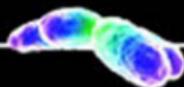


GERMS,
GENES,
&
CIVILIZATION



HOW EPIDEMICS
SHAPED WHO WE ARE TODAY



DAVID CLARK

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Preface

Humans typically labor under the illusion that they control their own destiny. This book argues that, in reality, invisible microbes often control human activities. Recent findings have shown that animals that develop without their natural bacterial inhabitants have defective immune systems and poor health. Thus, we and other animals depend on the bacteria for our healthy development. On a larger scale, we now recognize that microbes maintain the global ecosystem and are partly responsible for keeping our planet healthy. The amount of “good” bacteria that work to recycle nutrients and degrade waste is greater by far than the amount of “bad” bacteria that threaten human health.

Here I enter the intermediate zone between individual development and planetary ecology, to discuss how microbes have decided major historical events and shaped cultural trends. Furthermore, the emergence of resistance to infectious diseases has selected alterations in genes that affect human behavior.

This book is *not* a history of public health, medicine, or microbiology, although it does mention these issues. Instead, this book describes how infections have shaped both individual humans and their societies from the very beginning of civilization. Disease has influenced our cultural and religious beliefs, as well as determined the outcome of wars and major historical events. I have tried to show how beneficial long-term effects have resulted from epidemics that were terrible tragedies to those caught up in them.

Philosophically, we are just emerging from a period of transition between the perfectionist and selfish views of nature. The classic example, in the area of disease, is the idea that, over the ages, infectious agents will adapt to their hosts. Eventually, all diseases will become no worse than a bad cold. This is an attempt to retain a utopian future while allowing evolution to occur. Recently, we have come to realize that although some diseases become milder, others might evolve with greater virulence. We now see nature more as an arms race between life forms deploying assorted genetic strategies.

A second aspect of this more modern viewpoint, is to realize that the scale on which we view events is important. Improving a species through evolution inevitably involves the death of many less fit individuals. Applying this Darwinian idea to human populations lets us see that whereas mass fatalities from a plague are tragedies at the personal level, they can have positive effects when seen from a long-term perspective.

These positive effects vary from genetic changes that make us more resistant to the disease responsible for the epidemic (and often to related infections), to effects on human society that are hard to pin down and quantify. Epidemics have undoubtedly affected the outcome of many wars and conflicts. Whether these interventions were a good thing obviously depends on which side you support. Less ambiguous is the contribution of epidemics to the development of a free, technologically based society in the West. More ambiguous are the possible effects on religious belief and human behavior.

Modern progress in DNA technology and human genetics is generating a vast amount of data. Analyzing and checking this will take time. The next few years should reveal many

connections between infection, disease resistance, and alterations in genes that affect not only our physical characteristics, but also brain function or development and thus impact human behavior. We live in exciting times!

David Clark
Carbondale, Illinois

1

Introduction: our debt to disease

Early in the fifth century A.D., the Huns, led by Attila, emerged from the Asian steppes and swept across Europe. They faced no serious resistance. What was left of the greatest civilization the world had seen, the Roman Empire, was a tottering wreck. One more good shove and the remains of Roman civilization would have taken a final nose-dive. But strangely, on the verge of storming Rome itself, Attila withdrew. Why?

For many centuries the official answer was that God had intervened in some mysterious way to protect his chosen city, Rome, seat of the papacy. In more recent times, such supernatural explanations have fallen out of favor and the question has arisen anew. Some have suggested that Attila was overawed by the sanctity of Rome. But why would a pagan warlord like Attila stand in awe of a Christian center? Attila was by no means an ignorant barbarian: For example, he invited Roman and Greek engineers into Hun territory to install bathing facilities. However, his respect for Roman civilization

was clearly of a pragmatic rather than a religious nature. Another theory is that Attila was worried about leaving unattended his newly acquired homeland, in what is now Hungary. But then why did he venture out almost as far as Rome and hang around indecisively for so long before returning? All these explanations founder on the same point. It seems clear that Attila did indeed set out with every intention of taking Rome, but his expedition came to a premature halt.

Mounting modern evidence suggests that Attila was stopped by a virulent epidemic of dysentery, or some similar disease. Most of his men were too ill to stay on their horses, and a significant number died. In short, bacteria saved Rome. The ancient world had no knowledge of bacteria. Instead, most ancient cultures believed that epidemics were one of the main ways the gods expressed their displeasure. In the Bible, pestilence is often a punishment for wickedness, both for disobedience by the Israelites themselves and for intrusions by outsiders. For example, an epidemic saved the holy city of Jerusalem from the Assyrian invaders, providing a precedent for the failure of Attila to take Rome. So, in a curious way, the earlier explanation of God preserving Rome has reemerged in a modern scientific guise.

But before we rush to enroll the bacteria as honorary Roman citizens, we must consider another aspect of the issue. A major reason Rome itself was in such disarray when Attila approached was that it, too, had fallen victim to pestilence. Several catastrophic epidemics had swept through Rome in the period before the Huns surged into Europe. So whose side were the microbes really on?

Nowadays, floods, earthquakes, and volcanic eruptions are regarded as “acts of God,” at least by insurance companies. The implication is that neither the victims nor anyone else is responsible. This is not entirely true. People who

persistently rebuild their homes on a flood plain or along a fault line are at least partly to blame. Similarly, epidemics do not just happen to anyone at anytime anywhere without good reason. Neither the epidemics that struck Rome nor the disaster that overcame Attila's Huns were just random outbreaks of disease. What's more, their origins were interrelated.

Before Attila, Rome had several narrow escapes from other hordes of barbarians. Several times it looked as if the end was near and that the Romans would be overwhelmed. Yet somehow the Romans scraped by. Part of the credit must go to the Romans, who were an unusually determined people, not prone to giving up easily. Yet much of the credit also belongs to the unseen and unsung legions of microbes. It is relatively easy for us today to understand why an overcrowded, unhygienic ancient city suffered from persistent outbreaks of pestilence. Why disease so often intervened to protect the same city from successive waves of barbarians is more difficult to understand.

Imagine an ancient society that is moving along the path to urbanization. Large numbers of people are crowding into a growing city, such as Babylon, Athens, or Rome, which is much larger than neighboring communities. Infections normally spread more efficiently through crowded cities than through sparsely populated villages and rural areas. Sooner or later, some pestilence or plague will strike the emerging city. Its population will be decimated, and for a while it will be vulnerable. But if it recovers, its population will consist largely of those who are resistant to the plague of the day. In other words, denser populations are the first to build up resistance to the current infectious diseases in their region of the world. Next time a major conflict arises, the movements of armies or of refugees will spread infection around the war zone. People from rural communities or smaller towns will

have built up less resistance than the population of the city-state, so pestilence will fight on the side of the biggest city.

Once a major population center gains a significant lead over its competitors, the pestilence factor will make it extremely difficult to overthrow. This indeed is what happened to ancient Rome. A series of epidemics whose identities remain unknown devastated the Romans early in their history. Later, barbarians who ventured too close to Rome routinely succumbed to massive epidemics that had only mild effects on the Romans. As long as the Huns retained their nomadic lifestyle, they would have been little affected by epidemics. Even if an occasional marauder caught some infection from more settled and crowded regions, it was difficult for pestilence to spread among small, scattered groups of nomads. Once the Huns aggregated into a horde, under centralized leadership, the situation changed radically. On the one hand, they had little previous exposure to pestilence, so they lacked resistance. On the other hand they now formed a large, dense population, ripe for the spread of invading microorganisms. In a way, Attila's tragedy was the result of this vulnerable intermediate situation between nomadism and urbanization.

The general principle that *pestilence favors societies that have become resistant because of prior infection* has had a vast effect on human history. It has not only directed the growth and survival of the empires of the Old World, but it also was the major factor in European invaders' takeover of the American continent.

Epidemics select genetic alterations

Another result of ancient epidemics that experts have only recently come to understand is the accumulation of alterations

in the human genome. Through the millennia, a never-ending stream of hostile microbes has attacked and decimated human populations. Each time a human population is devastated by infectious disease, genetic selection takes place. People carrying genetic alterations that confer resistance, even if only partially, have a greater chance of survival. Consequently, their descendents will make up a greater proportion of the surviving population.

The result of constant epidemics is that, over the ages, distinct acquired genetic changes now protect us against many individual infections. We still carry these modifications in our DNA sequences, and recent investigations are revealing a steady stream of such genetic alterations, many surprisingly recent. Thus, in many ways, we are what disease has made us.

Yet another convoluted twist of fate appears here. Several well-known hereditary defects turn out to be side effects of resistance to disease. For example, sickle cell anemia is the result of hereditary resistance to malaria, and cystic fibrosis is associated with resistance to intestinal diseases that cause diarrhea and dehydration. A single copy of the cystic fibrosis mutation reduces water loss, thus protecting against a range of diseases whose most dangerous effect is dehydration. Two copies of the cystic fibrosis mutation slow water movements in the lung too much. So one copy of the mutation protects against disease, and two copies of the same mutation cause a hereditary defect.

The case of cystic fibrosis is especially revealing. The cystic fibrosis mutation is unusually common in those of north-west European ancestry. Calculations based on mutation rates and population genetics suggest that these mutations arose shortly after the collapse of the Roman Empire. This collapse led to a massive loss of general hygiene, especially in

the water supply. Doubtless waterborne intestinal diseases spread like wildfire, and eventually, mutations providing resistance accumulated.

Every cloud has a silver lining: our debt to disease

The way epidemics have intervened in history shows that disease is not just a uniformly negative matter. The outcome of an epidemic may be quite complex, especially over the long term. Whether we regard any particular outcome as “good” or “bad” depends partly whose side we are on and partly on the relative weight we give to short-term versus long-term effects. In this book, I point out the positive effects of epidemics. This is not because disease is beneficial overall, but because these less obvious beneficial side effects often are overlooked. If a virulent plague rages through society, the obvious response is to stop it by whatever means possible, not to sit around fantasizing about its effect on future centuries.

Not surprisingly, we normally think of infectious disease as our enemy. When a successful program of vaccination wipes out a blight such as smallpox, we feel no remorse that a unique life form has suffered extinction. When we learn that throughout the course of human history infectious disease has been responsible for more deaths than war, famine, or any other cause, this only confirms our viewpoint. Indeed, the victories we have achieved over infectious disease are among modern man’s greatest triumphs. Today industrialized nations have largely brought infectious disease under control. Unlike our predecessors of only a century or two ago, nowadays we mostly die from heart disease and cancer. Our longer lives give us time to reflect on the other side of this issue, and

I argue that, paradoxically, we also owe a great debt to infectious disease.

This approach is not merely idle intellectual self-indulgence. Infections that still threaten us either tend to cause disease in a subtler manner, or else they remain dangerous for other complicated reasons. The classic modern-day example is AIDS. This disease does not actually kill directly. Instead, it damages the immune system, allowing other diseases, impotent by themselves, to gain a foothold. Perhaps it is time for humanity to also take a more indirect and subversive attitude.

Over the long term, a positive side to disease emerges. Granted, if large black swellings are appearing in your armpits and you're about to die of bubonic plague, you'll find it difficult to maintain an unbiased perspective. Nonetheless, although the Black Death epidemics that ravaged Europe in the Middle Ages were devastating at the time, they had beneficial effects on a more global and futuristic scale. They shook up the repressive feudal system and, in the long term, made a major contribution to the evolution of Western democracy.

On the negative side of the balance sheet, we have the millions who died painful deaths in the plague epidemics. On the positive side, we must not forget those other millions who would have died in misery and poverty if industrial democracy had been delayed significantly. In our horrified emotional reaction to epidemics, we normally forget this latter aspect. We do not know for sure how many children would have died in infancy each century if the feudal system had continued. However, if we compare the infant mortality of 30%–50% that prevailed before industrial democracy with

the less than 1% infant mortality of today, we can clearly see that millions of innocent lives have indeed been saved.

On a more individual level, Charles Darwin probably caught Chagas's disease while on his famous voyage on the *Beagle* around South America and the Galapagos Islands. His resulting poor health kept Darwin at home for much of the rest of his life. Instead of wandering off on more expeditions to observe nature and collect specimens, he stayed put and pondered the origins of living things. This may well have played a major role in Darwin's compilation of the most influential book of the last few centuries, *The Origin of Species*.

As already remarked, whether such indirect effects are "good" or "bad" depends on your perspective. Should we consider the happiness of the individual, the benefit to a particular group, or the overall betterment of mankind? For that matter, how do we define the "betterment" of mankind? Whatever your outlook, the effects of infectious disease have been undeniably important in changing the course of history. Perhaps it is not too fanciful to think of "good" and "bad" diseases. Some diseases, like bubonic plague, may have had some beneficial long-term side effects on human society as a whole. Others, like sleeping sickness, have no positive aspect. Whatever our moral perspective, the effects of an epidemic on the overall fortune of a tribe, nation, or even a whole continent may be quite different than the immediate effects on the victims.

Crowding and culling

Pestilence has molded both our cultures and our genes over the long term. But before tackling these long-term effects, let's look at what actually happened to human civilizations

when diseases struck. Over time, humans increased in numbers and gathered together in villages, towns, and then cities. Populations grew larger and denser as civilization progressed. Sooner or later, when people are crowded together, infectious disease takes the opportunity to spread itself around, too.

Let's focus on severe infections with high mortality rates (such as smallpox, Ebolavirus, or bubonic plague). Each time pestilence passes through society, a sizable fraction is wiped out. The survivors give birth to the next generation, and numbers gradually increase again. Once the population is dense enough, another epidemic strikes and the cycle repeats. Over many generations, genetic resistance develops, so virulent pestilences wane into childhood diseases and may eventually fade away completely. Meanwhile, novel infections emerge and spread, taking the place of yesterday's retired plagues.

A crucial point for understanding the long-term effects of an epidemic is that death is distributed neither equally nor at random. Infectious disease strikes harder at some segments of the population than others. Let's start with factors that are wholly or mostly biological in nature.

First, older people and young children are especially susceptible. This is because the human immune system is not fully developed in the very young and is beginning to fade away in the very old. Conversely, some individuals may be immune to certain infections. Nowadays, such immunity is mostly due to artificial vaccination. Before this was available, immunity was normally acquired the hard way by catching the disease and surviving.

Second is the phenomenon of genetic resistance to disease. In contrast to immunity, which is acquired during an individual's lifetime, genetically based resistance is inherited

from one's ancestors. Individual people differ greatly in their inherent susceptibility to different diseases. When a population suffers from a dangerous disease, those with genetically based resistance survive more often than others. Consequently, inherited resistance gradually builds up over several generations. For example, the earliest reliable accounts of smallpox in Asia and Europe suggest that it was fatal 75% or more of the time. Yet over the next thousand years, the mortality rate fell to around 10%–30%. Then when smallpox was carried to the New World, the mortality rate among the American Indians was 75% or more. Thus, a virulent disease is vastly more devastating in a population that has never been previously exposed and has had no opportunity to build up resistance.

Many other factors affect our susceptibility to disease. These range from mainly biological to largely social in nature. For example, those who are poorly fed or live in bad housing and are cold, wet, and dirty are much more at risk than well-fed people who are dry, warm, and clean. Obviously, the closer people are crowded together, the easier it is for infectious disease to spread. These factors all lie on the interface where social conditions merge with biological effects.

Many of these factors can be lumped together, at least crudely. To put it bluntly, poor people are both more likely to become infected and also more likely to die if they are infected. Unfair as it may be, this is inevitably true in all real-life human societies. Today this is most clearly seen in the contrast between the industrial nations and the Third World. However, throughout recorded history prosperity and status have had their advantages. Even in societies of apes and baboons, higher-status animals tend to be better fed, a factor that helps them fight off many infections.

But how do you get to be rich or poor, high or low? To be sure, one way is to inherit money or social position (as distinct from genes) from your parents. But this ignores how your ancestors got rich to start with. Do competent, industrious, attractive, healthy, and brave people tend to rise through the ranks of society? Or is it the ruthless, greedy, cowardly, and corrupt who claw their way to the top? Whichever of these alternatives you espouse, for better or for worse, during a virulent epidemic, fewer people at the top will die than those at the bottom.

The message of this book

Humans typically labor under the illusion that they control their own destiny. However, I argue in this book that infectious disease has had a massive unrecognized effect on human history and culture. Moreover, constant epidemics with high death tolls have occurred throughout history and have selected major genetic alterations in the survivors. Modern DNA analysis, including the recent Human Genome Project, has revealed that alterations have occurred in certain individual genes. But many more changes remain to be discovered.

Some of these genetic alterations have mainly physical effects, but others may affect brain and behavior. For example, it is possible, though not fully proven, that genetic alterations that predispose humans to schizophrenia also protect against viral infections. As yet, the genes presumed responsible have not been identified.

Before dealing with these issues, we need to understand that many of our infectious diseases have emerged only very recently, after humans developed agriculture and settled into towns and cities (as discussed in Chapter 2, “Where Did Our

Diseases Come From?”). We also need to realize that a disease’s mode of transmission can alter its virulence over a relatively short period of historical time (as discussed in Chapter 3, “Transmission, Overcrowding, and Virulence”).

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