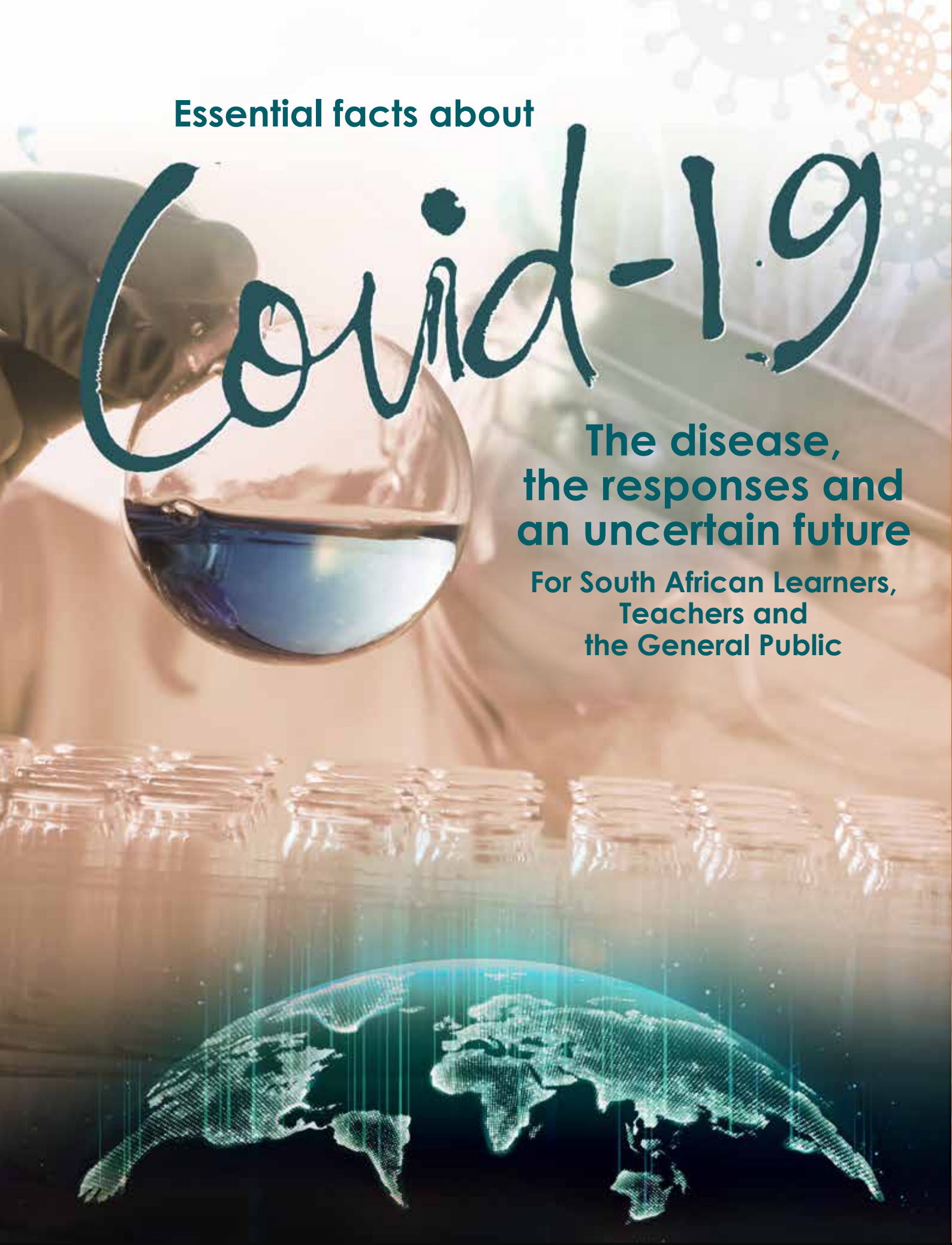
Essential facts about

Covid-19

The disease, the responses and an uncertain future

For South African Learners, Teachers and the General Public



Commissioned by the Academy of Science of South Africa (ASSAf)

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Applying scientific thinking in the service of society

The **Academy of Science of South Africa** (ASSAf) was inaugurated in May 1996. It was formed in response to the need for an Academy of Science consonant with the dawn of democracy in South Africa: **activist** in its mission of using science and scholarship for the **benefit of society**, with a mandate encompassing all scholarly disciplines that use an **open-minded** and **evidence-based** approach to build **knowledge**. ASSAf thus adopted in its name the term 'science' in the singular as reflecting a common way of enquiring rather than an aggregation of different disciplines. Its Members are elected on the basis of a combination of two principal criteria, **academic excellence** and **significant contributions to society**.

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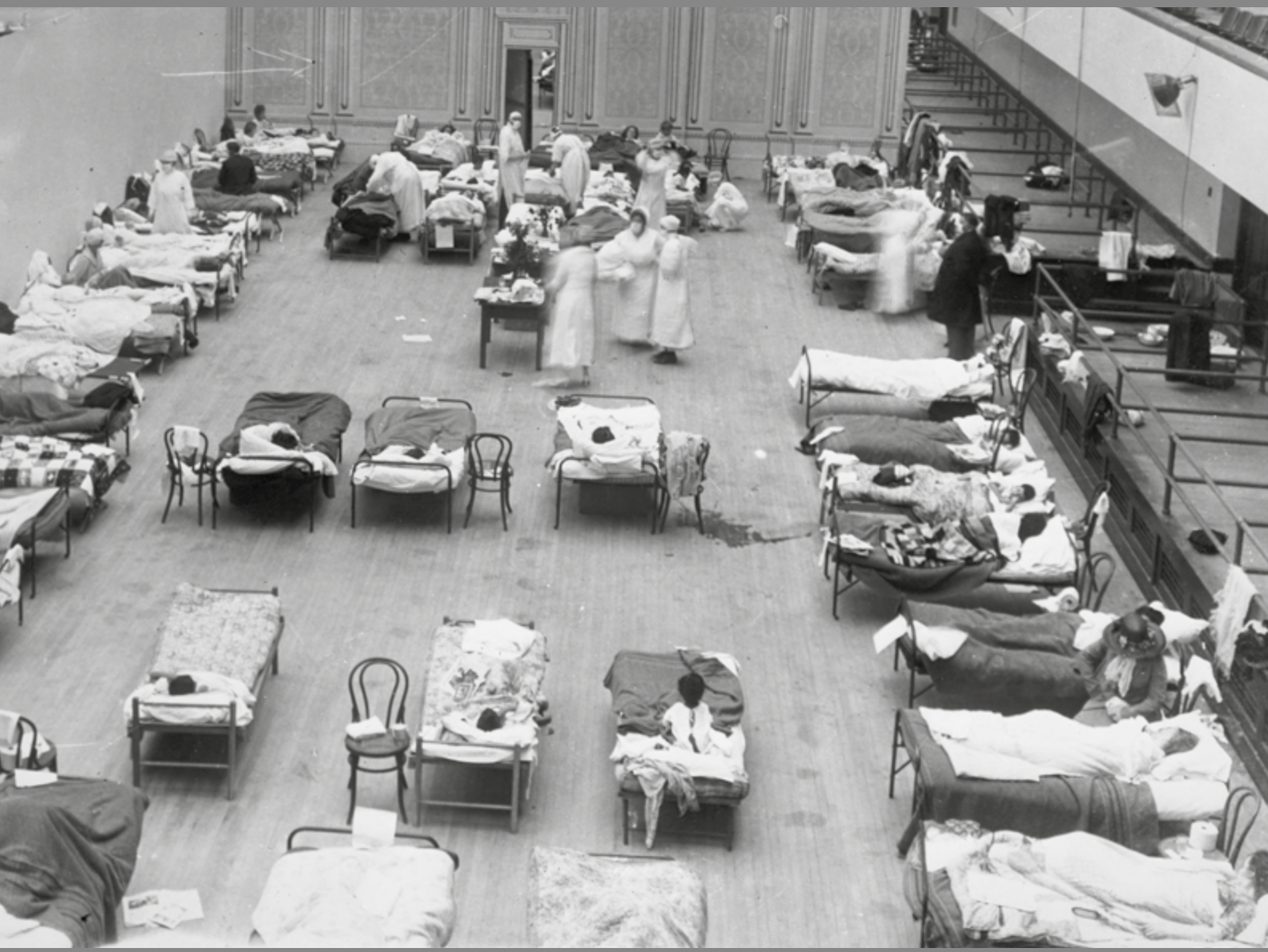
CHAPTER **3**

Infectious Diseases in World History

Viruses and viral infections are probably as old as life is on this planet. There is evidence that our human ancestors were exposed to viruses, but because populations were small and isolated, these were not pandemics as we know them today. The establishment of agricultural communities, animal domestication, and much later colonialism caused new viral epidemics and brought us into modern times of vaccine and antibiotic development.



Volunteer nurses from the American Red Cross tending influenza patients in a temporary hospital.
Source: https://commons.wikimedia.org

In Chapter 2, we saw how epidemics have periodically had devastating consequences in South Africa. We now look at epidemics throughout history in a broader perspective, looking further back in history and throughout the world. It is useful to understand how human evolution, history, and pre-history have been shaped by our interaction with viral and bacterial pathogens.

Pre-history

During our pre-history, say the Neolithic period (this is at the dawn of agriculture), the way viruses interacted with humans was different. Because population sizes were much smaller, there were fewer opportunities for sustained virus transmission. The viruses that did cross over from animal populations (which are generally RNA viruses, like coronaviruses and Ebola-like viruses) could not evolve to sustainable levels because there were simply not enough people to infect. People who study mathematical biology have shown that sustained transmission between humans requires populations greater than a minimal size and with sufficient contacts.

Epidemics and colonialism

The role of viruses changed as our populations became much bigger and there was differentiation into different countries and nations. Over time these worlds started colliding. For instance, during the colonial era the Americas and Africa were colonised by European nations. The so-called Old World came into contact with the so-called New World, and with the colonists came new diseases. Very often the viruses associated with the Old World were not known in the New World, with the consequence that people in the New World often lacked natural immunities. For example, when the Spanish army invaded the Aztecs in the 1500's, a major factor in the Aztecs' defeat was the introduction of smallpox and other infectious diseases by one or two Spanish soldiers. As smallpox spread through the Aztec population, their armies and civilians were largely decimated by this new virus.

The so-called Old World came into contact with the so-called New World, and with the colonists came new diseases.

Impact of our association with animals

RNA viruses became more prominent as our population sizes grew and as our agricultural practices changed. A major reason for annual flu epidemics is probably the ability of the influenza virus to replicate in human, bird, pig, and duck hosts, as well as wild birds. This sharing of hosts is also what makes the virus so effective in changing. The genetic material of the influenza virus is segmented. If a strain from a chicken mixes with a strain from a pig, which can happen if two viruses infect the same animal (see the diagram), they may swap genetic segments in a random

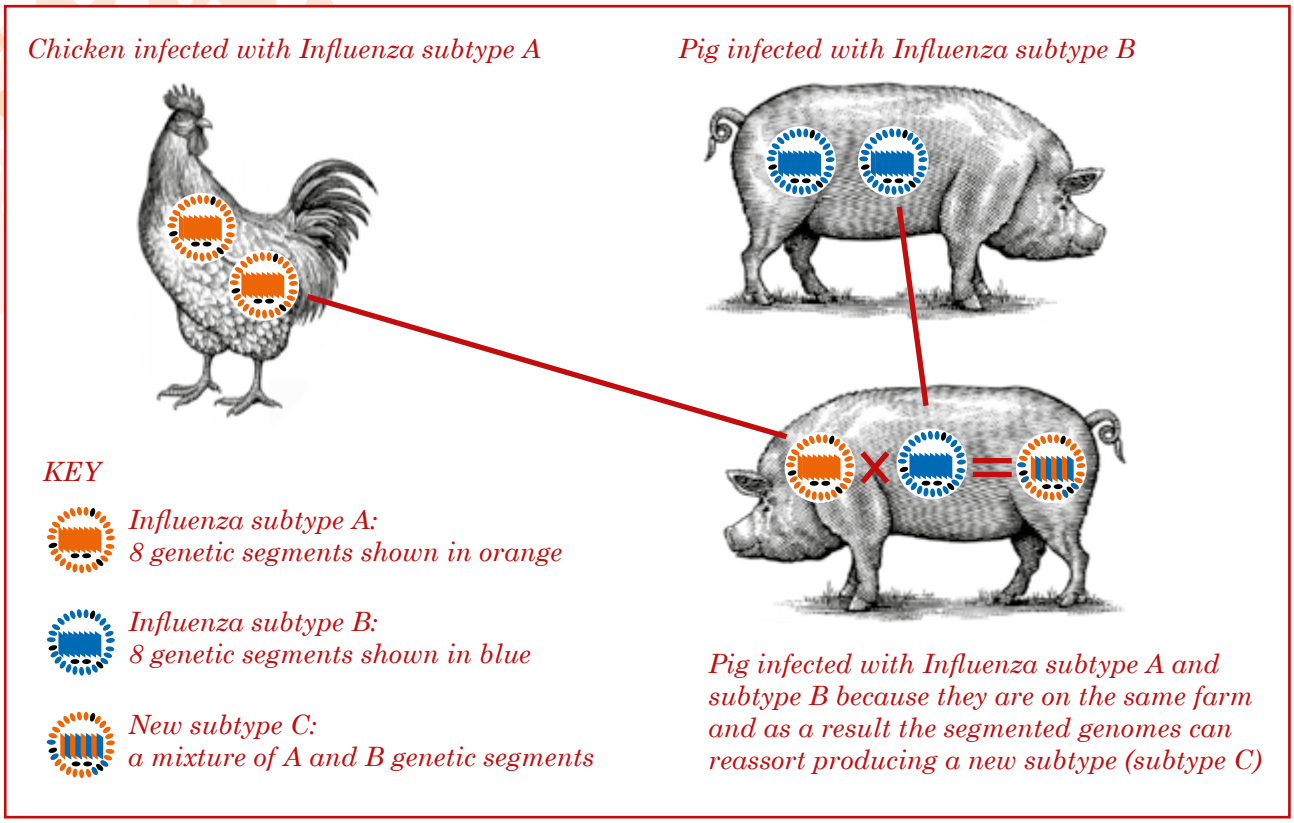


Figure 3.1 How influenza virus may produce a new subtype by genetic reassortment

Copyright: Steven I. Durbach

process called genetic reassortment (or recombination) to produce new virus subtypes.

While we are currently facing a major coronavirus pandemic, the flu, because of this mechanism of genetic change and our association with farm animals, continues to pose a threat, and in the last hundred years has produced several major epidemics. Most famously, the 'Spanish' flu pandemic, which took place around the time of World War I. This pandemic killed an estimated 50-100 million people (3-5% of the world's population at that time). The Spanish flu virus probably originated from birds. Although typically these viruses can replicate efficiently in humans, they cannot transmit from person to person unless they undergo a series of mutations in some key genes. The more often a human is infected by a bird-associated flu virus, the more likely the mutations required for a human epidemic will take place. It is a simple 'numbers game'. That is why when flu outbreaks occur in chickens, the entire chicken population must be destroyed to prevent the potentially devastating consequences of the bird flu spreading to humans. More recently, major flu epidemics that killed more than 100 000 people occurred in 1957 and 1968 (the Hong Kong flu) in Asia, and worldwide in 2009.

Dramatic examples of how agricultural and food-making practices have brought humans closer to animal populations and thus to novel RNA viruses also abound.

For example, the Ebola RNA virus comes from humans eating wild animal meat such as monkey meat (called bush meat). The National Institute of Communicable Diseases in Johannesburg was instrumental in tracking these viruses and was the first to discover the source of the Ebola virus about 40 years ago, through work by the famous South African Virologist Margareta Isaacson who tracked the virus down to its source in Zaire in 1976. Ebola has a very high mortality rate, of about 60-70%, and is an excellent example of how a virus can be too lethal for its own good. Unlike the flu, which can infect millions annually, in large part because it does not debilitate its host too much, Ebola makes its host so sick that infected people generally isolate and, therefore, transmit the virus less frequently. Moreover, Ebola relies on contact with bodily fluid for its transmission, which also makes it more difficult to spread than airborne viruses. Nevertheless, one of the most recent Ebola outbreaks in East Africa (2013-2016) claimed more than 11 000 lives. This epidemic, however, prompted the development of a novel vaccine. In the wake of this outbreak, the Coalition for Epidemic Preparedness Innovations (CEPI) was formed to foster a coordinated approach to developing new vaccines in order to provide countries with a vehicle to develop and prioritise the most appropriate vaccines to deal with future outbreaks.

When a virus jumps to humans from animals, as in the case of Ebola, the virus is most virulent, but sometimes evolves over time to become less virulent.

Fortunately, viruses often also evolve to become less virulent. This allows a virus to spread to larger numbers of people. Often when a virus jumps to humans from animals, as in the case of Ebola, the virus is most virulent, but sometimes evolves over time to become less virulent.

Ebola periodically jumps to humans from an animal reservoir. Wild animals represent a potentially extraordinarily rich reservoir of different types of RNA viruses that can on the rare occasion cross the species barrier to us. The SARS CoV-2 virus, for example, is hypothesised to have originated in a so-called 'wet market' in China where people trade in wild animals. These wet markets bring humans into close contact with wild animals and increase the probability of successful transfer from an animal to a human host. This probably happens often but the transfer leads nowhere in most cases due to a lack of sufficient human-to-human transmission. Viruses spreading among animals are generally not adapted to human hosts, so they are usually not successful in triggering an epidemic among humans. But the more animal to human transmission occurs, the greater the chance that rare variants with a lucky mutation (because mutations are entirely random) arise that can efficiently replicate in a human host, and, as with SARS CoV-2, have devastating consequences.

The bubonic plague and other epidemics

Throughout history, human society has periodically been impacted by massive epidemics leading to the death of a significant proportion of the human population at the time. These include various plagues or epidemics caused by both bacteria and viruses. Above we described the influenza virus, but the range of infectious diseases is enormous. An epidemic can be relatively minor, or it can decimate large swathes of a population, as occurred with the bubonic plague, caused by the bacterium Yersinia pestis. The plague, now easily treatable with antibiotics, probably spread to Europe in the Middle Ages via the expanding trade routes brought about by increased shipping. The disease was spread by rats that were largely immune to the bacterium. Fleas that bit the rats went on to bite people, thus transmitting the bacterium. The earliest known outbreak was in Rome in 590 AD. The most devastating outbreak was in Europe, Asia, and North Africa in 1346-1353. In those seven years, it killed 75–200 million people, which included 60% of the population of Europe.

The people of Tournai bury victims of the Black Death. (Tournai, c. 1353).
Source: https://commons.wikimedia.org/wiki/File:DoutielI3.jpg

It is also interesting to note how human behaviour can affect the re-emergence of certain outbreaks. Measles, for example, was well controlled by vaccination that was developed in the 1950's and was declared to be eliminated in the US by 2000. However, strong opposition to vaccination by concerted misinformation by anti-vaccination campaigns has led recently to a resurgence of the disease.

History of vaccination

The biggest breakthrough our species has had against viruses has been with the advent of vaccination. Vaccination has a surprisingly long history, but has been taken up into the Western scientific canon only in the last 220 years. This occurred when Edward Jenner noted that cow maids whose job it was to milk cows would occasionally catch a mild pox disease from cows called cowpox. The women so infected were often relieved as this usually meant they would not catch the dreaded

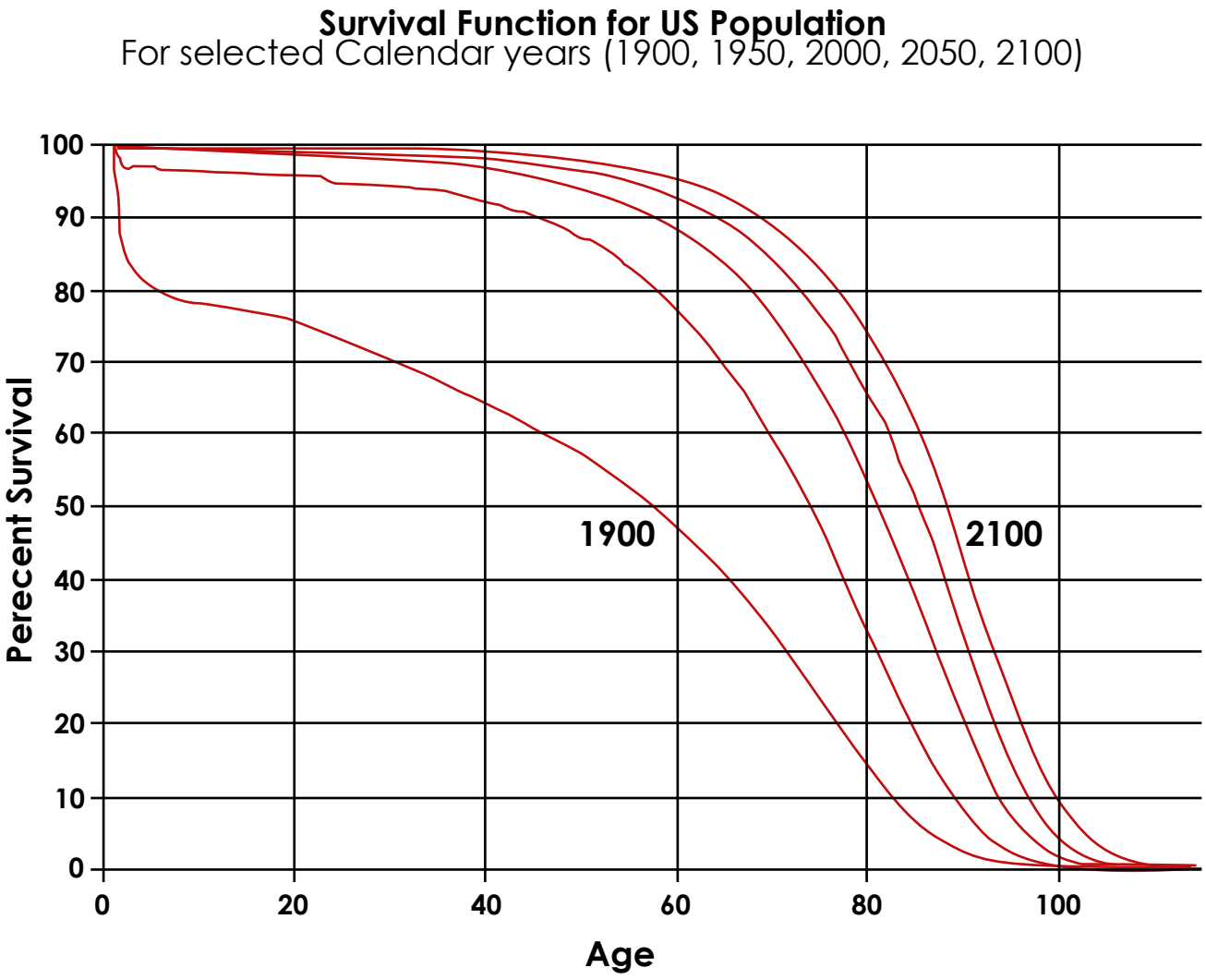


Figure 3.2 Survival Function for US population
Courtesy of US Social Security Administration, https://www.ssa.gov/oact/NOTES/as120/LifeTables_Body.html

smallpox disease. Jenner set about taking material from one of these cowpox lesions and inoculated it under the skin of a young boy, James Phipps, whom he later inoculated with material from an actual smallpox lesion. The boy did not go on to get smallpox. For hundreds of years prior to this in China, Africa (for example in the Sudan), and Turkey–and probably elsewhere as well, people had been responding with varying success to smallpox by a process called variolation, where material from lesions of mild smallpox cases was scratched into the skin of potential smallpox cases. In many cases, these people never developed the full-scale smallpox disease.

Although bacteria and viruses are by no means the same, their spread can be similar and their effects can be similar in how they make us sick, because they do so by replicating in our cells. Some bacteria, like the food-borne pathogen Salmonella, replicate in our cells and some like a Staphylococcus, the bacteria responsible for many skin infections, simply replicate in our tissues without invading our cells. Remember that, unlike viruses, bacteria do not depend on a host cell for their replication. Other bacteria, such as Mycobacterium tuberculosis that causes tuberculosis, are similar to the SARS-CoV-2 coronavirus in that they are also transmitted by small droplets produced by coughing (or sneezing). Today we treat bacterial infections with antibiotics. Although antibiotics are in no way like vaccines, they are our main means to combat bacteria. Their impact on human society is about as profound as the impact of vaccines. Antibiotics completely changed the

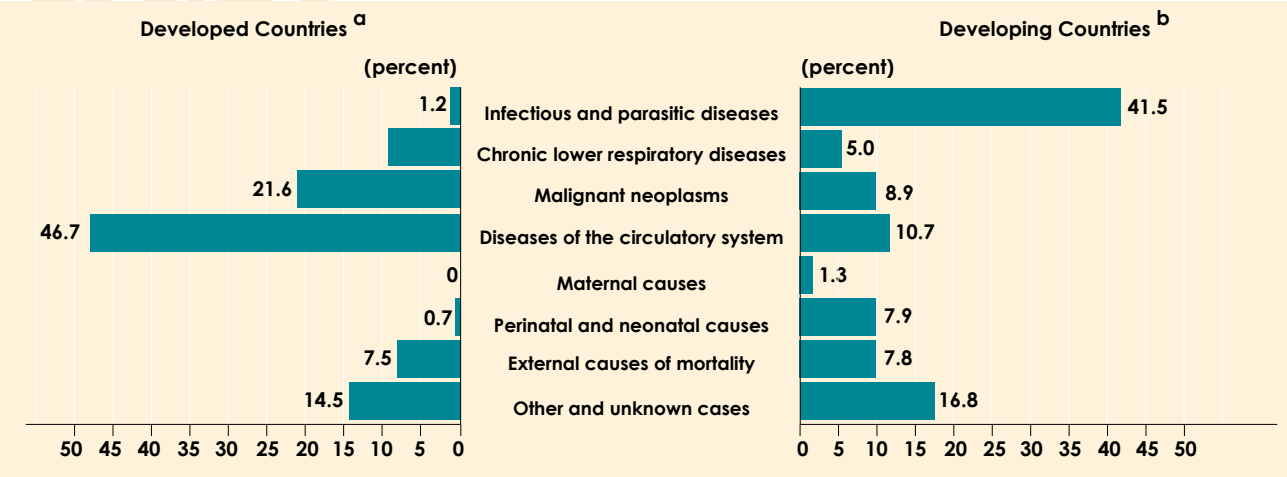


Figure 3.3: Causes of death in developed and developing countries (deaths per thousand)
Source: World Health Organisation (WHO) The World Health Report 1995. Bridging the Gaps (WHO, Geneva, 1995)

threat that micro-organisms had on our lives. It certainly made us very confident in our position in the natural world. Now we are not only at the top of the food chain. We are also no longer at the extraordinary mercy of the microbial world.

The US actuarial data in Figure 3.2 show that a little over a century ago, at least in the US, one in five infants did not make it to the age of five, and one out of three did not live beyond 40. The situation, however, has greatly improved. In 1900 the probability of surviving to 50 years old was 50%, whereas in 2000 50% are projected to live to well into their 80s. The most impressive feature is the massive improvement in child mortality, which is all but eliminated in children born from the 1950's onwards. This is primarily the result of large-scale vaccination programs. Similar improvements have occurred elsewhere, although the developing world lags behind, or has been partly neglected in this success story.

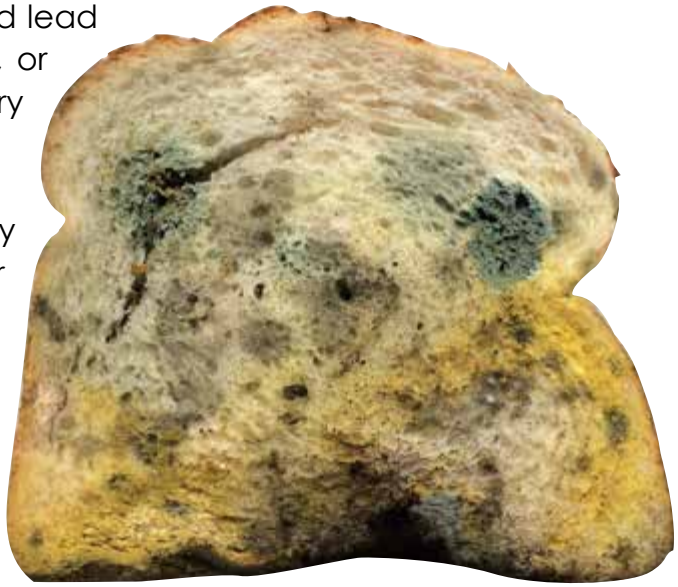
Because of the huge research and development costs needed to develop new antibiotics and vaccines, pharmaceutical companies often invest little in vaccines and drugs for countries that cannot afford them. Organisations such as the Bill and Melinda Gates Foundation have contributed huge amounts of money for developing drugs for diseases primarily afflicting the Third World. Great progress has been made for diseases such as TB as a consequence of this effort. South Africa has been a great beneficiary, and important research at local universities and institutes has been able to flourish towards this end. But a great disparity still exists if you consider the Figure 3.3 from the WHO. Note that non-infectious diseases are more prevalent in developed countries, but mortality due to infectious diseases is significantly higher in developing countries.

The discovery and impact of antibiotics

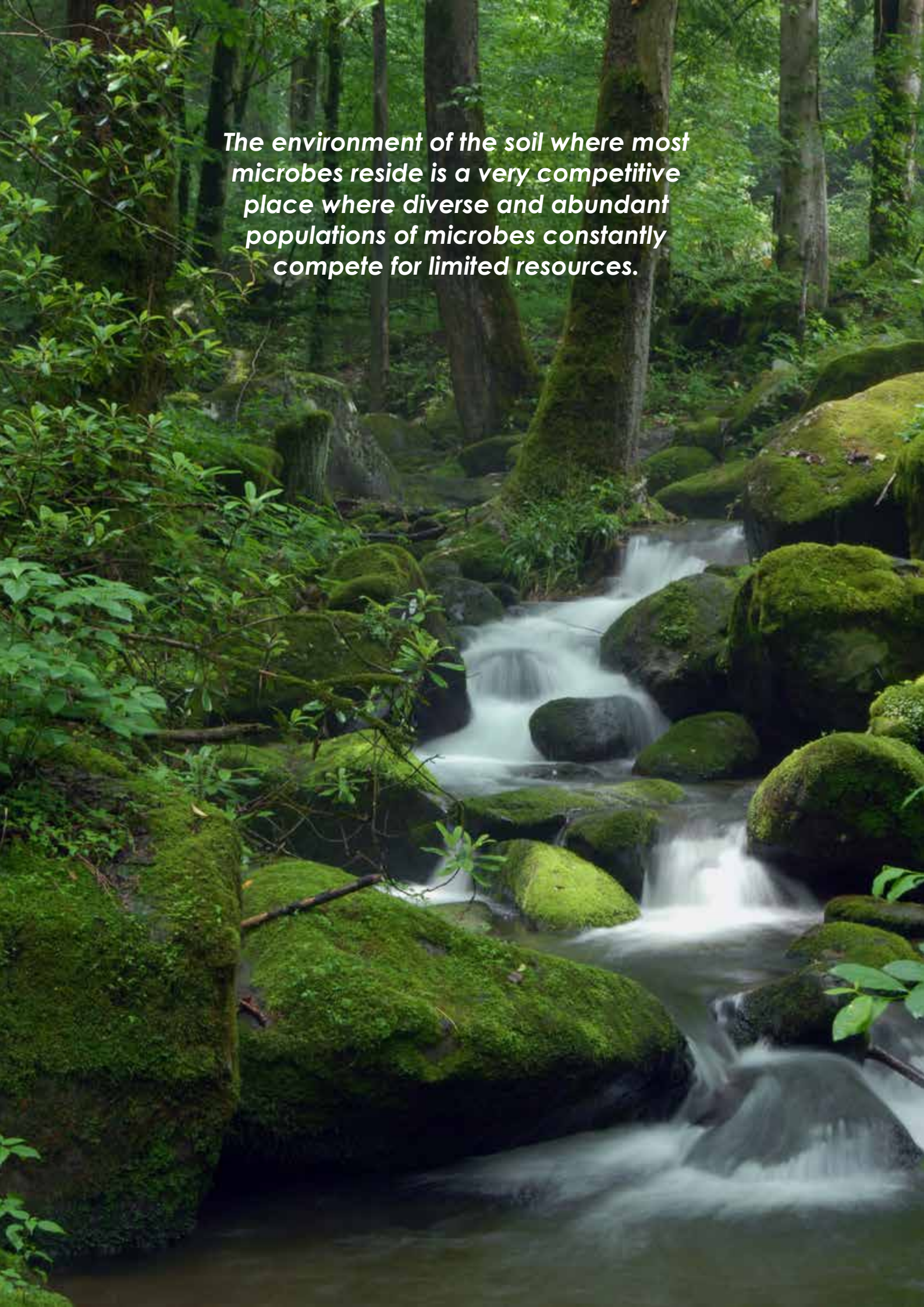
We briefly look at how antibiotics were first discovered. The environment of the soil where most microbes reside is a very competitive place where diverse and abundant populations of microbes constantly compete for limited resources. Consequently, many of these microbes produce chemical compounds that inhibit the growth–or kill–neighbouring competitor microbes. Some of these compounds can be quite specific, only harming the competitor. These compounds have been isolated by microbiologists and purified or synthesised by chemists. They are known as antibiotics. It is important to remember that antibiotics do not kill or inactivate viruses. They are, however, also useful and often necessary if bacterial super-infection takes place during a viral infection, as is commonly the case in the upper respiratory tract – that is, in the nose, sinuses, throat, bronchi, or lung tissue. The medical judgment needed to make such clinical decisions is considerable, and the growing problem of antibiotic resistance is intimately concerned with overuse of antibiotics in poor or 'defensive' medical practice. (Another major cause is the use of antibiotics in farm animals to stimulate their growth.)

About 2,500 years ago, the ancient Egyptians under the Pharaoh Imhotep discovered by trial and error (one component of the scientific method) that wounds healed quicker if covered with mouldy bread! That is because the mould on your bread is often a fungus called Penicillium, which produces the compound we have named penicillin that inhibits the growth of certain bacteria that cause infection. This is the earliest known expression of the antibiotic effect. Alexander Fleming famously (around 1928) noted the petri dishes in which he had grown a culture of bacteria were inhibited by a fungus contaminating his experiment. This is a common and annoying experience for microbiologists. But, importantly, Fleming did not just abandon these dishes. Rather he turned this mess into a serendipitous discovery by asking: what does this mean? He proceeded to find that the contaminating fungus was producing a compound that later on would be purified and called penicillin, which would save millions of lives. Penicillin, for example, prevented devastating outcomes from often quite superficial wounds that, due to the growth of contaminating bacteria in the wounds, could lead to gangrene, requiring amputation of limbs, or sepsis (bacteria in the blood), which is very hard to treat and often leads to death.

Following the discovery of penicillin, many other antibiotics have been discovered for treating a variety of bacterial infections. A major problem today is the overuse, or abuse,

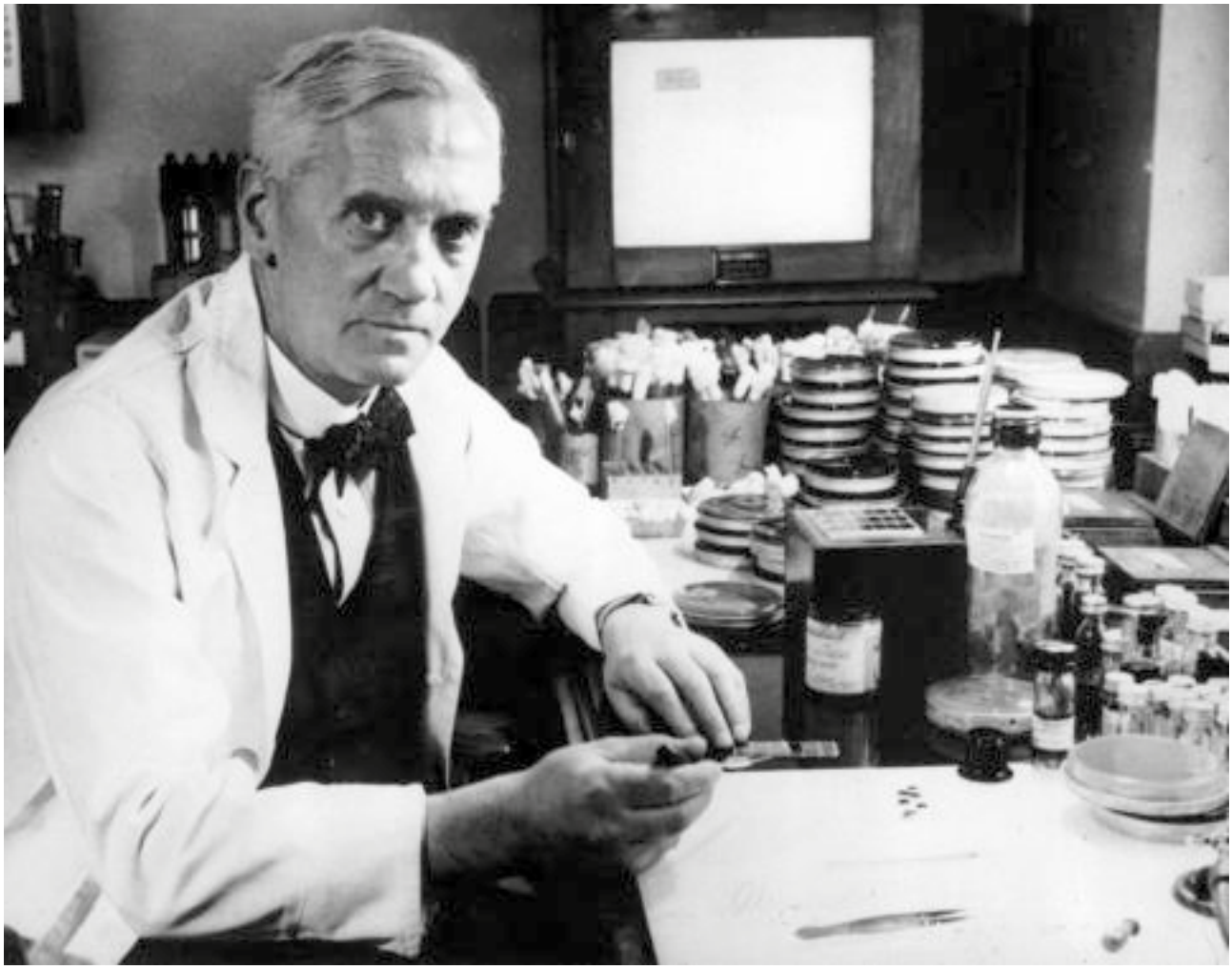


The mould on your bread is often a fungus called Penicillium.
Source: https://commons.wikimedia.org



The environment of the soil where most microbes reside is a very competitive place where diverse and abundant populations of microbes constantly compete for limited resources.

of antibiotics. Recall that the soil where most of these microbes reside is a highly competitive environment. Bacteria on the receiving end of these antibiotics also have their own tricks to subvert the assault from a neighbour's antibiotic. They may contain genes that produce enzymes that inactivate the antibiotic. Bacteria with such genes are said to be antibiotic resistant. This is a classic arms race. The genetic elements conferring antibiotic resistance often reside in plasmids and transposons that can be passed between bacteria. This is Nature's way of speeding up evolution. Genetics, microbiology, and evolutionary science teach us how microbes evolve and adapt to ever-changing environments, and why we should be cautious about the overuse of antibiotics.



Alexander Fleming
Source: https://commons.wikimedia.org

ISBN 978-1-928496-37-3
DOI http://dx.doi.org/10.17159/assaf.2021/0072
July 2021
Published by: Academy of Science of South Africa (ASSAf)
PO Box 72135, Lynnwood Ridge, Pretoria, South Africa, 0040
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The Parliament of South Africa passed the Academy of Science of South Africa Act (No 67 of 2001), which came into force on 15 May 2002. This made ASSAf the only academy of science in South Africa officially recognised by government and representing the country in the international community of science academies and elsewhere.

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