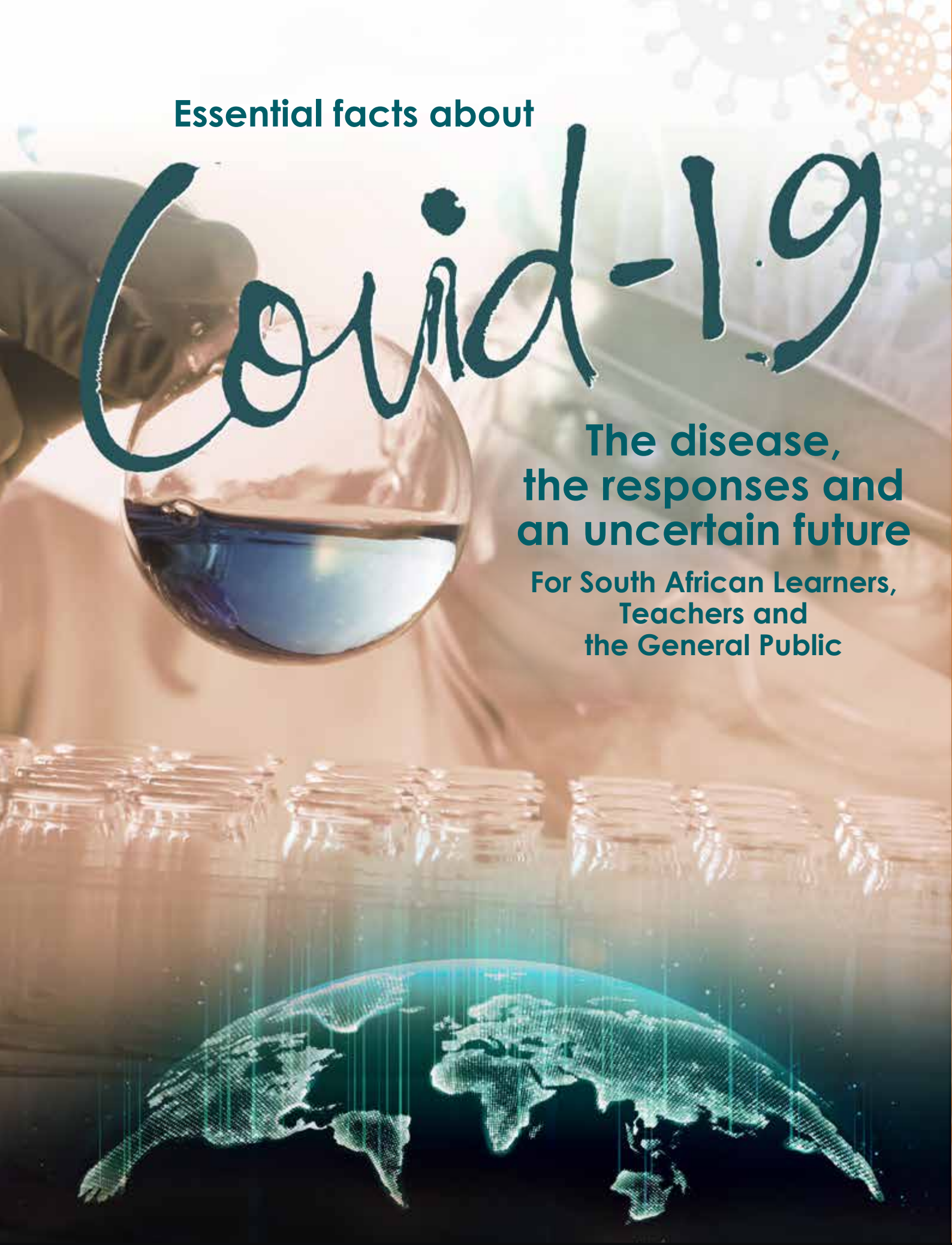
Essential facts about

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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APPENDIX **C**

WHAT IS THE SCIENTIFIC METHOD AND EVIDENCE-BASED MEDICINE?

History of the scientific method

The history of the scientific method dates back several thousands of years. One of the oldest medical textbooks is an Egyptian papyrus (the Edwin Smith papyrus) written around 1600 BCE. It is assumed that this papyrus is a military surgery manual. It describes around 50 types of injuries. Remarkably, this document follows a modern empirical approach to medical science based on examination, diagnosis, treatment, and prognosis.

Modern science dates back to the scientific revolution initiated by Nicolaus Copernicus, Johannes Kepler, and Galileo Galilei. These scientists used evidence from astronomical observation to refute the view that the Earth lies at the centre of the Universe. They proposed the alternative view that planets revolve around the Sun. At the time, this scientific revolution was not greeted with universal enthusiasm. The Catholic Church had incorporated the Greek scientist Ptolemy's (100-170) 'geocentric' view as part of its dogma. Galileo Galilei (1564-1642) was threatened by the Church with being burnt alive for contradicting its belief that the Sun revolved around the Earth.

A similar revolution occurred in medicine, when the French biologist and chemist Louis Pasteur (1822-1895) established the connection between micro-organisms and diseases. Louis Pasteur applied the scientific method to disprove the theory of spontaneous generation. According to this theory, living organisms could be created spontaneously from non-living matter, for example air. Pasteur's hypothesis, on the other hand, was that without contamination, living matter (i.e., microorganisms) could not form. To this end, Pasteur boiled meat broth in a gooseneck flask–a flask with a tube in the shape of a gooseneck attached, in order to slow down the flow of air. After boiling, the liquid in the flask remained sterile until it got in touch with the liquid in the tube. This was proof that the germs contained in the air caused the generation and not the air itself (spontaneous generation). An immediate application of the germ theory was the suggestion of a process, still used today, to prevent the bacterial contamination of milk, wine and food, through heating. This process is now called pasteurisation. Pasteur's germ theory is a good example of the scientific method.

A good example of how science moves us forwards is to consider the fact that later scientists, notably amongst them the French-American microbiologist Rene Dubos, concluded that the 'germ theory' of disease was indeed correct but incomplete, and that the role of the host was the second-most important factor that determined the ways in which infectious diseases actually manifest in individual members of a population–the

strength and precise nature of the multi-component immune system, the genetic background, gender, and other variables.

Basic Steps of the Scientific Method

The scientific method is a strategy to develop models to understand phenomena that we observe. In a nutshell, it consists of the following sequence of five steps:

- We make an observation.
- We ask a question related to the observation.
- We develop a hypothesis that could explain the observation. It is crucial that this hypothesis can be tested.
- We use the hypothesis to make a prediction.
- We test the prediction with the help of an experiment.

Of course, the above steps might have to be repeated, as our initial hypothesis may turn out to be wrong.

In the case of Pasteur's approach described above, the steps were:

- He observed that microscopic organisms grew in contaminated liquids.
- He asked the question whether contamination and not air could cause the generation of microbes.
- He developed the hypothesis that a boiled liquid would stay uncontaminated if not exposed.
- He made the prediction that by boiling a liquid (the meat broth) and preventing the access of air, germs would not develop. He tested the prediction by boiling the meat broth in a gooseneck bottle. The use of the gooseneck bottle served just the purpose of testing this hypothesis.

It is important to understand that science proceeds according to an hypothesis, which is then validated or not according to the evidence collected. Science is not a belief system. This is why science is the engine of progress and why scientists speak with factual, evidence-based knowledge.

How has the methodology of modern medicine improved on past practices? Intuition vs experiment.

The scientific method pioneered in medicine by Pasteur immediately led to further advances in medicine. Joseph Lister (1827-1912) was inspired by reading the papers of Pasteur. Lister wanted to understand what caused infections in wounds. He repeated some of Pasteur's experiments and applied the same procedures to wounds. He could prove that it is bacteria entering the wounds that cause the infections that, in many cases, could lead to death. Lister discovered that by

spraying surgical instruments and cleaning the wounds with a solution of carbolic acid, bacterial infections could be avoided. Needless to say, antiseptic surgery is now the standard of surgery.

For his contribution to medicine, Joseph Lister was honoured by Queen Victoria with the title of Baron. A popular mouthwash "Listerine" is named after him and is still promoted with the slogan: "Kills the germs that cause bad breath"!

What are some past practices in medicine that have turned out to be unfounded?

The application of the scientific method to medicine also helped to reveal some popular methods and therapies as unfounded. A typical example is the treatment of bloodletting, introduced about 2000 years ago and widely used until the 19th century. According to Claudius Galen (c.129-216/217 CE), a famous physician of the Roman Empire, bloodletting was the 'cure' of choice for fevers, apoplexy, and headaches. This procedure, often performed by barbers, was based on the 'humoural theory', which held that blood, phlegm, black bile, and yellow bile should be balanced in the human body. If one of the 'humours' was out of balance, a disease would result. The theory was aligned to the four fundamental elements of air, water, earth and fire. As a more scientific analysis was applied to this procedure, its use steadily declined.

How do we decide whether a drug is effective?

During the Age of Navigation, roughly from the 16th to 18th century, about 50% of sailors were reported to have died of scurvy. Today we know that this disease is caused by a lack of Vitamin C. A Scottish military surgeon aboard a vessel performed an experiment. James Lind divided the crew in six groups and administered different treatments to each group. By monitoring the effects of the different treatments, he observed that the group given lemons and oranges to eat recovered from signs of the scurvy. The publication of these results was probably the first account of a systematic clinical trial.

Clinical trials are essentially the fifth step of the scientific method applied to medical research.

Clinical trials are now common practice in medical research. Clinical trials are essentially the fifth step of the scientific method applied to medical research. A clinical trial is an experiment designed to test a hypothesis.

What is the process for developing a new drug? How does one ensure drug safety? And efficacy?

Before we can test a drug, we need to develop it. This is what is called the pre-clinical development of new pharmaceuticals. Once a new compound has been found, it is tested on healthy individuals to determine its safety and to determine the proper dosage. Then the new drug is applied to a small number of patients with the

specific disease. Only after these trials is the drug administered to a large number of patients. Only after three phases of testing have been successful can a drug be considered for licensing, with rare emergency exceptions.

What are some biases to guard against?

Of course, the best clinical trial is not perfect and some systematic errors, called biases, might contaminate the study. A common bias is the sampling bias. In this case, the pool of patients used for the clinical trial is not representative of the intended study population.

Another bias is called the placebo effect. Often people believe to have been cured after taking a fake drug without the active ingredient. Such a drug is known as a placebo. Consequently, drug trial studies typically use two groups: a control group, which is given the placebo, and another group given the real drug. The patient, and often also their doctor, does not know whether they have received the drug or the placebo. The study is analysed in terms of the difference in outcome between the two groups.

What are some of the ethical dilemmas that arise in drug testing?

In order to speed up the evaluation of newly developed coronavirus vaccines, some scientists have suggested to deliberately infect volunteers. For a new virus, a clinical trial will typically take at least one year. A carefully designed 'human challenge' trial could reduce the time of the trial to a couple of months. This raises the ethical question about the high risks involved for the volunteers, especially in the case of diseases such as Covid-19, where no effective cure exists yet.

The tremendous success of mass vaccination relies on more than a certain threshold fraction of the population being vaccinated, in order to benefit from herd immunity.

How safe are vaccines?

As described in detail in Chapter 7, vaccines reduce the risk of getting a disease. Extensive testing takes place to test vaccines both for efficacy and safety, and many candidate vaccines do not make it to the market as the result of these tests. Public confidence in the safety of vaccination is crucial.

We mention an important recent success of sustained vaccination. This year the WHO declared Africa free from polio. The eradication of the wild polio virus was only possible because of a systematic vaccination effort spanning over many years. The virus remains endemic only in Afghanistan and Pakistan.

The tremendous success of mass vaccination relies on more than a certain threshold fraction of the population being vaccinated, in order to benefit from the 'herd immunity' explained in Chapter 5. When less than this fraction is vaccinated in some areas or communities, outbreaks can and do occur. Mass vaccination relies

on widespread public acceptance of vaccines–of their safety, efficacy, and importance. Consequently, false claims that vaccines are not safe can undermine vaccination programs and threaten public health.

The false claims of a link between the measles, mumps, and rubella (MMR) vaccine and autism and its consequences serve as an example. In 1998, the British doctor Andrew Jeremy Wakefield and collaborators published an article in the medical journal, The Lancet, claiming to have discovered such a link. This led to much discussion and the rise of an anti-vaxxer movement. A sharp decline in vaccination uptake followed, leading to a number of outbreaks of measles around the world, with thousands of cases and many deaths. The findings of such a link were subsequently refuted by other researchers and the original article was withdrawn by most of Wakefield's collaborators. It was further uncovered that Wakefield failed to disclose conflicts of interest resulting from his involvement in litigation surrounding the safety of the vaccine.

The anti-vax movement, nevertheless, continues to this day and threatens the widespread acceptance of coronavirus vaccines. In a recent survey held in the United Kingdom, people were asked whether they will undergo the administration of an anti-coronavirus vaccine if one were developed. Apparently, many said 'no', indicating the power of the growing anti-vax movements and the suspicions around the scientific enterprise.

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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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