Modern Epidemics

FROM THE SPANISH FLU TO COVID-19

Salvador Macip

CONTENTS

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Translated from Catalan by Julie Wark

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Dedication

For my mother:

Thank you for all these years of unconditional support

The smallest unit of life – a single bacterial cell – is a monument of pattern and process unrivalled in the universe as we know it.

Lynn Margulis and Dorion Sagan, *Microcosmos: Four Billion Years of Microbial Evolution* (University of California Press, 1986)

But there is something terrifying about the fact that nothing can stop the implacable evolution of these viruses as they test, through mindless mutation, ever more strategies to facilitate their survival, a survival that just may represent disease and death for us humans.

C. J. Peters and Mark Olshaker, *Virus Hunter: Thirty Years of Battling Hot Viruses around the World* (Anchor Books, 1997)

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Introduction

An ever-present danger

In spring 2009, there was an outbreak in Mexico of an influenza pandemic that spread unstoppably around the world in just a few weeks. Many people were taken by surprise as they hadn't imagined that, with all the advances in medicine today, we could still feel so helpless when faced with such a common virus. Yet, scientists had been predicting it for quite some time. When the first edition of this book was published, over a decade ago, by which time that pandemic had started to abate, I was interviewed by some newspapers and repeated the same thing several times: it was indisputable that there would be another pandemic in a few years' time, and we had better prepare in case the virus that would be circulating then turned out to be more aggressive than A(H1N1), the so-called 'swine flu' virus, which was creating so many problems. Such long-term prophecies are easy to make because, if you are wrong, no one remembers, so you don't get taken to task about it afterwards. But, in this case, it wasn't prediction but certainty. All the experts I had spoken to or read while writing this book agreed that it was inevitable. Everyone who had sufficiently studied the matter came to the same conclusion: it wasn't a matter of waiting to see *if* it would happen but *when* it would happen.

When I said this, people looked at me not so much with fear as with an amused or incredulous expression. Another alarmist, they must have thought. In the Epilogue of this book, I explain how the publishers of the first version were also surprised when I anticipated the 2009 pandemic some months before it happened. They had an excuse, because they hadn’t experienced an infectious disease of such dimensions, but the attitude should have changed after the A(H1N1) flu, which could be regarded as the first pandemic of the modern era, the first to have attacked a globalized, frontierless world. This should have warned us of what can happen when, faced with the appearance of an unknown virus against which we have no defences, we are obliged to act swiftly in order to avert a possible tragedy. But, even so, the outbreak of COVID-19, the disease caused by the new virus called SARS-CoV-2, caught us unawares.

The responses to this second great twenty-first century world health crisis (in terms of viruses) are very similar to those of the first one, namely confusion, panic and uncertainty. Once again, mismanaged information has sown distrust among the public. Perhaps there is one slight improvement in that many countries have responded faster and have shared important data more efficiently. Despite the doubts and unnecessary delays of the early weeks, protective measures are now being more firmly applied. Yet, there are many issues still to be resolved if we want to be better prepared for future pandemics.

Fortunately, SARS-CoV-2 isn’t the ‘supervirus’ that I talk about later in these pages, but it does raise more logistical problems than any of the flu viruses we’ve seen recently. Although we are still not well enough informed about it, we do know that it spreads very fast (partly because those affected are contagious for a long period without symptoms), and that it has a relatively low mortality rate of probably somewhere near 1 per cent. To give some perspective, this is ten times higher than the 0.1 per cent for seasonal flu but much lower than the 50–80 per cent for Ebola. If we add up these factors, as well as the many uncertainties, there are more than enough reasons to be cautious and to act as fast as possible. It’s true that the symptoms it presents are relatively mild in most cases, but in some, especially for certain groups of the population (for example, elderly people and those with serious illnesses), it can be fatal. This, together with the great ease of contagion, can create very serious problems of global health, which is why it is essential to prevent its spread as soon as possible.

However, although COVID-19 is taking up so much media space, it isn’t the only infectious disease we should be worried about. In terms of health impact, the four big epidemics and pandemics are still influenza, AIDS, malaria and tuberculosis. It’s true that we’ve recently had the biggest Ebola outbreak in history, but it’s still a disease that is restricted to certain areas of the globe. At the same time, we’ve seen how the coronavirus family has gained prominence, and how these microbes are capable of creating worldwide alerts. The first serious illness caused by these viruses was SARS which, though it was seen as a possible long-term risk at the beginning of the century, appears to be fairly well under control for the moment. After SARS, in 2012 there was MERS (Middle East Respiratory Syndrome), but this, too, remained quite localized. It wasn’t until the appearance of the third great coronavirus, SARS-CoV-2, that all the alarms went off.

So, are the coronaviruses the latest danger for humanity? Would they deserve a chapter alongside the other four major infectious diseases? Right now, it’s hard to know. Coronaviruses usually come from bats, which act as reservoirs, the places where the viruses survive and reproduce. And it’s highly probable that other strains will end up jumping to humans in areas where there’s more contact with animals (and China is one of the main loci of the problem because of its traditions and lax regulation of public markets where wild animals are sold). But we will need to wait and see whether or not this ends up becoming a major health problem in the coming decades.

As for COVID-19, its impact will depend on how quickly an effective vaccine is found, produced and administered, and on the virus's ability to keep changing. It seems clear that it's a big enough threat to be taken seriously, and that it's going to cause major problems for quite some time. But, the most likely thing is that we will end up getting the better of it, if all goes well. It's possible that, afterwards, there will still be outbreaks but, in normal circumstances – once a good part of the population has a certain immunity after coming into contact with the virus, and when we have the appropriate complementary tools (vaccine, antivirals, and so on) – it would never cause another pandemic like that of 2020. Nevertheless, this doesn't mean that we can lower our guard. I must insist that there will be more pandemics, and the danger that one of them will be caused by an even more aggressive virus is always going to be present.

Let's do our homework

Meanwhile, what can we do? Prepare ourselves for the future. It's easy to forget the latent problem of pandemics when we've just overcome one and, in statistical terms, it's not very likely that the next one will appear any time soon. But governments have the obligation to plan rapid response measures and, even more important, to instruct the population. Unless people – all the people – participate, we won't be able to confront infections with any guarantee of success. We've already seen this twice in the twenty-first century: when there's a crisis at the global level, it's necessary to count on everyone to root out the problem. The conclusions we can draw in 2020 are the same as those reached in 2009. Most importantly: when a new virus appears, rapid, coordinated action is necessary until we understand the extent of the symptoms it's causing, even if they seem mild at first. And we can only achieve this if we all understand how an infectious disease works and what the real power of microbes is.

Though it may seem excessive, isolating infected populations, encouraging hygiene and avoiding large gatherings of people are highly effective strategies in these situations, especially when it comes to making sure that the disease doesn't cause its own particular kind of collapse of a country's health system, which would end up with many collateral victims. This is crucial in the early phases of an epidemic. But it's also necessary to improve public management of the crisis, which is invariably one of the weak points. And there will always be someone who believes the whole thing is a plot or an exaggeration, but we must manage to ensure that this position remains marginal, and that people listen to those who know what they are talking about. Hence, there needs to be a sound, well-coordinated communication strategy and, if possible, one with a single, reliable source of information (maybe the WHO, or maybe a new body) backed by all the authorities and the media and making the details widely available. And all of us also need to make an effort to learn a bit more about microbes.

SARS and MERS have been warnings of the danger that a microbe from this family could represent in the right conditions, and scientists spoke out loud and clear to announce it. Many people thought they were exaggerating because neither of the two epidemics turned out to be as serious as originally predicted. Now, with millions affected by COVID-19, from Asia to America and everywhere in-between, the fear of being vulnerable to the microbes around us has become generalized. Which position is more correct? Shrugging it off to the point of ignoring the experts' warnings, or panicking about going outside and breathing air that's full of invisible killers? The best idea, of course, is to find a middle course.

However, in order to make these kinds of decisions, we need clear information about the present risks of suffering from a serious infection and what we can do to prevent it. It isn't always easy to obtain this because we are constantly finding clashing opinions in the media, ranging from those announcing an apocalypse to others who believe there is nothing to worry about. Who is right? We must respect viruses and bacteria and understand that we can't always defeat them, and now, well into the twenty-first century, we also need to know the extent to which it's possible that a pandemic can cause millions of deaths, as has happened several times throughout history.

A tool for understanding the present and preparing for the future

This is where we scientists can help a little. Popular science books like this can make a humble contribution to general knowledge and, in doing so, gradually ensure that microbes cease to be the great unknowns we only talk about when it's already too late. Here, you will find some tools offering a better understanding of how infections work and what resources we have for stopping them. This information could be useful in the future, but it has special relevance now when COVID-19 has caused such an upheaval to our way of life. That is the reasoning behind publication of this updated, expanded edition, which includes everything we know so far about coronaviruses.

In the following pages, I've tried to fill in the gaps in general knowledge about microbes and to provide readers with a direct account of, and basic data about, such common but, in fact, little understood diseases like flu and

AIDS, which are caused by the most important microbes. On some fronts of our struggle against infections, we remain in a tactical draw, with no guarantees that the situation will continue like this indefinitely. On others, we are clearly losing the game. And according to some experts, the situation can get worse at any time and we won't be able to do anything to prevent it. We shouldn't even count on our few victories because all the ground we've gained could be lost overnight if we are not careful.

Few fields arouse as much fear and incomprehension as microbiology, the study of invisible organisms that are as likely to help us to survive as to wipe us off the face of the Earth. In recent years, we've not only seen the spectre of influenza making front-page news; we've also learned to live with AIDS – the most significant pandemic our species has suffered for centuries – and to such an extent that many people have lost respect for it. We've heard news of the advance of a type of tuberculosis that can't be cured with any drug, but we think that this is a problem that will never affect us. Thanks to irresponsible media campaigns, we've become so scared of vaccines that child health has regressed by several decades. We've discovered that a small amount of white powder inside an envelope can keep a whole country terrified for months. We've feared that the next war could be fought by throwing deadly bacteria at civilian populations. We've seen how the military considered that a disease we believed was eradicated could be more effective than an atomic bomb. And lurking behind all this are always the same culprits: microbes.

We must realize that viruses and bacteria haven't only shaped the history of humanity, they are also responsible for millions of deaths, although they are not always front-page news. We need to know the subject well enough not to be flummoxed by the inflated reports we find in the media but, at the same time, to know when we have to act quickly.

We must be aware of the strategies we have within our reach for combating microorganisms and the extent to which they can protect us. And, above all, we need to put an end to a series of myths and false beliefs that are hindering advances in the area of health. My aim as an educator is to remedy some of these shortcomings.

The book is divided into two parts, which are independent and can be read in the order the reader prefers. In the first, more general part, I will give an account of what microorganisms are and describe some of the historic pandemics that have seriously threatened our survival. The second part focuses on the main infectious diseases we haven't yet managed to control; namely, what we can rightly call the four great modern plagues: influenza, AIDS, tuberculosis and malaria. They are important because of the number of people they affect around the world, their serious economic and social impact, their aggressiveness and, in some cases, the scant means we still have for fighting them. Some have already spread all over the planet. Others are circumscribed to certain areas, but that doesn't mean they don't cause large numbers of casualties. I will assess how far we are from defeating them and the risks of seeing them turning into tragedies beyond our control. I will also discuss, in particular, the gravity of the present pandemic and how it's expected to evolve.

In this book, I want to raise several questions that I believe are necessary. Does our future depend on microorganisms? Why do antibiotics stop being effective? How much longer will they serve us? Will an AIDS vaccine ever be found? Or a cure? Why are we so afraid of influenza coming from animals, like bird or swine flu? Could a flu epidemic today wipe out half the world's population? Do we have the means to stop dangerous infections before they spread? Should we fear an attack with biological weapons? Are we immune to infectious diseases that have been eradicated?

What can we do to avoid being infected? Can vaccines cause autism? We will now move on to delve into the fascinating world of viruses and bacteria in order to find the answers.

I don’t think anyone would doubt today that infectious diseases are a global problem. They start in one corner of the planet, but our lifestyle helps them to spread like wildfire. Pandemics are still frequent, and we must learn from every episode so we can do better next time. These are problems we can’t ignore. I hope this book will help readers to see what it means to share the planet with all these invisible enemies and that, at the end of the day, we will be able to find together that much-needed point between alarm and caution which will allow us to survive as a species for many more millennia.

Part I
Sharing the World with Microorganisms

1
Travel Companions

We humans have managed to escape from our predators. In the security of urban settings, we don’t have to worry about being devoured by lions, tigers or other carnivores that are stronger and faster than we are. As a result, we’ve successfully occupied all the ecosystems and multiply like no other animal has ever done before. We therefore tend to think we are invulnerable, at least when it comes to competing with other inhabitants of the Earth for our everyday survival.

This idea couldn’t be more wrong. We are immersed in a constant struggle against an adversary so powerful it can eliminate the human race in a matter of months. Indeed, it’s been on the point of doing so more than once. I refer to microorganisms, our invisible enemies, the millions of microscopic beings sharing our habitat, the bacteria, viruses and many other minuscule life forms with which we have a very special love–hate relationship. Thanks to them, we’re alive. Because of them, some 14 million people die every year. Why are we still vulnerable to such infinitesimal organisms? This chapter will introduce the main kinds of microbes and describe how they interact with humans.

They were here first

Microbes are the oldest inhabitants of this planet. They’ve been around for between 3,000 and 4,000 million years, but humans didn’t discover them until a little more than a century ago when science was sufficiently advanced to let us see them close up with the aid of a microscope. During the first 2,000 million years, microbes, and specifically bacteria, had the Earth to themselves. They were the first to appear and will doubtless be the last to leave because they are not only the most diverse form of life but are also the one that most easily adapts to any conditions. If a catastrophe wiped out most life on Earth, they would probably be the only survivors.

There are more than a million kinds of microorganisms, most of them inoffensive. The main ones are bacteria and viruses, but to these must be added certain fungi, algae and amoebas. In both number and weight, microorganisms are predominant among living beings. If we could put all the microbes on one side of the scale and all the animals on the other, the microbes would weigh twenty-five times more. The fastest growing microbes duplicate every thirteen minutes, and the slowest every fourteen days. At this rate, if a single bacterium had all the possible nutrients and the right conditions, it could generate a colony that would weigh as much as the whole Earth in three days.

We shouldn’t forget that it’s thanks to microbes that this planet is habitable. Some 2,700 million years ago, there appeared a certain kind of bacterium that was able to use sunlight to transform water and CO_2 into energy. A secondary effect of this process, which is called *photosynthesis*, is generation of oxygen. Like toxic exhaust fumes given off by a car engine, the oxygen kept accumulating in huge quantities and ‘contaminating’ the Earth’s atmosphere. This inadvertent pollution ended up being providential for us as it permitted the appearance of a new class of beings – humans among them – that needed oxygen for their basic functions. To this very day, bacteria are important for keeping the planet in balance. Without them, life on Earth would be wiped out.

Space: the last frontier

Bacteria could also survive in outer space. Some very tiny species have been found (among them *Herminiimonas glaciei*, which was discovered in 2009). They can endure for more than 120,000 years under layers of ice three kilometres thick, practically without oxygen and nutrients. These conditions are very similar to those that might be found outside our planet.

We should be grateful for other things, too. Bacteria are also our ancestors. As I said, life on Earth was at first limited to minuscule single cell organisms. They gradually began to come together in groups of cells that, acting in concert, went on to specialize in different functions, now in the form of what are known as *multicellular* organisms. This is the path that led to the fabulous biological diversity we have today. As proof of our humble origins, there are still structures in human cells that come directly from those original bacteria. And they are essential for human life.

Peaceful passengers

We shouldn’t necessarily see microorganisms as a threat. On the contrary, coexistence with many of them is highly beneficial for humans and determines proper functioning of the organism. The human body, one of the most complex multicellular organisms in existence, consists of approximately 100 billion cells. But this needs to be clarified: I mean 100 billion *human* cells. If we are to be exact, we also need to count all the microorganisms that inhabit us. Initially, it was calculated that they might be ten times more numerous than our own cells, but more recent data suggest that a closer estimate would be one microbe for each human cell. In any case, we can venture that the human body is colonized by millions of microorganisms, of some 400 different species, which normally don't cause any illness. Put together they would weigh a kilogram. These data are mind-boggling, enough to make us wonder what a human being really is. A mixture of highly specialized cells and microbes that live in harmony? From this standpoint, we are perhaps nothing more than a walking ecosystem in which a series of microorganisms peaceably survive.

The microbes that are always with us are not only freeloaders but 'stowaways' that are very important for our metabolism. Humans, like all other animals, depend on them to survive. From them, we obtain vitamins, nutrients and protection against infections caused by their more toxic kin. Cows, for example, couldn't ingest grass without the help of the bacteria they have in their digestive tract, and neither could termites benefit from the cellulose in wood. There are plants we use as food, peas and beans for example, that need bacteria in order to fix the essential nitrogen from the sun.

Further proof of their importance is that it is thought that, when giving birth, mothers pass on to their children the 'good' bacteria that will settle in their digestive systems and protect them in the future. Hence, there are studies exploring what happens to babies born by caesarean, because these children haven't had to pass through the vaginal canal that would equip them with their first microorganisms. It's not yet sure what effect this might have on their future health.

Nomenclature

By convention, microorganisms, like all other living beings, are designated by using a first name (with the first letter capitalized) and a second name, both in Latin. The first is the genus name and the second the species name. The genus name can be abbreviated to the initial alone, and both tend to be italicized. Example: *Mycobacterium tuberculosis* (or *M. tuberculosis*) is a species of bacteria of the genus of microbacteria that causes tuberculosis.

In the domain of health, more and more importance is being given to what's known as the *microbiota*, or the set of all the microorganisms each person carries inside (and on the surface). It's believed that, depending on which microbes inhabit this microbiota, we can be more or less prone to certain illnesses or conditions.

One example of this would be that the type of bacteria found in intestines could determine whether we gain weight or not, as was first suggested in a study from 2006. After isolating intestinal bacteria from mice of normal weight and from others that were obese, scientists found that bacteria from the latter contributed towards weight gain in the former, even when they continued with the same diet. Humans have between 500 and 1,000 different species of bacteria in the digestive tract and it might well be that these also have an influence on a person's susceptibility to gaining weight. More recent studies support this theory. For example, in 2009 it was found that obese women have a high presence in their saliva of bacteria called *Selenomonas noxia*. By contrast, thin women show a very different set of bacteria.

Secondary effects

It’s been known for some time now that antibiotics can disrupt the balance of ‘good’ bacteria. Medicines eliminate infections but are unable to distinguish between aggressive and innocuous microbes. Depending on the treatment, even weeks can go by in some cases before the bacterial composition of the intestine, for example, completely recovers. This can then give rise to diarrhoea or new infections caused by other harmful bacteria, especially in people already weakened by illness.

This shows that it is not only our intestines that are full of microorganisms. Our mouths, too, normally have between six and thirty different types of bacteria. And skin is another organ that is home to thousands more. It was once believed that most of them were of the genus *Staphylococcus*, because when samples taken from human skin were cultivated in the laboratory, they were the most visible. But this doesn’t mean that there aren’t many more. There are others that don’t divide so quickly. Indeed, with the new tools of genetic analysis, it’s been possible to see that the set of denizens of human skin is much more complex than was previously thought, with up to 1,000 different species, which is to say, a number that’s comparable with that for the intestines. The skin behind the ear is the zone with the least diversity of bacteria, with only fifteen kinds, while the forearm has as many as forty-four. This varying distribution might explain whysome skin diseases appear in certain zones and not in others. As in the intestines, bacteria on the skin have important functions, so, for example, oilier zones have some bacteria that produce a moisturizing substance to stop the skin from cracking.

In recent years, several studies have set about the task of identifying all the microorganisms that are to be found in different organs, generally using modern techniques to read their genes in order to relate them to obesity or illness. These studies give us a general idea of the microbes we carry around with us, although each person's flora is, in fact, unique. Almost like our DNA. It depends more on the zone in which we live than on our genes, and personal habits have a considerable influence as well. An article published in January 2009 demonstrated that sets of intestinal bacteria vary even between twins. Nevertheless, the members of a family living under the same roof have similar flora. The article also indicated that obesity reduces the diversity of flora, as well as altering the genes and metabolism of microorganisms. It's speculated that this might have consequences for our health, but we still aren't sure what they might be.

This knowledge we are acquiring about the microbes that coexist with us has led to questions about whether they can be used for therapeutic purposes. There are now studies looking into ways of changing the composition of a person's microbiota as a way of curing illnesses and even regulating the metabolism with the aim of weight loss. The easiest way is to take microbes from a healthy person's faeces and transfer them to the patient. Informally known as a stool transplant, this isn't such a simple process as it may appear, because it requires, first of all, filtering out the bad microbes and other contaminants.

It's still not known whether this procedure might have any real benefit, but what is undeniable is that the microbiota plays an important role in our health, both positively and negatively. This could be more far-reaching than initially imagined. Some studies have even shown that the microbes inhabiting our intestines could affect the brain and somehow influence behaviour.

The dark side

It’s well known that not all microbes are as beneficial as the ones I’ve just described. A group called *pathogens*, amounting to only 1,415 of all those that exist, have been found to cause infectious diseases in humans. Although they are clearly a minority, their impact on society has been, and is, immense.

Infections occur when one of these pathogens manages to enter our organism and overcome its defence systems. Problems arise when the microbe starts drawing on the resources of the organisms it has invaded to multiply nonstop. If this isn’t checked fast enough, it will end up interfering with the normal functioning of the body, presenting the symptoms characteristic of each infection, depending on the organs the invader prefers. Some of these symptoms are shared by many infectious diseases, for example, fever, shivers or feeling unwell in general.

It’s commonly believed that, thanks to the discovery of antibiotics, pathogenic microbes have ceased to be the terrible threat they were until just a few decades ago. To some extent, this is true. Nevertheless, we are a long way from being able to feel relaxed about this. On the one hand, bacteria that are resistant to the most commonly used antibiotics are constantly appearing. On the other, some serious illnesses still exist for which there are no vaccines or treatment. And there are still others that have both but, even so, we can’t stop them. Moreover, it should be recalled that antibiotics are only useful against bacteria, but they don’t work with viruses. It’s true that we have antivirals to fight these microbes, but they aren’t so effective, and we still haven’t produced such a wide range either. This, then, is a neverending struggle.

A bit of terminology

With regard to infections, there’s a series of terms that are frequently used to define their reach. For example, an *outbreak* is an infection localized among a relatively small group of people, for example, a family, a school or even a village. A typical case would be food poisoning, which tends to affect only those who have eaten food containing pathogenic microbes.

The next level is an *epidemic*, which is defined rather arbitrarily as an accumulation of infected people that’s bigger than ‘normal’. For example, if a disease is very rare, a mere handful of cases could be regarded as an epidemic. When an epidemic has spread through more than a continent or even the whole planet, we call it a *pandemic*. Technically speaking, the WHO officially declares a pandemic only when a disease goes beyond six phases, ranging from detection of the microbe in animals (phase 1) through to the continuing presence of the disease in more than one of the regions defined by the organization (phase 6).

An infectious disease that’s constantly present in a region without any significant fall or rise in the number of cases is said to be *endemic*. For example, malaria is endemic to many parts of Africa. Whether or not an outbreak turns into an epidemic, a pandemic or becomes endemic depends on many factors, among them the speed at which it spreads and the virulence of the disease it causes.