal activities.
3. Significant weight loss without dieting, or appetite change.
4. Increased or decreased quantity of sleep.
5. Either marked sluggishness or hyperactivity.
6. Fatigue every day.
7. Excessive feelings of worthlessness or guilt.
8. Diminished ability to concentrate; Indecisiveness.
9. Recurrent thoughts of death, thoughts of suicide, planning suicide, or attempting suicide.

B. These symptoms cannot be accounted for by another psychiatric syndrome, drug abuse, hormonal problems, or recent bereavement.

C. These symptoms cause significant distress in social, occupational, or other important activities.

From Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), *4th ed. (Washington, DC: American Psychiatric Association, 1994), 327. Not to be used for medical diagnosis.*

Diagnosis of Mania

A. Persistently elevated, expansive, or irritable mood, either lasting for more than one week or requiring hospitalization.

B. Three or more of the following symptoms have been significantly present:

1. Inflated self-esteem
2. Decreased need for sleep
3. Highly talkative
4. Racing thoughts
5. Distractibility
6. Increase in sexual or social behavior; physical agitation
7. Excessive spending or investment; sexual indiscretions

C. Symptoms do not meet criteria for other affect episodes.

D. Marked impairment of work, social, or family interactions; threat to self

E. Exclusions: Symptoms not due to

1. Medication
2. Substance abuse
3. General medical condition (e.g., hyperthyroidism)

From Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), *4th ed. (Washington, DC: American Psychiatric Association, 1994), 332. Not to be used for medical diagnosis.*

22.16 The sociopath combines subjective well-being with pathological Darwinian outcomes

Personality disorders give rise to behavior that is not usually "crazy," but law enforcement and families have considerable difficulty dealing with individuals who have personality disorders. Vague popular notions of personality disorders are common. **Narcissists**, **histrionics**, and **sociopaths** are just three personality disorders that are widely misunderstood. Many women think that their ex-husband or their attorney is a narcissist. Many men think that their ex-wife or girlfriend is a histrionic. And everybody thinks, at least sometimes, that unscrupulous politicians and bad drivers are sociopaths.

There may be some truth to all of these suspicions. There are more than ten clinically recognized personality disorders, each with a long list of diagnostic criteria and clinical features. Most of the personality disorders blend into each other, and patients with multiple disorders are commonly diagnosed by psychiatrists. However, one personality disorder stands out from the rest: antisocial personality disorder, which is often called sociopathy. This disorder is the most reliably diagnosed, among the personality disorders, and it has the most profound consequences. The diagnostic criteria for this disorder are given in this module.

Sociopaths generally lack loyalty, love, grief, and so on. Sociopaths commit a lot of crimes, perhaps as many as half of all crimes against property, despite making up only about 1 percent of most populations. This should give them a lot of experience at evading capture. Instead, they are remarkably easy to arrest. There is nothing unusual about a sociopath being captured within a few yards of a police station.

One of the most interesting features of sociopaths is their freedom from many types of psychological aberration or distress. Their intelligence is not markedly reduced. They do not exhibit clinical depression or mania. In many ways, they are relaxed. Yet their lives are completely disordered. They do not sustain marriages or careers. Often they are highly promiscuous; most unusually, sociopathic women may have a predilection for group sex and other dangerous sexual practices. Clinical case histories record a pattern of extensive social deviance, ranging from murder to inappropriate practical jokes.

It has been proposed repeatedly in the scientific literature that sociopaths are cheaters from the standpoint of evolutionary game theory; and this cheating, it has been argued, is evolutionarily beneficial. In other words, it has been argued that sociopaths do not suffer from a Darwinian brain disorder—unlike, say, schizophrenics. Sociopaths just take whatever they need and ignore the consequences.

This model might make sense of other personality disorders, perhaps narcissism or histrionics, which can be successfully manipulative. But the problem with applying it to sociopaths is that sociopaths do not follow through on long-term plans of any kind. It's not that they get into trouble because they are extraordinarily selfish in their choices. They are sometimes very generous. They just do not seem to be able to follow any sort of strategy.

An alternative Darwinian interpretation of this disorder is that it arises when there is a breakdown in signaling from one part of the brain to another, signaling that is normally experienced in the form of both positive and negative affect, anxiety and contentment. (This idea is outlined at the end of Chapter 21.) That is, sociopaths may suffer from a class of brain disorders in which the direction of behavior toward Darwinian ends fails. In a sense, then, sociopaths could be Darwinian idiots.

One piece of evidence in favor of this model is the phenomenon of pseudo-psychopaths. When people sitting in the front passenger seats of cars do not use seat belts, their crashes become experiments in brain function. It is not uncommon for people who go through car windshields to receive extensive damage to the **frontal lobes** of their brain, above and behind the eyes. Some of these patients exhibit a "couch potato" syndrome. They tend to lose motivation, overeat, and watch television programs endlessly. Other patients seem to become instant sociopaths: socially aggressive, self-centered, and uninhibited (see the box). Lesions to the frontal lobes thus can create most of the elements of the sociopathic personality. This suggests that sociopaths are not examples of a particular strategy choice. Instead, they lack at least some of a Darwinian capacity of coordinating choices to the end of increasing fitness. Some part(s) of their brains have lost key functions. Sociopathy is a Darwinian brain disorder, on this interpretation.

General Diagnostic Criteria for Personality Disorders

A. Consistent deviation from social expectations in two (or more) of the following respects:
   1. Perception of self and other people
   2. Appropriateness of affect
   3. Social interactions
   4. Impulsiveness

B. The deviant pattern is pervasive across a broad range of situations.

C. The deviant pattern causes distress or impairment of functioning in social, occupational, and other respects.

D. The pattern has been stable since adolescence or early adulthood.

E. The pattern cannot be accounted for in terms of some other psychiatric disorder.

F. The pattern cannot be explained by drug use, medication, trauma, or any other medical condition.

Diagnostic Criteria for Antisocial Personality Disorder

A. Pervasive disregard of the rights of others since adolescence, as indicated by three (or more) of the following symptoms:

1. Repeated criminal acts
2. Recurrent lying, assumption of false identities, "conning"
3. Failure to plan ahead
4. Repeated physical fights or assaults
5. Reckless disregard for the safety of others
6. Repeated dismissal at work, failure to repay loans
7. Lack of remorse

B. The diagnosed individual is at least 18 years old.

C. Similar behavior before the age of 15 years.

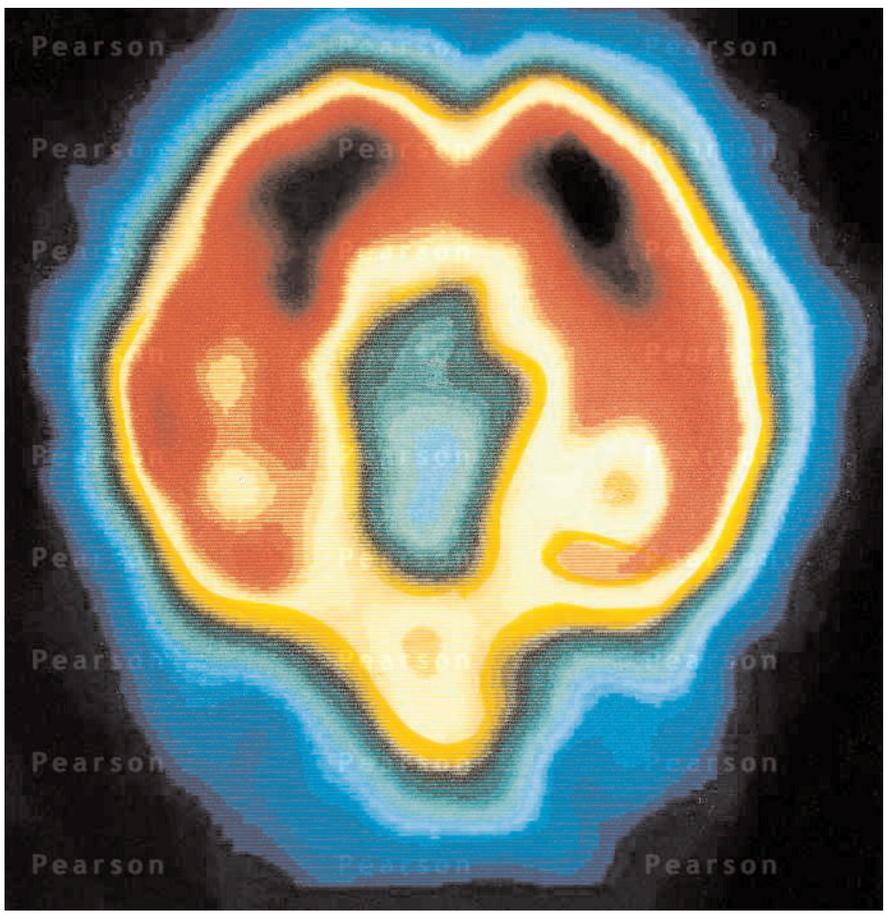
D. Antisocial behavior is not confined to psychotic episodes of schizophrenia or mania.

From Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), *4th ed. (Washington, DC: American Psychiatric Association, 1994), 633, 649. Not to be used for medical diagnosis.*

The Mysterious Case of Phineas Gage

Phineas Gage was 25 years old in Vermont's summer of 1848. He was in charge of a railroad construction gang, and he was highly regarded by his employers. While setting up an explosive charge Phineas was distracted and inadvertently set off an explosion at close range. An iron rod blasted into his face, shooting through the front part of his brain and out through the top of his skull. Amazingly, Gage regained consciousness soon after the accident. Due to the close care of a physician, Gage survived the infections that resulted from his injury and was pronounced cured in two months. His physical recovery was excellent.

But Gage's personality was transformed. He seemed to have lost his social inhibitions, becoming newly irreverent, capricious, and profane in speech. He no longer carried through on his plans. His employers wouldn't take him back. The only steady work he could find was as a "freak" in a traveling circus, where his wounds were exhibited to the public. Gage's life was forever disordered after his accident.



SUMMARY

1. Medicine has undergone considerable reform in the twentieth century, thanks to a substantial input of information from biological research. However, in the past this transfer of information from biology to medicine has largely neglected the Darwinian part of biology. In recent years, Darwinian biologists have attempted to rectify this oversight by contributing to the resolution of problems in medicine, ranging from contagious disease to aging to psychiatry.
2. One of the best-developed applications of Darwinian thinking to medicine has been the study of genetic diseases. One of these applications is the interpretation of the origin of genetic diseases. Darwinian biologists can also shed light on the prospects and value of engineering germlines and somatic cells.
3. The medicine of contagious disease has received some novel criticisms from Darwinian biologists. Of particular note is the differentiation of adaptive responses from pathological symptoms. Adaptive responses, like vomiting, may be distressing; but they may also save the patient's life if they are allowed to proceed. Physicians may overmedicate symptoms, thereby fostering the death of their patients.
4. Human aging is a problem with which conventional medicine has made little progress, at least in the past. Evolutionary analysis suggests that aging is a quintessential product of evolutionary mechanisms, not a side effect of cell biology. This insight suggests strategies for eventually treating human aging.
5. Psychiatry has never had a successful theoretical framework. Darwinian models of the human mind suggest one way to construct such a theoretical framework. As with the Darwinian analysis of contagious disease, it is important to distinguish between normal human brain functions that may cause distress and brain disorders that reduce Darwinian fitness. With such distinctions in mind, it is possible to make some sense of such phenomena as schizophrenia, phobia, depression, mania, and sociopathy.

REVIEW QUESTIONS

1. Why does evolutionary history produce universal human imperfections?
2. Pick one human genetic disease and analyze it from a Darwinian standpoint.
3. How plausible is it that HIV could eventually wipe out most of the human species?
4. If HIV did wipe out most humans, what would be the evolutionary prospects for the survivors?
5. Why should you take all the antibiotic that your physician prescribes?
6. If you had AIDS, would rather stay home or go to a hospital?
7. Are you, or someone you know, taking any measures to slow your aging? If you or they are, do you think that this measure will be effective?
8. Why do some people live more than 100 years, while others die from "natural causes" before reaching 50?
9. Do you have a relative with a major behavioral problem? If you do, analyze their condition from a Darwinian perspective.
10. Would you want to have a sociopath as a close friend?

KEY TERMS

ADA deficiency
affect
age-1
AIDS
antibiotic
antibiotic resistance
antiviral
anxiety
brain disorder
choking
cholera
dauer
delusion
depression
disease vector
Ebola
epiglottis
Ewald, Paul W.
frontal lobes
Gage, Phineas
genetic disease
geriatrics
germline engineering
gerontology
hallucination
histrionic
HIV
malaria
mania
maximum longevity
narcissist
Nesse, Randolph M.
phobia
personality disorder
pharynx
phenylketonuria (PKU)
phenylalanine
RNA virus
SARS
schizophrenia
smallpox
sociopath
somatic engineering
trachea
vaccine
virulence
Williams, George C.

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