CHAPTER 27

THE IMPORTANCE OF DISEASE

A species can change very rapidly if it is forced through a bottleneck (a situation in which only a few members of a species survive). For instance, imagine a species of ants that exists only on a small Caribbean island. Normally ants propagate by producing, at specific times of the year, flying males (drones) and females (queens) that mate in flight. The queen then lands, digs a burrow, breaks off her wings, and lives off her atrophying wing muscles while she raises her first brood. The first brood of worker ants then begins to take care of her while she continues to lay eggs and build the new colony. Suppose that, just at the time of the mating flight, which is synchronous among all the colonies of that species, a hurricane came along and blew all of the flying ants out to sea. However, in one colony, there were mutant defective ants whose wings did not develop properly and they could not fly. If they could mate on the ground, they would be the only survivors. Their children would carry the mutation and therefore also be unable to produce flying drones and queens. The ants on this island would thereafter be completely flightless. In one incident, the species would have changed radically. In this case we would say that there was a 100% selection for flightlessness.

We will consider what this term means, but remember also that the bottleneck process can work in another way. Suppose that there is a species, like pigeons, in which the color varies widely. In this hurricane, a pregnant female or a pair of white pigeons is blown to a new island. They can easily live on the island, and they continue to breed. However, of the wide range of colors known in the species, only white birds are found on this island. This is called founder effect, and is also an important aspect of evolution, as is seen in the Galapagos Islands (Chapter 7).

In laboratory settings, and sometimes in the field, we can measure the extent to which a single mutation favors or disfavors its bearer. We call this selection and, strictly speaking, it refers to the likelihood that the bearer will leave progeny to the next generation. The point is that the estimation of selection pressure can in the simplest case be an easy mathematical calculation. The calculation is as follows: Let us assume a type of flower, in which one homozygous form (page 185, Chapter 13) (RR) is red, the heterozygous form (Rr) is pink, and the other homozygous form (rr) is white. (I am avoiding using "dominant" and "recessive" because in this case it is not true dominance. However, it is easier to follow.) Let us now cross two pink flowers:

(1) $Rr \times Rr \rightarrow RR, rR, Rr, rr$

In other words, we should get 25% red, 50% pink, and 25% white flowers. What if we do not? In the worst case, we might get 33% red and 67% pink, but no white flowers at all. In this case we might conclude that the white flower cannot survive or, in technical terms, that it is a recessive lethal. We could check this in various ways, for instance by looking for imperfect seeds or seeds that did not sprout, or simply noticing that Rr × Rr crosses produced about 25% fewer seeds than RR × Rr crosses. In this case we would state that the rr genotype or r phenotype is lethal, and that there is 100% selection against it. If we found some, but fewer than 25%, white flowers, we could calculate the **selection pressure** simply as the ratio of those found to those expected. If, with large numbers of plants, we found 20% white flowers, then the pressure would be 80% (100 × 20/25) or 20% against white flowers. The calculation is actually a bit more complex, but this is the general idea.

We can also calculate what would happen, all other things being equal, if this pressure were maintained from one generation to the next. We could modify the calculation to take into account the fact that there were fewer white flowers in the next generation, and continue pursuing the calculation over numerous generations. In the simplest and crudest calculation, it would be as follows:

Presume that two purebreds meet.

(2) $RR(red) \times rr(white) - - > Rr(all\ red)$

The frequency of the gene "r" is 2 copies out of the 4 possible genes, or 2/4, or 0.5.

(3) $Rr \times Rr - - > RR, Rr, Rr, rr\ (3\ red\ to\ 1\ white).$

The frequency is still 4/8 or 0.5 However, let us assume that 20% of the whites die, perhaps without being seen. The expected frequency for r is 0.5, but what we find is the equivalent of RR=1; Rr=2; rr=0.8. The frequency with which we find r in the population is no longer 0.5 but (2+0.8+0.8)/(2+2+2+0.8+0.8) or the totals for r divided by the overall totals. The total for "r" is not 50% of the population, but 47% of the population. We then repeat the cross, plugging in the reduced frequency of "r" and again subtracting 20% of the resultant "rr".

Using this kind of calculation we could determine, for instance, whether or not a population could be converted in time from one type to another by the elimination of the less favored type or the greater success of the more favored type. The result depends on both the selection pressure and the size of the initial population. For instance, if one variation is favored over another by only 1% (for every 100 of the more favored variation that survive to leave young to the next generation, only 99 of the less favored variation survive to leave young) then the time needed to change the species to the more favored variation will be impossibly long. If the selection pressure is 10% (100 to 90 survival), then with an initial population of 600, it will take 68 generations before the entire population looks like the more favored variety, but if the new variation appears in a population of 6,000,000, then at the end of 100 generations it will still be seen in only 0.2% of the population or one in every 500—in other words, a rare variant. If the selection pressure is 50%

(one variant has a 2:1 advantage over the other) then if this new variant appears in a population of 600, it will completely replace the old variant in 16 generations. If the initial population is 6,000,000, then it will take 39 generations. What this says is that, first, most of this kind of change takes place in small, rather than large, populations (Chapter 29) and, second, that strong selection pressures can quickly force the conversion of a population from at least one characteristic to another (Fig. 27.1).

The thing about diseases is that they can quickly produce extremely strong selection pressures. If a disease breaks out that kills 95% of the population, and 5% survive because they carry a genetic trait that makes them resistant to the disease, then the population will quickly convert from being a sensitive to a resistant population. Since there are so few survivors, perhaps by accident or perhaps because of a connection of an otherwise irrelevant trait to the resistance, the survivors may well look or in other ways be different from the original population, and so the species will have changed.

Is this a realistic consideration for evolution? We have many examples in current events to indicate that such draconian selection does occur, and we have further evidence to suggest that it has happened before in history and that disease can play a major role in evolution. In fact, the whole purpose of sex may be to avoid disease. We will address each of these issues in turn.

Not the most obvious, but the easiest to understand, is a laboratory procedure conducted every day that is the basis of most of the most astonishing announcements from molecular biology. This is how to isolate a specific gene or to implant it into a certain cell. One can break up the DNA into gene-sized pieces and try to get the pieces into cells or bacteria, but how do you tell which cells have actually gotten a piece? The trick is to package the pieces with another piece of DNA, which has the information for resisting an antibiotic, usually a means of digesting the antibiotic (Fig. 27.2). Then the package is offered to cells that are normally killed by the antibiotic, and the cells are then grown in the presence of the antibiotic. All the cells that have not received the package are killed by the antibiotic, and only those that have absorbed the package—sometimes as few as 1 in 1,000,000—survive. We use this trick in research to quickly get rid of everything that we are not interested in but, within the universe of this Petri dish, it is evolution. Of the perhaps 10 or 100,000,000 bacteria in the dish, only a few, perhaps 10 to 1000, survive, and these are genetically different from all the rest. If the Petri dish had been the earth, the species would have changed.

Humans inadvertently conduct this type of selection on a regular basis. The poly-resistant bacteria (bacteria resistant to most antibiotics, “superbugs”) that make the headlines come from this process. Antibiotics are common in the environment. They get there through several means: Many are used in obvious medical situations, though failure of patients to use the full killing dose often results in the selection of the most resistant organisms. Although it is discouraged today, small supplements of antibiotics added to the feed of animals raised for meat often stimulate faster growth of the livestock at very low cost. It is possible that the antibiotics kill

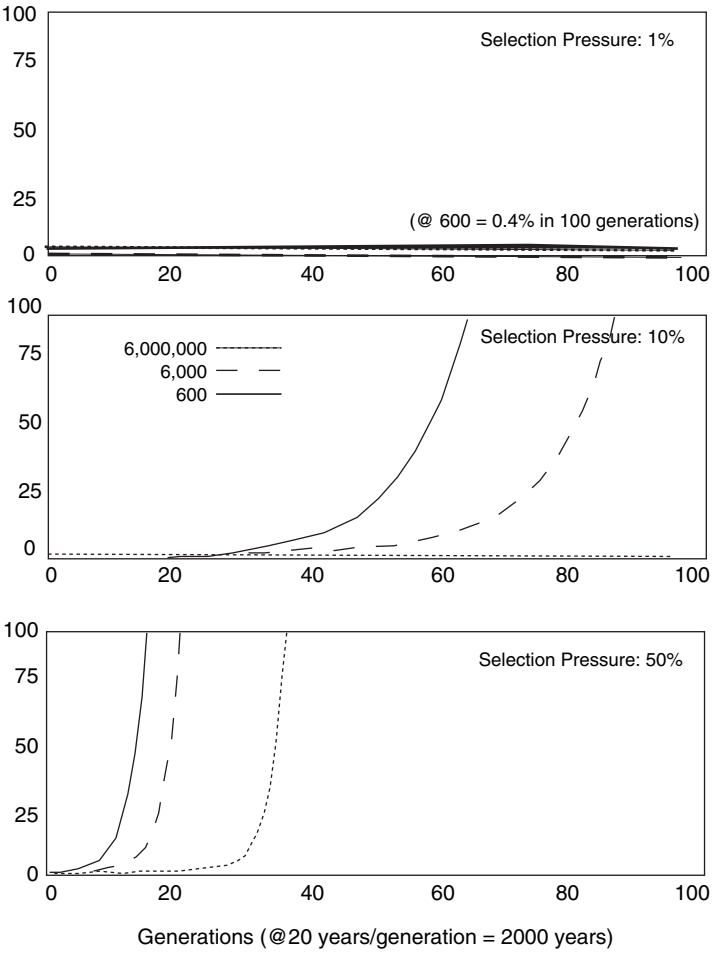

Figure 27.1. Selection pressures in theoretical populations. In each figure, the plots indicate the same selection pressures applied to populations of 600 individuals, 6,000 individuals, and 6,000,000 individuals. The selection is maintained over 100 generations, which would be approximately 2000 years for humans. The assumption is that a new recessive mutation appears in one individual in the population and is selected for at the pressure indicated. For a characteristic to go from essentially 0 frequency at the beginning to 100% frequency means that the entire population has been converted to the new characteristic. The selection pressures have been applied as follows: 50% selection (for every one individual of the normal type surviving to reproduce, two of the mutant survive to reproduce); 10% (for every ten normals, eleven mutants survive); and 1% (for every 100 normals, 101 mutants survive). With very low selection pressures, there is very little change. With very high selection pressures, even large size populations can be converted very quickly. With moderate (10%) selection, the freely-breeding population is converted only if it is relatively small. Calculations such as these, but of course considerably more complex, have led to the conclusion that relatively small human populations were under relatively severe selection pressure, leading to very rapid evolution

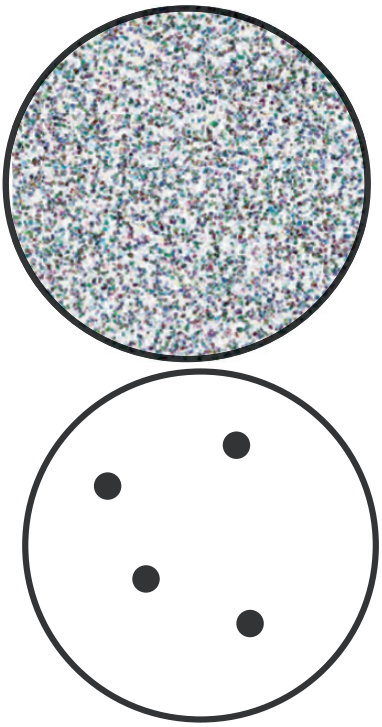

Figure 27.2. A Petri dish as a high selection pressure universe. Upper: 1,000,000 are placed in a Petri dish containing penicillin. Lower: Two days later, almost all of the bacteria have died, but 4 out of the 1,000,000 have survived and are now growing in the dish. Since each colony is a descendent of one bacterium, it is a clone and can easily grow to the numbers originally placed in the dish. If this dish were the world, the species would have changed

or limit the growth of the most noxious bacteria, thereby making the animals a bit healthier and faster growing, but the net result has been to expose all sorts of microorganisms to sublethal doses of antibiotics, thus selecting for those most resistant to the antibiotics. This practice has been a major means of generating bacterial resistance to antibiotics in our society. A third means of selecting for resistance has been misguided medical practice. For instance, during the Vietnam War, prostitutes in the Philippines were given prophylactic (preventative) doses of antibiotics to lower the spread of venereal disease. The theory was that the doses given, less than full curative treatment, would lower the number of bacteria that the prostitutes would carry and therefore protect them and their clients. Unfortunately prophylactic treatments work exactly in this fashion, allowing the survival of only the resistant bacteria. Thus syphilis and gonorrhea bacteria resistant to the most common antibiotics were selected for and their populations expanded.

Disease can frequently devastate a population. It is estimated that the native South American population decreased by 90% in the first 50 years after Europeans made

contact—a bit by war, but mostly because the native population had no resistance to the diseases carried by the Europeans (see page 45 and this chapter, page 367). Fungal diseases carried by travelers have in recent times wiped out the American elm and the American chestnut, both lovely and highly desirable trees, and of course a fungus carried from South or Central America to Ireland in the space of two years destroyed virtually the entire potato crop. Such tragedies happen routinely. In the beginning of the 21st Century, diseases are destroying Central American frog populations, large numbers of crows have succumbed to West Nile Virus, and Asian bird flu is threatening many bird populations. Usually such a sequence begins when, through expansion of range of either the host or the parasite (virus, bacterium, or fungus) the parasite encounters a vulnerable host.

There are two likely consequences of such an encounter. In the worst scenario, the parasite will achieve 100% kill. In this case both the host and the disease-causing organism are out of luck, since the host is now extinct and the parasite, at least in territory of the host, has no further prey to attack. However, the niche (lifestyle, see Chapter 24, page 336) is now unoccupied, and a new species may expand or evolve to replace the extinct one. For instance, if the victim was a bird that caught flying insects, another species of bird might expand into the territory or adapt to exploit this food resource. The second likely consequence, which is seen quite frequently, is that the entire species will not be exterminated, owing to an existence within the gene pool of the species of some genes that confer resistance to the disease. In this case the survivors will be resistant to the disease and, when it is all over, the species will have changed or evolved. In most cases the resistance will not be absolute, and the parasite and host will continue in such a manner that the parasite does some but not catastrophic damage to the host species. Often such a situation works to the advantage of both species (see red queen hypothesis, page 366). For

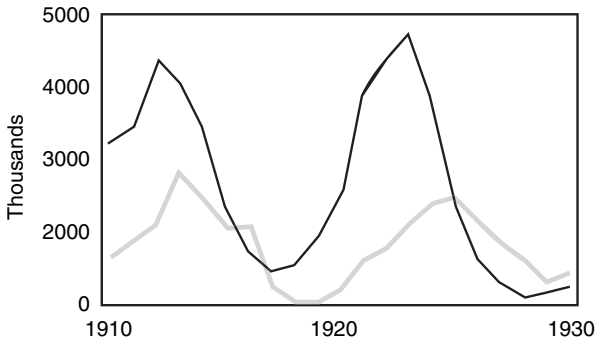

Figure 27.3. The population of lynxes depends on the population of hares and vice-versa. In this study by MacLulish in 1937, based on numbers of animals trapped in Canada, the lynx population (gray) increases approximately one year after the increase in the hare population (black). When the number of lynxes gets sufficiently high, they decimate the hare population, leading to starvation among the lynxes. The reduced number of lynxes then allows the hare population to build. The predator and prey cycle together, but neither wipes out the other. The scale for lynxes is 0 to 5000, since there are far more hares than lynxes

instance, the population of the lynx (a predator) tracks that of the snowshoe hare (Fig. 27.3). The populations oscillate, but then neither rises to unsupportable levels. This is very different from the misguided effort of the National Park Service to render the Grand Canyon more attractive to visitors. Considering that visitors liked to see deer and that the deer were attacked by coyotes, members of the service shot the coyotes. Sure enough, and as planned, over the next two years the numbers of deer rose, until the population had tripled. Unfortunately, there was an unforeseen complication. The many deer ate all available vegetation by December and almost all of them died before spring. It took many years before the population regained its original level. The lesson of biology was, better to choose your nemesis and live with it than to live without controls.

Besides the evidence of the damage that can be done to populations by the sudden outbreak of disease, there is substantial evidence that disease is a very strong driving force in evolution. The evidence ranges from the simple observation that what we, as humans, consider as ugliness in other humans is, far more often than not, an appearance caused by or very similar to an appearance caused by severe disease. It expands to the very large question of why animals and plants go to such lengths to maintain sexual reproduction. The first clue is to observe exactly what the courtship is all about. In most instances, males preen before females, and the females select their partners from among a few suitors. What determines their choice? Since birds undertake highly visible courtships involving aerial acrobatics or displays, bird courtship has been studied in some detail, but the rules apply to other animals as well. Usually the female notices one particular characteristic of the courting male. This may be any of a number of things: bright colors, symmetrical tail feathers, a strong, powerful, or magnificently varied song, or an elaborately built bower, filled with colorful objects. Male ospreys catch the largest fish that they can and display it, in flight, before females, to demonstrate what good providers they can be.

The preference of the females is toward the most of the characteristic, and the impact ranges from extravagant to ridiculous. Peacocks drag along ridiculously large tails, because when they are courting the female will choose the male whose tail has the most eyes. This can be easily demonstrated in zoos. One can take the male Don Juan or Rudolf Valentino, pluck a few of his tail feathers, and attach them to a less successful male. The less successful male will move up in the attractiveness rank, and the former champ will be far less successful in his courtship. Female swallows judge the symmetry of the courting male's tail. Again, if one captures a perfect, handsome, male and removes a few tail feathers, he immediately drops in the female's estimation.

This selectiveness on the part of the females can easily trend to the ridiculous. One can artificially exaggerate a characteristic that appears to be the object of selection, for instance by making display feathers even larger and, quite often, the female will be attracted to the artificially larger and more spectacular feature to the point of absurdity. From observations such as these, we conclude that some of the most bizarre structures and behaviors that we encounter in the animal world, such as giant antlers or the habit of American buffalo (bisons) to charge at each other over

the length of a football field, slamming their heads into each other in a collision that can be heard for miles, are the evolved result of sexual selection or its counterpart, competition among males for preeminence in the herd or social structure. Part of the answer may lie in the description of these modifications as "extravagant". These features become desirable precisely because they are useless. The peacock that can invest so much food energy in building the biggest and best tail, or the buffalo that can literally knock his opponent senseless, is obviously healthy, with excess energy available. Diseases or parasites sap energy, making the animals weaker and less capable of very demanding acrobatics or other feats of strength or agility, less capable of building elaborate tail feathers, and less capable of synthesizing complex but brilliant pigments. These results have been documented. A parasite-ridden bird may not synthesize perfect feathers, or may get into more scrapes than a parasite-free bird; unhealthy cardinals are less brilliantly colored than healthy ones. What is happening when the female selects the showiest or most spectacular male is that she is selecting the most disease-free partner. Thus sexual selection works to minimize disease in the population.

THE RED QUEEN HYPOTHESIS

There is a second aspect of sexual selection that again argues that the function of sex, and the reason that most animals and plants, invest enormous energy in sex, is the limitation of disease. This aspect can be best answered by asking the question, why do animals never evolve perfect defenses against their enemies? An approach to answering this question is to consider the Red Queen Hypothesis. In *Alice in Wonderland*, the Red Queen challenges Alice to a race, which they conduct, only to end up at the place where they started. This image in biology applies to the question of why the fox never manages to catch all the hares, or the hares never evolve to escape the fox. Like all these questions, we can address it on several levels. The first, of course, is the obvious: Both the fox and the hare are capable of evolving. If the hare proves better at escaping, the force of selection for the fox will be improvement in the fox's ability to catch the hare; if the fox becomes too good, it will select for hares that can escape the fox. Diagrammatically, it might look like this (with "become" or the arrows being shorthand for an evolutionary hypothesis):

Foxes catch more hares–>only fastest hares survive, hares become faster–>foxes starve, only best hunters survive, foxes become better hunters–>foxes catch more hares–>only fastest hares survive, hares become faster–>foxes starve, only best hunters survive, foxes become better hunters–>foxes catch more hares–>etc.

This is the Red Queen model: everyone runs and runs to stay in the same place. Phrased another way, and a bit more profoundly, neither the fox nor the hare can afford to be perfect. If the fox is perfect, it will eat all of its prey and starve to death. If the hare is perfect, there will be no predation, and it will quickly overpopulate the land, eat all available food, and starve to death. Thus fox and hare are condemned to live together in a mutual race in which neither is allowed to win.

How does this apply to disease and to sexual selection? First, it is a bit more difficult to follow, but the relationship of hare to fox is the same as the relationship of hare to tularemia or any other disease of hares: if the disease organism kills off the entire species, it has no further hosts and itself will die out, and if the hare is completely disease-free, it risks overbreeding and consuming all its food. Second, sexual selection generates the variety necessary to allow the target of the disease organism to keep its position in the Red Queen race. Consider a situation of fish in a pond that are subject to heavy infestation by parasites. The parasites attack the fish by attaching to a specific protein in the gills. Perhaps there are five varieties of this protein in different individuals of this species of fish. This gives 25 (5 * 5) different combinations of the protein in individual fish. If the parasite is particularly effective in interacting with protein type A, all fish bearing the A type will be heavily infested and may die. However, fish bearing proteins type B, C, D, and E will be less infested. When type A dies, parasites that can identify only type A will also die, but among the parasites, which are also sexual, there are some parasites that can interact with fish bearing protein type B. Thus the parasite will evolve to attack these fish, and the cycle will repeat, until ultimately we will return to the few survivors carrying type A. If the fish were not sexual, but reproduced as clones like the aphids mentioned above, the varieties would not be available and one round of parasitism would kill off the population. Sexual recombination provides the variation necessary to survive parasites and disease.

Finally, disease may have played an important part in the development of modern society. Jared Diamond, in a monumental work (*Guns*, *Germs*, *and Steel*) argues that western societies spread across and dominated other societies because of a happenstance of geography. In one of the few regions of the world in which both animals and plants capable of being domesticated lived, humans in the Middle East domesticated both grains and large animals. The animals gave them the power to build large edifices and the speed and endurance to travel long distances rapidly—both giving strong military advantages—but also other advantages. For during the period during which the cattle, horses, and other animals were domesticated, probably many people contracted diseases from the animals and probably died. The survivors were those resistant to these diseases. When, however, the possessors of the animals explored further afield, such as Europeans reaching the New World, they carried the germs of diseases that to them were mild but that were devastating to the indigenous peoples. In some areas of Central and South America, as many as 90% of the native population died within 10 years of their first contact with Europeans. As Diamond notes, no wonder the natives were terrified of these strange, pale interlopers.

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STUDY QUESTIONS

1. Look up information about the effect of the arrival of explorers on the native populations in any land that you choose, and evaluate the impact of disease on the two populations.
2. Many people, though requested to complete the full prescription of an antibiotic, stop taking the antibiotic as soon as they feel better. What is likely to happen to the bacteria in this situation?
3. Look up the biological history of the potato famine of Ireland. What happened? Why?
4. Do the current spread of diseases such as West Nile Virus, Asian bird flu, or Mad Cow Disease, threaten severe selection to humans? How about to the animals that they infect? Argue your position with real data as gathered from appropriate reports.
5. Will the human population change because of AIDS?
6. Can you identify any alternative explanation that would address the high prevalence of sexuality among both animals and plants?