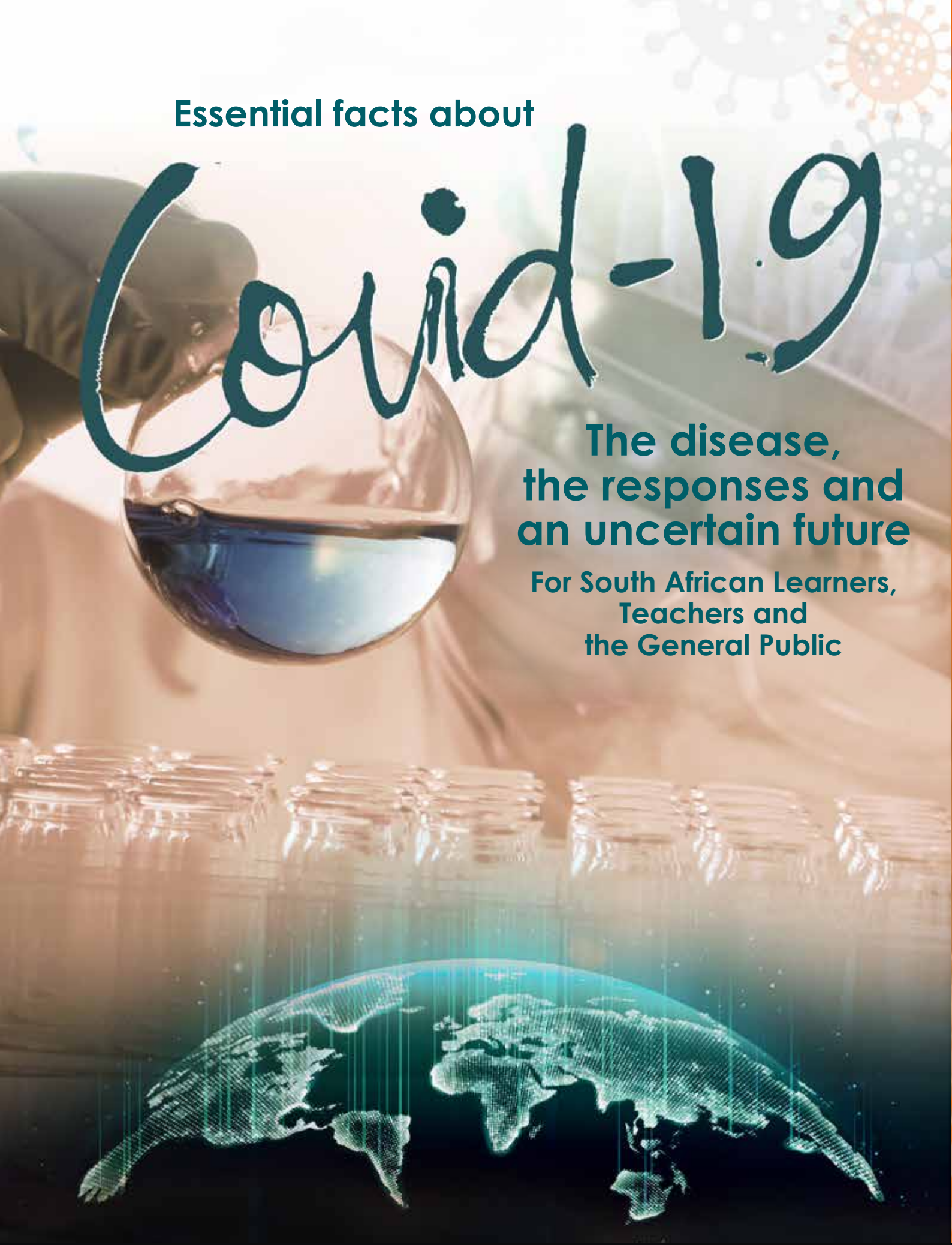
Essential facts about

Covid-19

The disease, the responses and an uncertain future

For South African Learners, Teachers and the General Public



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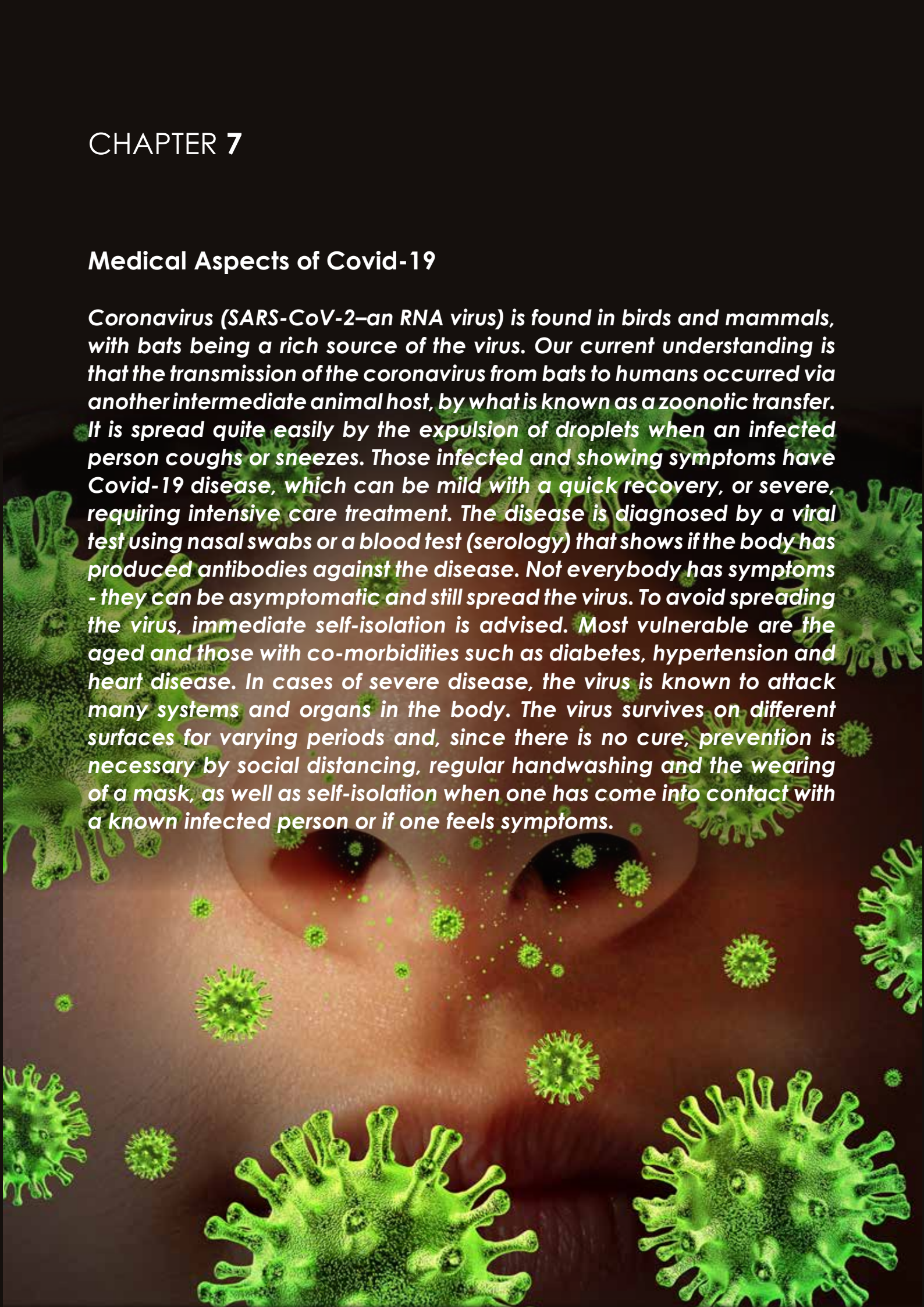
CHAPTER **7**

Medical Aspects of Covid-19

Coronavirus (SARS-CoV-2–an RNA virus) is found in birds and mammals, with bats being a rich source of the virus. Our current understanding is that the transmission of the coronavirus from bats to humans occurred via another intermediate animal host, by what is known as a zoonotic transfer. It is spread quite easily by the expulsion of droplets when an infected person coughs or sneezes. Those infected and showing symptoms have Covid-19 disease, which can be mild with a quick recovery, or severe, requiring intensive care treatment. The disease is diagnosed by a viral test using nasal swabs or a blood test (serology) that shows if the body has produced antibodies against the disease. Not everybody has symptoms - they can be asymptomatic and still spread the virus. To avoid spreading the virus, immediate self-isolation is advised. Most vulnerable are the aged and those with co-morbidities such as diabetes, hypertension and heart disease. In cases of severe disease, the virus is known to attack many systems and organs in the body. The virus survives on different surfaces for varying periods and, since there is no cure, prevention is necessary by social distancing, regular handwashing and the wearing of a mask, as well as self-isolation when one has come into contact with a known infected person or if one feels symptoms.



SARS -CoV-2 nomenclature

Virus: SARS-CoV-2 (Severe acute respiratory syndrome-related to coronavirus 2)
Disease: Covid-19 (coronavirus disease 2019)

What we know about coronaviruses and humans?

Coronaviruses, first discovered in the 1960s, are found in birds and mammals, especially in bats, civets, camels, and rats. The causative agent of Covid-19 (SARS-CoV-2) belongs to the genus Coronavirus, family Coronaviridae, and order Nidovirales. SARS-CoV-2 is the 7th coronavirus known to infect humans. Notwithstanding restricted geospatial transmission, SARS-CoV (Asia) in 2003 and MERS-CoV (Middle East) in 2012 caused severe disease. In contrast, coronaviruses HKU1, NL63, OC43 and 229E are associated with mild symptoms and represent the cause of about a fifth of 'common colds' in most parts of the world.

Bats are a rich source of coronaviruses, although only a few of these coronaviruses can infect humans. SARS and MERS viruses have zoonotic transmission, originating from bats and passing through palm civets and camels, respectively, as the intermediate hosts. The most recent reports have suggested that SARS-CoV-2 is a modified coronavirus of bat origin, which came to humans as a result of zoonotic transmission by first adapting to an intermediary host.

Origin and characteristics of SARS CoV-2

The true origin of SARS-CoV-2 in humans remains to be established. Phylogenetic analysis (the study of evolutionary relationships among biological entities–often species, individuals or genes–where viruses isolated from humans and or other animal species are sequenced and compared to identify common ancestry or where differences exist between species) suggests that bats are the original host, while an animal sold at the seafood market in Wuhan might be an intermediate host facilitating the emergence of the virus in humans.

Phylogenetic analyses show that the pangolin coronavirus is genetically related to the SARS-CoV-2 and other bat coronaviruses. It carries the same receptor binding domain as does SARS-CoV-2 but the rest of the virus is only 90% genetically similar. Pangolins may therefore not be the intermediary host. SARS-CoV-2 binds with high affinity to human Angiotensin-converting enzyme 2 (ACE-2) as its cellular receptor and uses it as an entry point to invade target cells in humans. ACE-2 receptor expression is much higher in the lower lobes of our lungs compared with the upper respiratory tracts.

Is the virus likely to mutate into forms that are more or less dangerous?

SARS-CoV-2 is a large RNA virus and appears to have an effective repair system when errors are made in copying its single RNA strand during replication in infected host cells. Most of the mutations since the start of the pandemic have not drastically changed the properties of the virus, although there have been plenty of 'neutral' mutations that have been detected by whole-genome sequencing of samples from all over the world. Analysis of these is a fast-developing way of tracking the source of particular outbreaks and responding appropriately to them. However in the past year a few variants that spread more readily have become a major cause of concern.

Bilateral multi-lobular lung involvement is common in Covid-19, but we now know that it is a multi-organ disease affecting human beings from head to toes. Not everyone who gets infected gets sick. In fact, the majority remain asymptomatic. Not everyone who gets ill develops Acute Respiratory Distress Syndrome (ARDS) requiring mechanical ventilation.

Respiratory droplets and aerosols transmit the virus through exhalation, such as sneezing, coughing, singing, and talking. There is much evidence to suggest that the virus is air-borne in aerosols, which remain in the air much longer and can migrate further than virus contained in the much larger droplets that fall quickly onto surfaces like the ground or floor.

Does everyone who gets exposed to SARS-CoV-2 get the disease?

Not everyone exposed to SARS-CoV-2 develops the disease. Those at greatest risk of infection are persons who have had prolonged, unprotected close contact (i.e., within 2 metres for 15 minutes or longer) with a person with 'active' (confirmed or unconfirmed) SARS-CoV-2 infection. The virus is spread by infected persons regardless of whether the person has symptoms or not. In fact, the peak concentration of the virus in an infected person is just before the onset of symptoms.

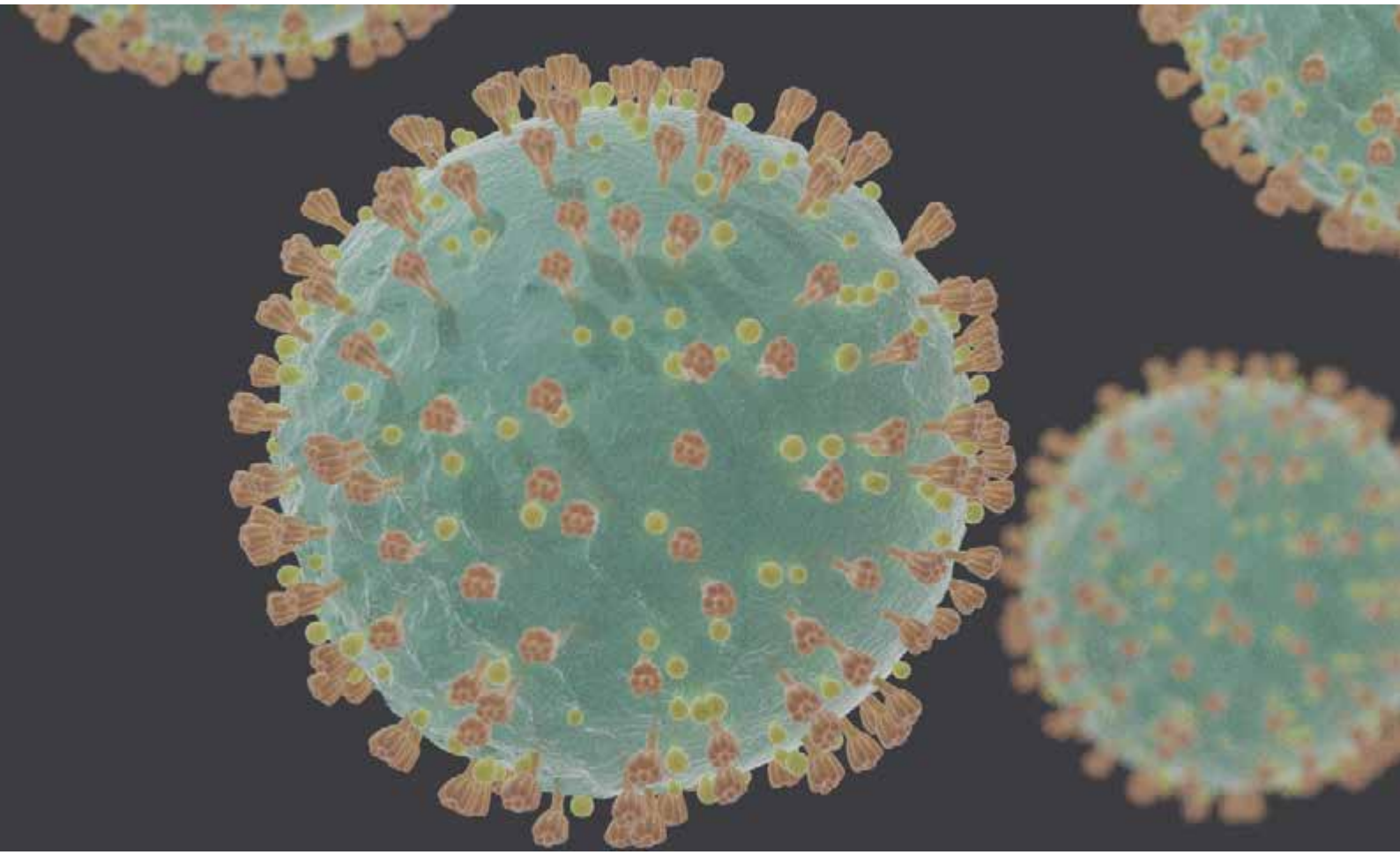
While everyone exposed to SARS-CoV-2 appears to be at some risk of acquiring the infection, the severity of the resulting clinical disease differs markedly by age. According to the Chinese Centre for Disease Control and Prevention, which analysed more than 44,672 confirmed cases, age is the most important predictor of severe disease and death. The case fatality rate was <1% among <60 years old; 3.6% for those 60-69 years; 8.0% in people 70-79 years; and 14.8% among those 80 years or older.

What is the course of a Covid-19 infection?

The time from exposure to development of symptoms for SARS-CoV-2 infection ranges from 2–14 days with an average incubation time of 4-5 days.

Common presenting symptoms of the disease:

- fever (88%)
- cough (68%, 33% productive)
- fatigue (38%)
- shortness of breath (dyspnoea)(19%)
- sore throat (14%)
- muscle pain (myalgia) (15%)
- loss of sense of smell (anosmia) (variable but frequent)
- loss of sense of taste (ageusia) (variable, less frequent)
- severe headaches (14%)
- nasal congestion (5%)
- diarrhoea (4%)



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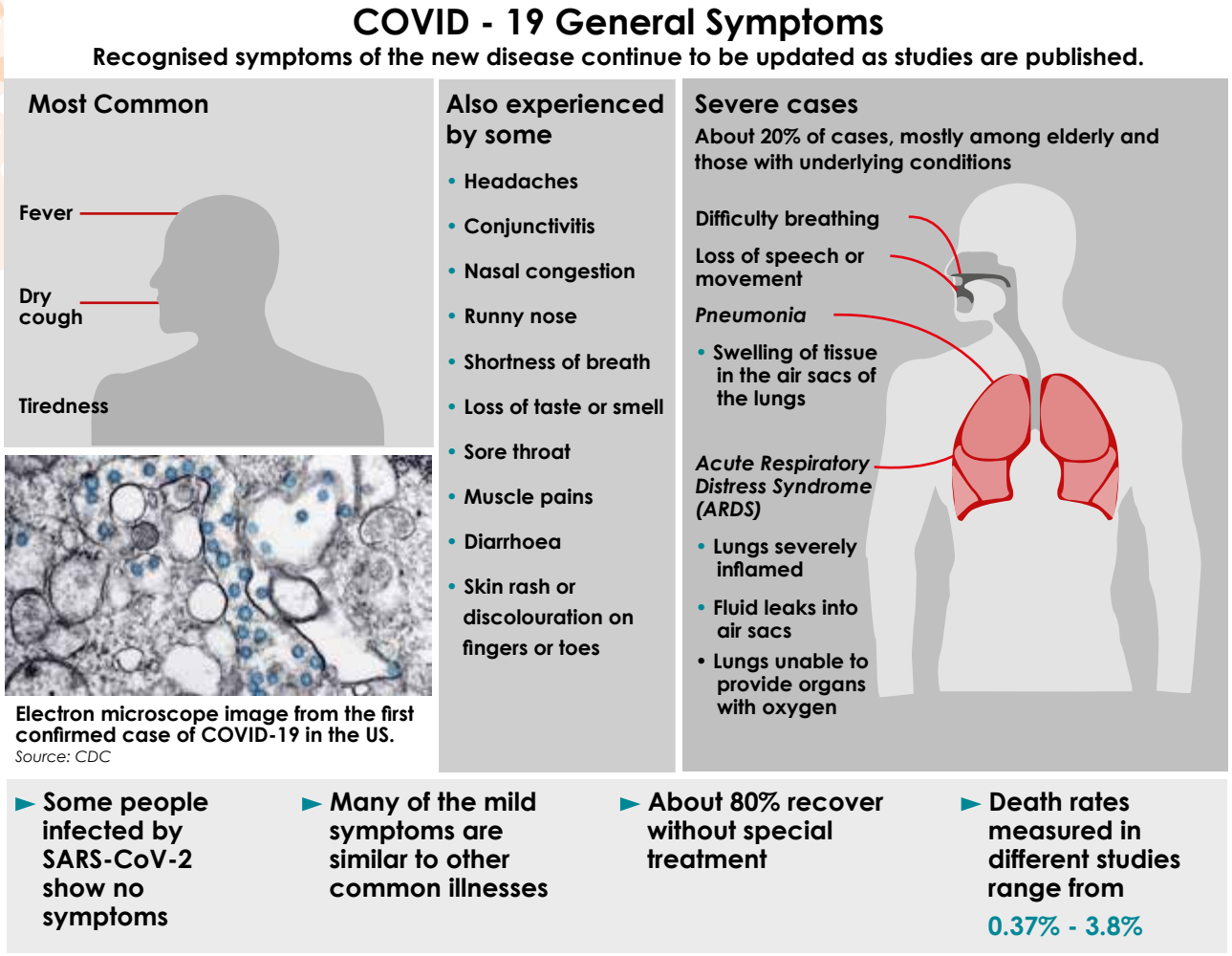


Figure 7.1: Covid-19 general symptoms

Source: WHO/CDC

An asymptomatic infection–a person infected with Covid-19 who does not develop any symptoms.

Symptomatic infection–these symptoms can range from mild to critical. Most people (about 80 per cent) recover from the disease without needing special treatment.

Around one out of every six people who gets symptomatic Covid-19 becomes seriously ill and develops difficulty breathing.

Severity of disease presentation: (WHO clinical guidelines of grading)
Mild–fever, cough, fatigue, anorexia, shortness of breath, myalgia. Other non-specific symptoms, such as sore throat, nasal congestion, headache, diarrhoea, nausea and vomiting, anosmia and ageusia.
Moderate–Above symptoms with clinical signs of pneumonia and SpO_2 >90%
Severe–Respiratory distress with SpO_2 <90%
Critical–Acute Respiratory Distress Syndrome (ARDS)

Coronavirus progression in majority of cases

Exposure to the virus

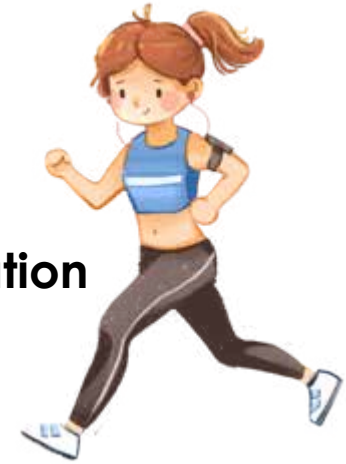
Incubation period
4 to 6 days (average)
Can be up to 14 days

Person develops symptoms

Infectious period
8 to 10 days
(but can be longer)
Starts from 1-3 days before symptoms develop

Illness 10 days
But can be longer

No more symptoms
3 days



Released from isolation

Figure 7.2 : The natural history and disease progression of Covid-19

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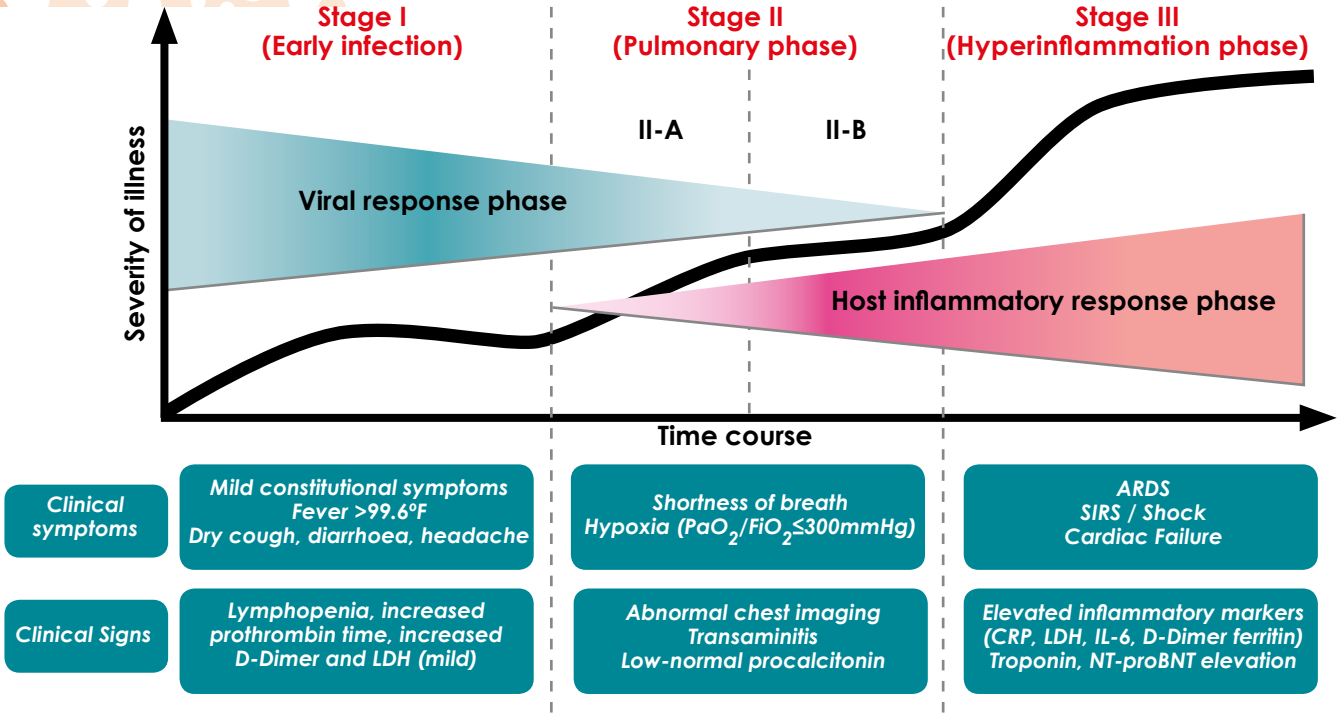

Figure 7.3: Schematic representation of the natural history of Covid-19 from the onset to recovery or death

Source: US NIH

There are basically three stages or phases in the natural history of Covid-19, regarding disease severity. The first phase is related to the onset of the disease and is generally characterised by the development of influenza-like symptoms from mild to moderate. Some individuals recover and some progress to the second phase. Depending on the severity of phase 2, patients can improve or worsen with the necessity of intubation and ventilation. Phase 3 is characterised by hyper-inflammation and sepsis of lungs. Patients often require intensive care and most of them, unfortunately, cannot overcome the infection and may eventually die.

What is the spectrum of disease?

SARS-CoV-2 affects different organ systems at different times. There is a growing body of evidence suggesting that Covid-19 is a multi-system disease, with the causative virus capable of infecting and affecting any organ in which its receptor is present. The spikes on the surface of SARS-CoV-2 virus particles each comprise three identical subunits, each of which, in turn, is made up of two functional components; the S1 part is responsible for binding to the host cell receptor and the S2 part is for the fusion of the viral and cellular membranes. Angiotensin converting enzyme 2 (ACE2) embedded in the surface membrane of many cells is the functional receptor for SARS-CoV-2 to gain access to human cells. The ACE2 receptor is highly expressed in lung epithelial cells, kidneys, gastrointestinal tract, liver, vascular endothelial cells, and arterial smooth muscle cells. Thus, all of these organs and systems with high expression of ACE2 receptors are targets for SARS-CoV-2 infection. Covid-19 may induce a widespread inflammatory response involving all these organs.

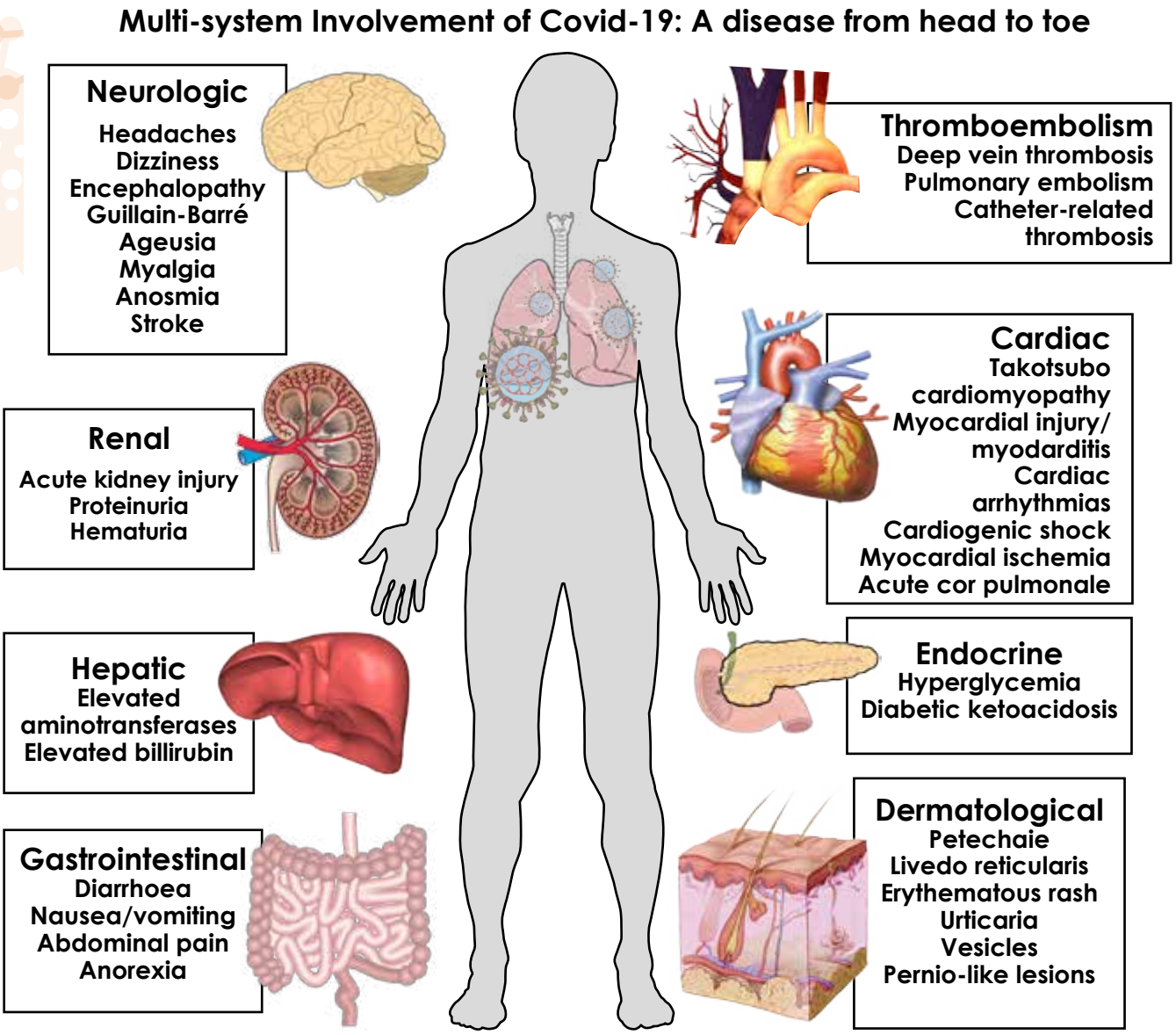

Figure 7.4: Multi-system involvement of Covid-19: A disease from head to toe

Why does Covid-19 make so many people sick?

- It is an emerging infectious disease, which means the human population has not previously been infected and, therefore, people do not have immunity to the virus.
- The virus spreads rapidly and easily.
- Each person's immune system must apply all its components to try to find the right defences to protect the body. This takes from hours to days to weeks, during which time the virus continues to replicate and spread.
- The majority of people infected with the virus don't develop any symptoms but are still infectious i.e. they continue to spread the virus.
- About 80% of infections are transmitted by 'super-spreaders', who are infected individuals who might shed more virus into the environment than others if their

immune system has trouble subduing the invader. (We now know that some examples of 'super-spreading' are not so much due to the infectiousness of the infecting person, but the circumstances in which large numbers of other people are exposed to an infected person, e.g., a large number of party-goers crowded together in an indoor venue, laughing and singing and not wearing masks.)

How does Covid-19 spread from person to person? Droplets, aerosols, and surfaces?

Transmission in most instances takes place via inhalation or ingestion of respiratory droplets (generated through coughing and sneezing) or the much smaller and lighter respiratory aerosols (generated by singing or talking loudly or breathing heavily during exercise), and by direct transfer of virus particles from contaminated surfaces to the mouth, nose or eyes.

The stability of virus in air and on various surfaces is: Air; Copper (4 hours); Cardboard (24 hours); Stainless Steel (48 hours); Plastic (72 hours).

Droplet or aerosol transmission usually occurs when a person is in close contact (within 1 metre) for longer than a few minutes with someone who has active virus, whether symptomatic or not. It can also occur by direct contact with still-active virus left on surfaces in the immediate environment of, or on objects used by, actively infected persons (e.g., stethoscope or thermometer).

In hospitals or ICUs, airborne transmission by droplets or aerosols is especially likely in specific circumstances and settings in which procedures or support treatments

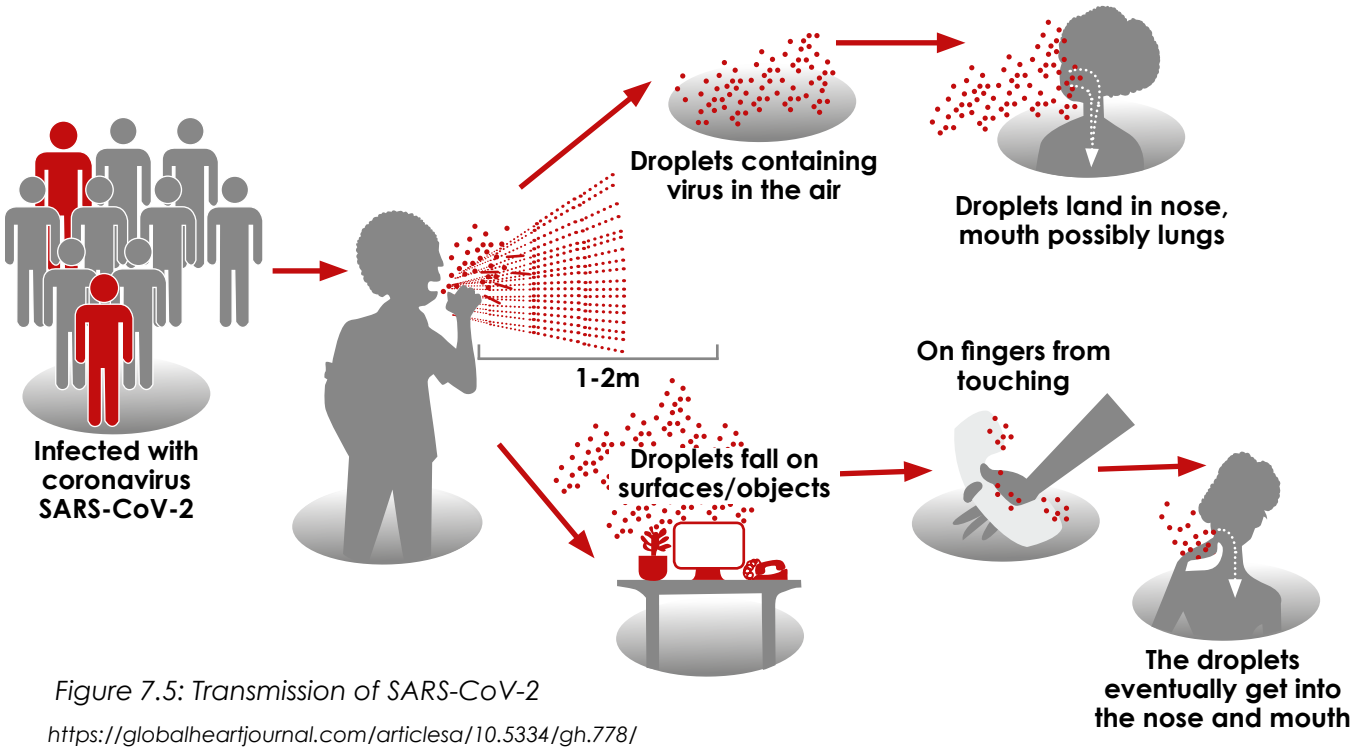

Figure 7.5: Transmission of SARS-CoV-2

https://globalheartjournal.com/articlesa/10.5334/gh.778/

that generate aerosols are performed; i.e.,endotracheal intubation, bronchoscopy, open suctioning, administration of nebulised treatment, manual ventilation before intubation.

Some general observations:

- The virus is usually detectable in the nasopharynx/oropharynx 1-3 days before the onset of symptoms.
- The viral load peaks around the time of symptom onset.
- Viral loads are generally higher in sputum samples than in nasopharyngeal or oro-pharyngeal swabs.
- The virus is detectable by PCR in the nasopharynx/oropharynx for ≥7 days after the onset of illness in most cases, but culturable virus seems to be rare after day 7.
- Pre-symptomatic transmission is an important contributor to community transmission (wide range of estimates–up to 50%).
- Transmission occurs from symptomatic cases in the first few days of symptoms.
- Transmission after 7 days of illness is likely to be rare.

Why is it so difficult to stop the spread of the virus?

Pre-symptomatic infectiousness–people spreading it, without knowing it, before they get ill.
Asymptomatic infectiousness–people spreading it without ever knowing they have the infection.
Rapid spread–infected person infects more than one other person (Chapter 5).
Super-spreaders–such as patient 31 in South Korea who infected over 1000 people in a few days.
Repeated waves/resurgence–even when initial epidemic is controlled, there is an ever-present risk of new epidemics.
Emergence of new variants–that are able to escape natural or vaccine induced immune responses.

What makes SARS-CoV-2 infection so serious?

Case fatality rates (how many people die from the disease) are not high, but….
The virus has a genetic advantage in the form of the spike protein's high affinity for a widely distributed cell-surface receptor.

The virus spreads easily and remains viable outside the body for several hours or days depending on the way it leaves and the material of any surfaces it lands on.

Stopping spread is complicated as the virus is highly infectious and spreads even before an infected person has symptoms (pre-symptomatic spread) and, at the same time, the majority of exposed and infected individuals remain asymptomatic. The transmission rate is therefore high–on average, one person infects between two and three others; but, in the circumstances in which spreading is most effective (closed, unventilated spaces with many people not wearing masks and talking loudly or singing, etc.), super-spreading can occur with tens or hundreds of people being infected in a single evening. It is estimated that about 80% of transmissions take place at such super-spreading events from only <10% of infected individuals. Even when substantial reductions in new infections have been achieved, there can readily be a resurgence/second wave of infection.

The virus replicates and spreads rapidly within a matter of days. This rapid spread and surge of infections can easily overwhelm health services, resulting in higher death rates than would be the case if all patients received optimal treatment. Greater vulnerability with increasing age, and the presence of co-morbidities. During winter it is challenging to differentiate between flu and Covid-19.

What should one do if one has symptoms consistent with Covid-19?

Once persons suspect that they may have Covid-19, they should:

- **Self-isolate:** Self-isolating means staying at home and staying away from other family members to avoid spreading the virus. Ideally, people who have symptoms of Covid-19 should remain in one room and use a separate bathroom to other members of the household. Self-isolation is appropriate for those with mild symptoms.

- **Seek medical help if needed:** A person should contact a doctor by phone to report their symptoms and seek further advice and should not show up at a doctor's office without prior approval from the facility. People should call the emergency services if their symptoms are severe or include breathing difficulties.

Who is most at risk? Comorbidities, morbidity, and mortality.

While cases of Covid-19 have only recently been detected in countries with substantial HIV epidemics, there are no data available on whether the virus will exacerbate HIV infection or how HIV infection may impact the SARS-CoV-2 virus. Data from other respiratory illnesses, such as influenza, suggest that people with compromised immunity, such as those living with HIV, particularly those with low CD4 T-cell counts, are likely to be at higher risk of developing severe Covid-19 illness. In countries like South Africa that have generalised HIV epidemics and an already overburdened health care system, the impact of Covid-19 is likely to put severe strain on the services.

Other predictors of disease progression include malnutrition (both under-weight and overweight/obesity) and non-communicable diseases (NCDs), including hypertension and diabetes. Malnutrition and NCDs are prevalent in South Africa and have been associated with higher risk and severe outcomes related to other influenza-like illnesses.

Older age (being over 60 years) and pre-existing medical conditions (diabetes; hypertension; HIV; TB; cardiovascular disease; cancer patients) appear to be important factors for severe illness and death. There is growing evidence that Covid-19 can also itself either cause or exacerbate metabolic syndrome (pre-diabetic condition) and hypertension.

How can doctors help patients with serious Covid-19?

Not all patients with Covid-19 will require medical supportive care or hospital admission.

Clinical management for hospitalised patients with Covid-19 is focused on supportive care for complications, including supplemental oxygen and advanced organ support for respiratory failure, septic shock, and multi-organ failure.

What is acute respiratory distress syndrome (ARDS)? How is it treated?

The majority of mortality attributable to SARS-CoV-2 infection occurs through the development of viral pneumonia-induced acute respiratory distress syndrome (ARDS). While the exact mechanisms through which SARS-CoV-2 causes ARDS and how certain host factors confer an increased risk of developing severe disease remain unclear, one factor has emerged as a dominant predictor of disease severity and risk of mortality: age.

This is an inflammatory process which can lead to insults to the lung, either direct or indirect.

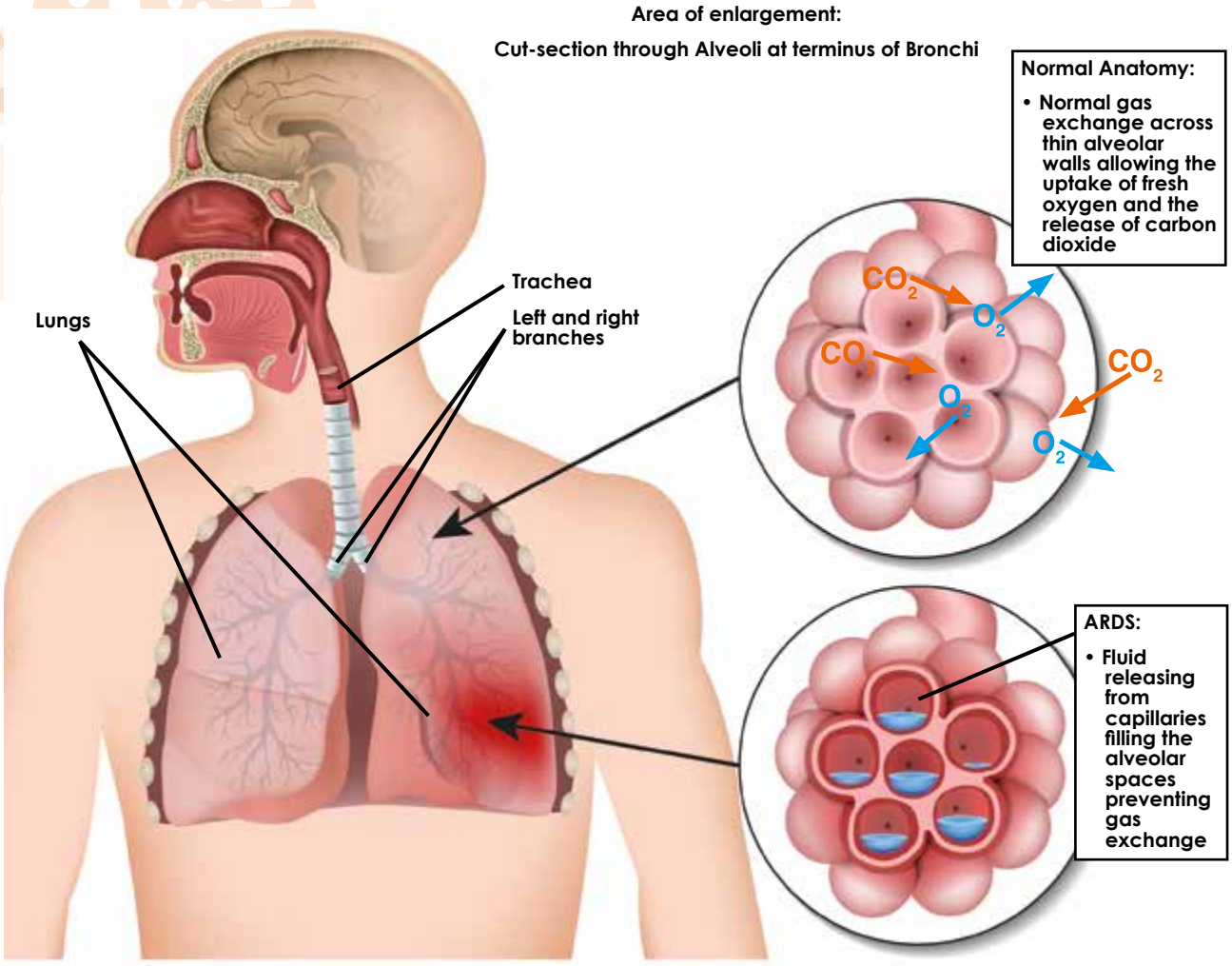

Figure 7.6

Figure 7.6: The early exudative stage presents diffuse alveolar damage with destruction of epithelial and endothelial cells. ARDS is characterized by an increase in the permeability of the alveolar-capillary barrier, leading to an influx of fluid into the alveoli. Fluid builds up in the tiny, elastic air sacs (alveoli) in your lungs. The fluid keeps your lungs from filling with enough air, which means less oxygen reaches your bloodstream. This deprives your organs of the oxygen they need to function.

Patients who have severe difficulty breathing and require oxygen may need mechanical ventilation.

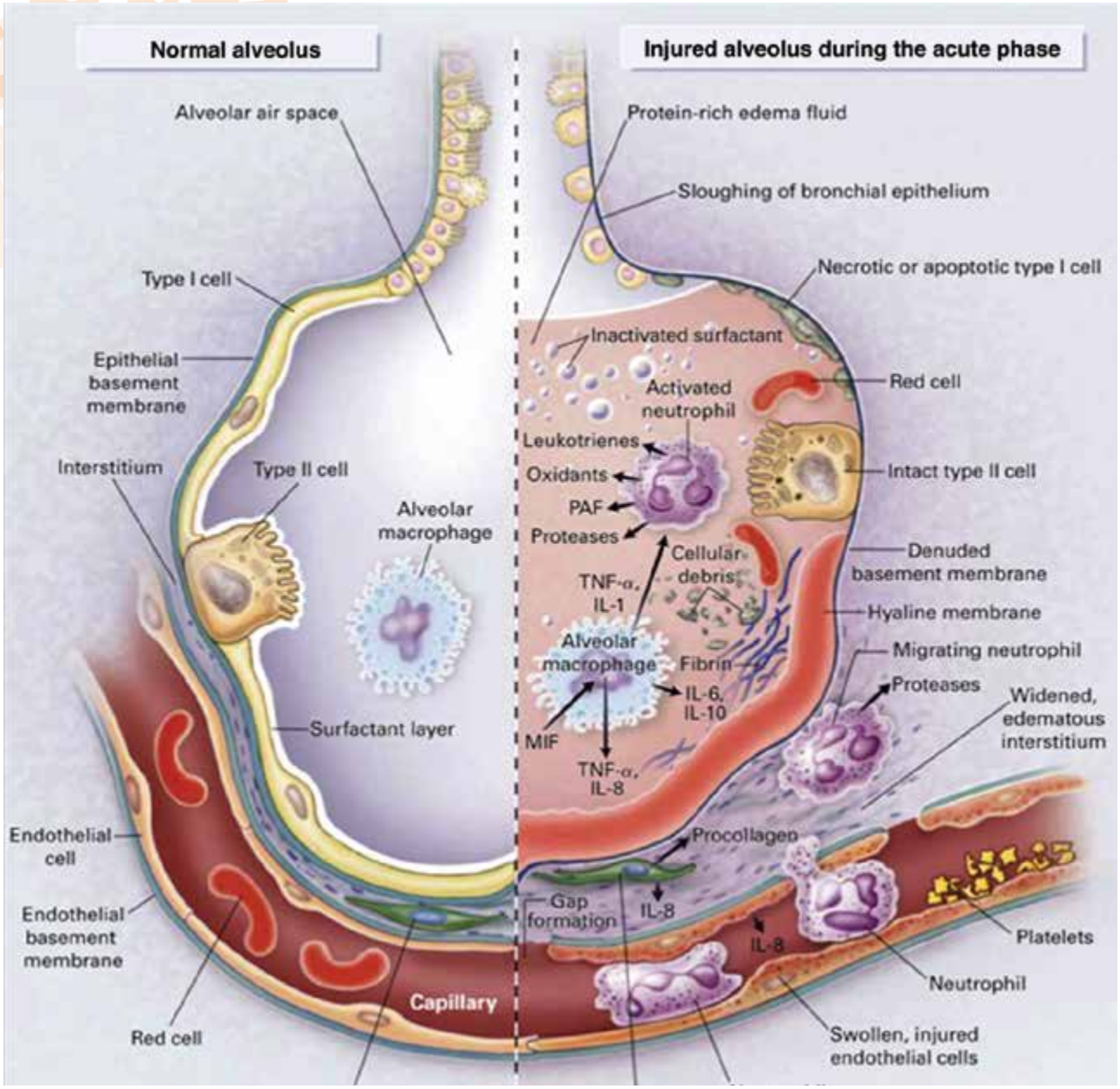

Figure 7.7 Formation of protein-rich pulmonary edema fluid. Normal and injured alveolar-capillary barriers are illustrated in left and right panels

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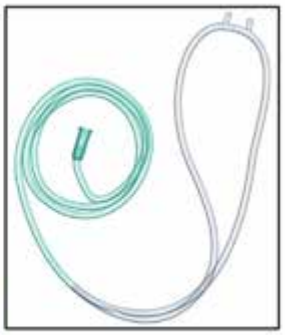
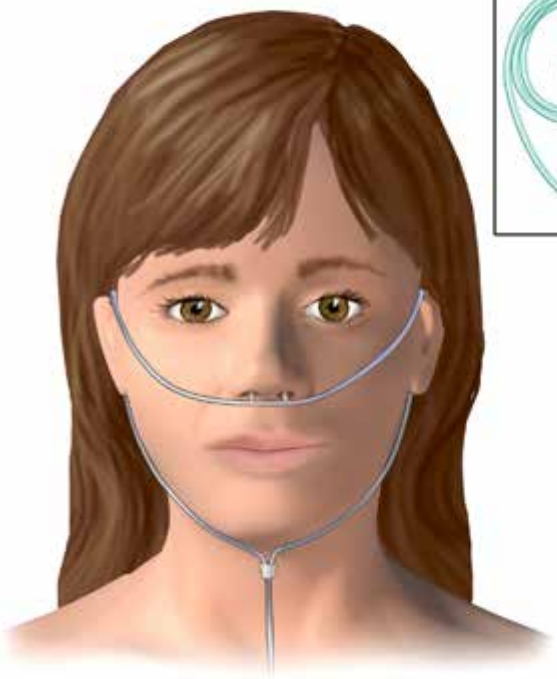
About 5–15% of patients with Covid-19 infection require intensive care surveillance and ventilatory support, mainly for one reason: severe hypoxemia (an abnormally low concentration of oxygen in the blood). The goal of treatment should be maintenance of oxygen saturation >90%. That means supplementation of oxygen via several ways.

There are no clear evidence-based guidelines for the ideal time to proceed to mechanical ventilation in patients with Covid-19. Availability of ventilators, intensive care capacity, considerations of palliative care and end-of-life resources as well as individual patient characteristics all play a role in decisions to institute mechanical ventilation.

Nasal Cannula



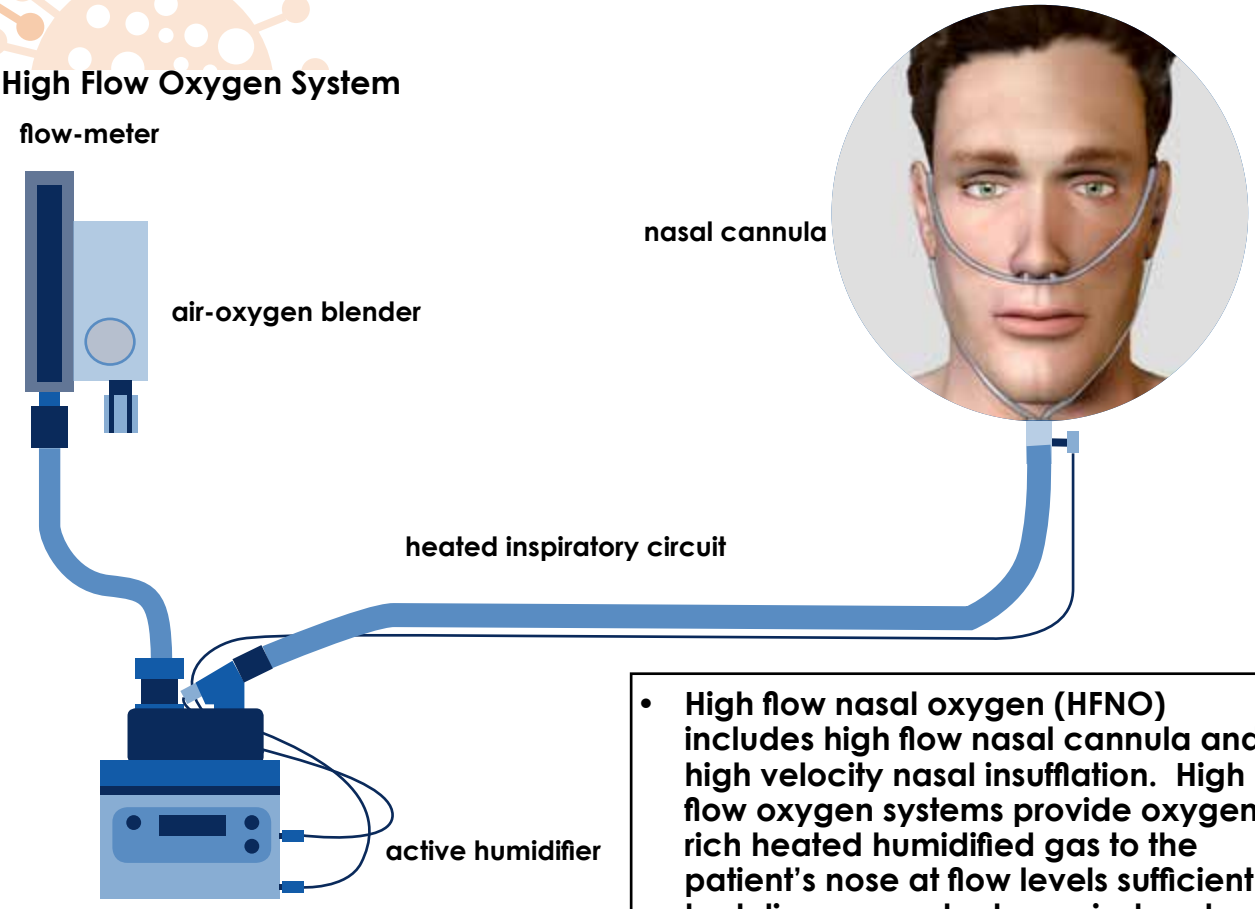


- Effective for mildly hypoxic patients, supplemental oxygen delivered by nasal cannula can induce significant dispersion of exhaled air, even at low flow rates.
- Supplemental oxygen by nasal cannula provides up to about 5-6 L/min

Simple Face Mask

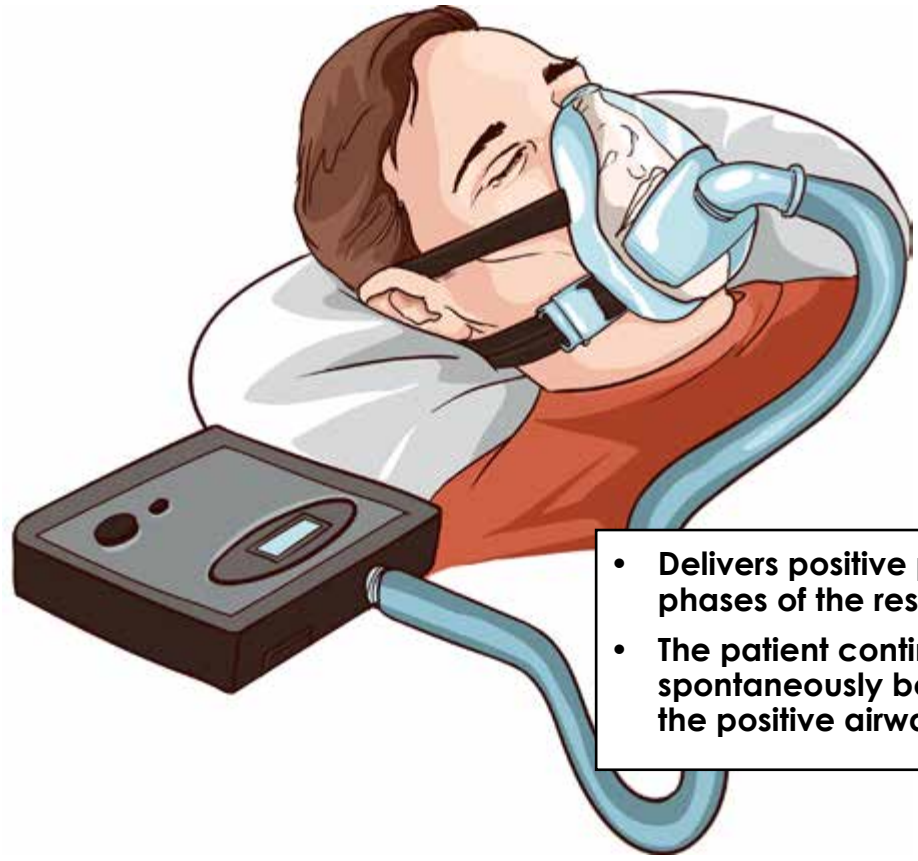
- Oxygen supplementation via a simple mask is only marginally greater than that of nasal cannula.
- Simple masks provide supplemental oxygen with flow rates up to approximately 5-10 L/min

High Flow Oxygen System



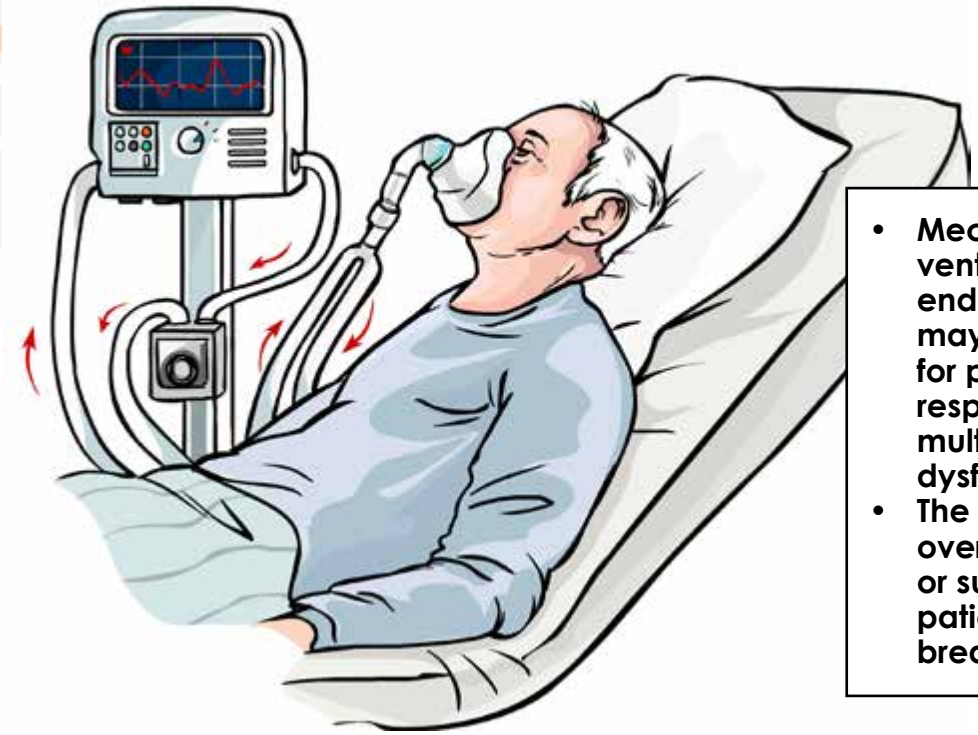
- High flow nasal oxygen (HFNO) includes high flow nasal cannula and high velocity nasal insufflation. High flow oxygen systems provide oxygen rich heated humidified gas to the patient's nose at flow levels sufficient to deliver a constant, precisely set high FiO_2.

Continuous positive airway pressure (CPAP)



- Delivers positive pressure through all phases of the respiratory cycle.
- The patient continues to breathe spontaneously both with and against the positive airway pressure.

Mechanical ventilation



- **Mechanical ventilation through an endotracheal tube may be necessary for patients with frank respiratory failure or multisystem organ dysfunction.**
- **The machine takes over completely or supports the patient's spontaneous breathing**

Figure 7.8

Clotting and strokes

Strokes occur when the brain's blood supply is interrupted, usually by a blood clot. Covid-19 causes complications to younger patients being hospitalised for, and sometimes dying from, serious strokes. It is unknown if coronavirus itself stimulates blood clots to form, or if they are a result of an over-active immune response to the virus.

These strokes are found in patients who test positive for coronavirus but who do not have any traditional risk factors for stroke. They tend to have no Covid-19 symptoms, or only mild symptoms. The type of stroke occurring in these patients typically occurs in much older patients.

Covid-related strokes occur because of a body wide increase in blood clot formation, which can damage any organ, not just the brain. A blood clot in the lungs is called pulmonary embolism and can cause shortness of breath, chest pain, or death. A blood clot in or near the heart can cause a heart attack. Blood clots in the kidneys can cause kidney damage requiring dialysis.

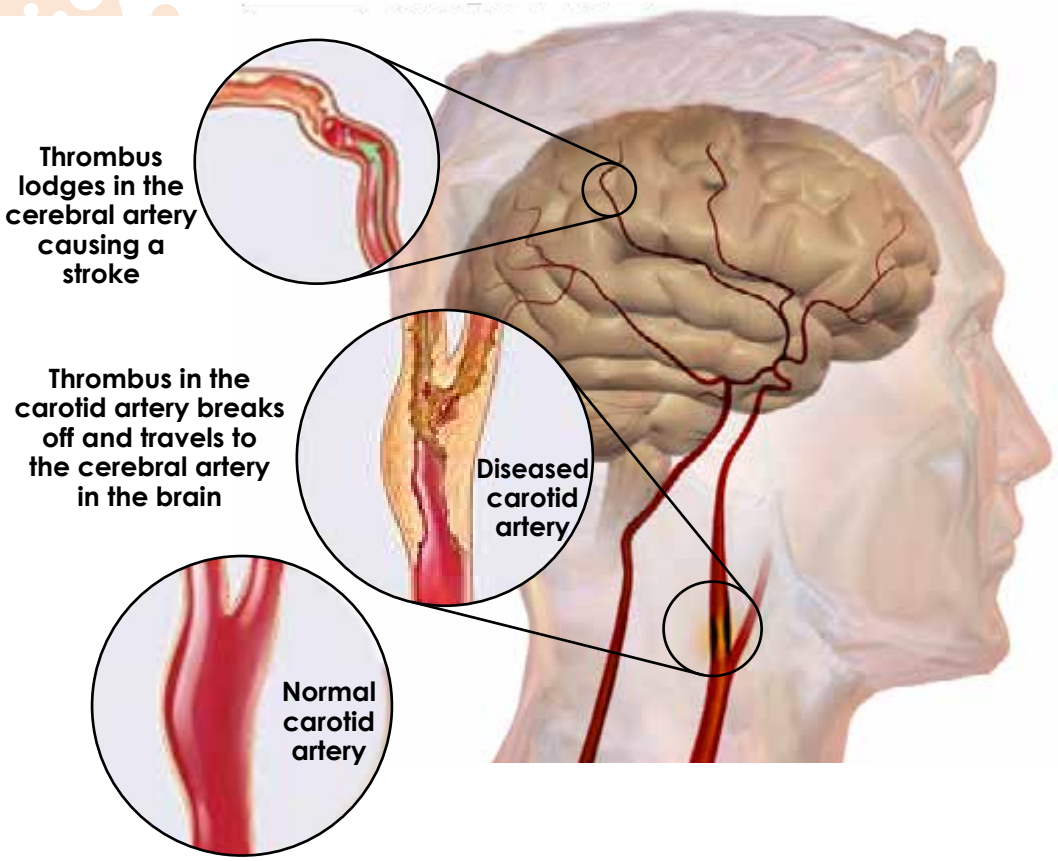


Figure 7.9

How does one minimise the risk of spread of Covid-19?

The best measures are directly relatable to the ways in which SARS-CoV-2 is spread. As already described, Covid-19 is transmitted through inhalation or ingestion of respiratory droplets and/or aerosols emitted by an infected person (respectively generated through coughing and sneezing, and talking or singing or breathing heavily). Individuals can also be infected from touching surfaces contaminated with the virus and then touching their faces (e.g., eyes, nose, mouth).

As with other respiratory infections like the flu or the common cold, public health measures are critical to slow the spread of illnesses. Public health measures are everyday preventive actions that include use of **non-pharmaceutical interventions:**

- Staying home when sick;
- Covering mouth and nose with flexed elbow or tissue when coughing or sneezing;
- Disposing of used tissues immediately;
- Washing hands often with soap and water or sanitiser for at least 20 seconds;
- Cleaning frequently touched surfaces and objects;
- Using face barriers such as layered cloth masks or medical masks;
- Maintaining social distance (>2 metres)- an extreme form of social distance is a national lockdown; other forms include stay at home/remote working;
- Using personal protective equipment (PPE) in the case of all health care workers (respirators; surgical masks; face shields; goggles; gloves; plastic gowns or aprons)

How does one test for Covid-19 and what do the tests tell you?

There are currently two types of diagnostic tests available for Covid-19: viral tests and antibody tests. In South Africa, only the viral test is utilised for diagnosing infection.

A viral test tells you if you have a current infection

The timing of testing is critically important. If one tests too early after exposure the test can be negative. You can also test negative if you use this test after the peak stage of infection. The molecular real-time polymerase chain reaction (RT-PCR) test detects the virus's genetic material. This test is conducted by inserting a swab deep into your nose or throat to collect a specimen for testing. False-positive results can occur with PCR tests, because the coronavirus's genetic material may linger in the body long after recovery from an infection in some individuals. While we think the virus is dead 10 days post-infection, the test remains positive. In fact, in South Africa, given the shortage of test-kits, repeat testing after 10 days of a confirmed infection is discouraged. False-negative results from antigen tests may range as high as 20 to 30 percent.

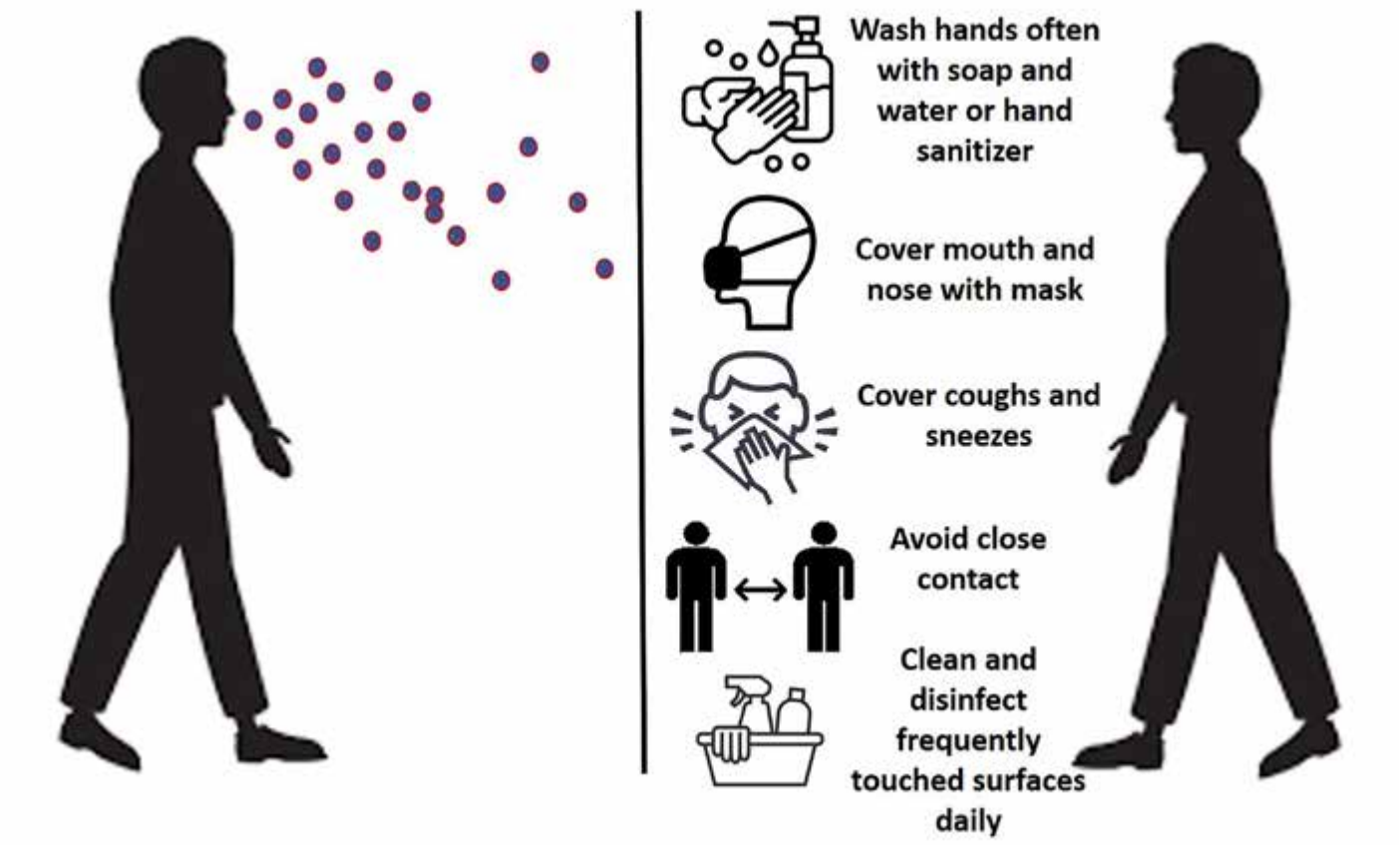


Figure 7.10: Preventive measures to avoid the spread of SARS-CoV-2. The virus spreads mainly from person-to-person between people who are in close contact with one another and through respiratory droplets produced when an infected person coughs, sneezes or talks. The best way to prevent Covid-19 is to avoid being exposed to the virus.

Source: Dos Santos WG. Natural History of COVID-19 and current knowledge on treatment therapeutic options. Biomed Pharmacother. 2020 Sep;129:110493. doi: 10.1016/j.biopha.2020.110493

An antibody test, detecting antibodies in your blood specific for proteins on the surface of the virus, tells you if you had a past infection but is not good at picking up current infection because it can take 1–3 weeks after infection for your body to make detectable antibodies. Having antibodies to the virus that causes Covid-19 might provide protection from getting infected with the virus again, but we do not know this for sure as a few cases of re-infection have recently been identified in China and the USA. We do not know how much protection antibodies provide or how long this protection might last.

Another serological test measures a person's levels of different kinds of antibodies, called immunoglobulins, all of which can be created as an immune response to an invader. They are called IgM (early), IgG (later) and IgA (formed at mucosal surfaces like the airways and intestines, but also found in the blood). These antibodies are all proteins produced by the immune system in response to an infection, but they appear at different times in the course of an infection, and they are all specific to that particular infection. They are found in the clear part of blood when it is separated from the red blood cells, which is called serum (after clotting) or plasma (without clotting).

What do SARS-CoV-2 IgG and IgM levels tell us?

Since SARS-CoV-2 is a new virus, we are still learning how our immune response works against Covid-19 and exactly how long antibodies last. Tests of total IgG and IgM levels cannot distinguish between early (IgM) and late (IgG) antibody responses and, as a result, don't provide a clear picture about whether an individual has potentially developed a longer-term immune response (IgG) or is currently infected (IgM). Alternatively, an IgG-specific serology test reveals if a person had coronavirus in the past and has developed antibodies that are highly specific to the virus.

While we don't yet know if IgG antibodies offer lasting SARS-CoV-2 immunity, the IgG-specific test does tell clinicians of past infection, which can provide important information regarding individual and population immunity levels.

In South Africa, antibody tests have only recently been approved and are primarily used for surveillance purposes (monitoring who has been infected at a population level) rather than for diagnostic purposes.

Children and Covid-19

To date, data on Covid-19 in children and adolescents remain scarce. Such young people can be asymptomatic or may present with fever, respiratory and/or gastrointestinal symptoms. Recent studies have demonstrated that Covid-19 is generally a mild disease in children when compared with older patients. It is not

yet known what the reasons for the difference in severity of disease are, but three possibilities exist:

- Children may have lower viral loads even if they get Covid-19. There may be a correlation between the severity of Covid-19 and the viral loads (or the duration of virus-shedding period).
- Children have lower expression levels of ACE2, when compared to adults, and, therefore, have fewer receptor sites for the SARS-CoV-2 to bind to.
- There may be a simultaneous presence of other viruses in the mucosa of the lungs and airways, common in young children, and these viruses may compete with SARS-CoV-2 virus and limit its growth.

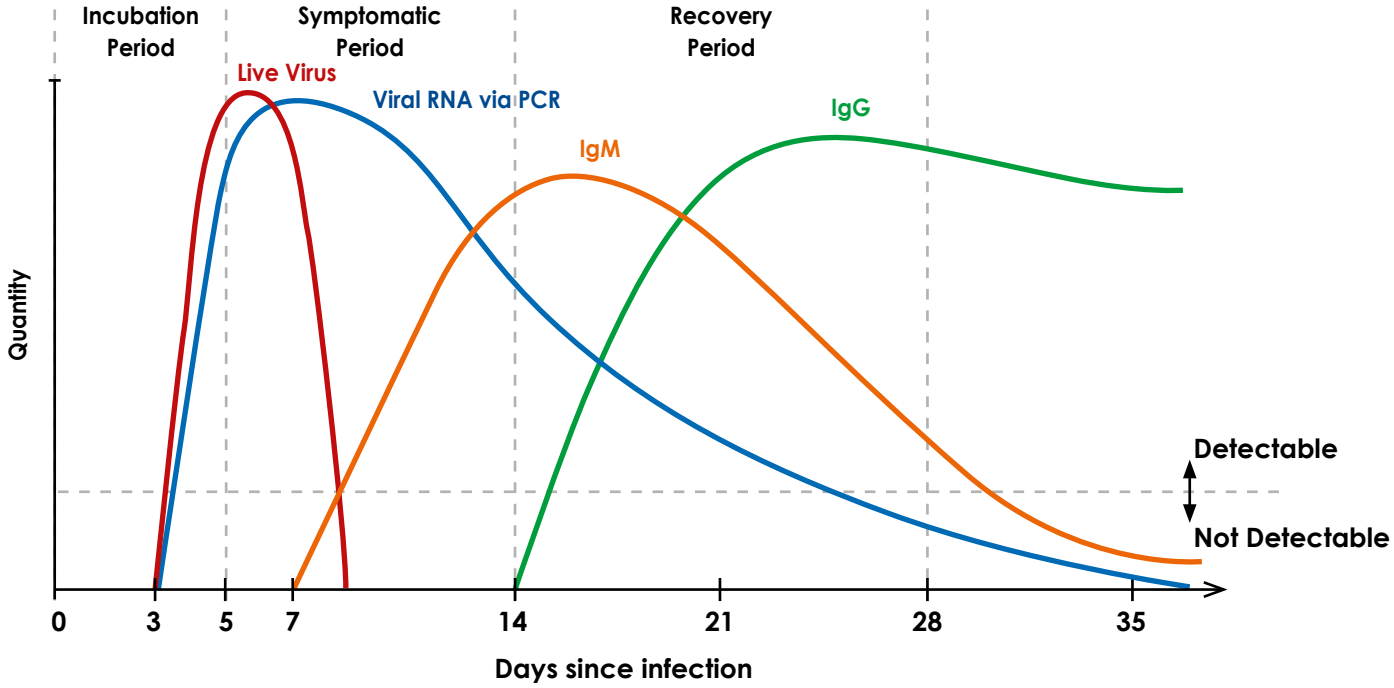


Figure 7.11: Window for detection of SARS-CoV-2 infection

Reprinted with permission from: Denning et al., British Dental Journal 229 (2020) 521

There has been a record of children and adolescents with a very rare Covid19-associated multi-system inflammatory condition, which seems to develop after the infection rather than during the acute stage of Covid-19. The clinical features of these paediatric cases are both similar and distinct from other well-described inflammatory syndromes in children, including Kawasaki disease, Kawasaki disease shock syndrome, and toxic shock syndrome. This Covid-19 associated multi-system inflammatory syndrome in children and adolescents is referred to interchangeably as paediatric inflammatory multi-system syndrome temporally associated with SARS-CoV-2 (PIMSTS) or multi-system inflammatory syndrome in children (MISC) associated with Covid-19.

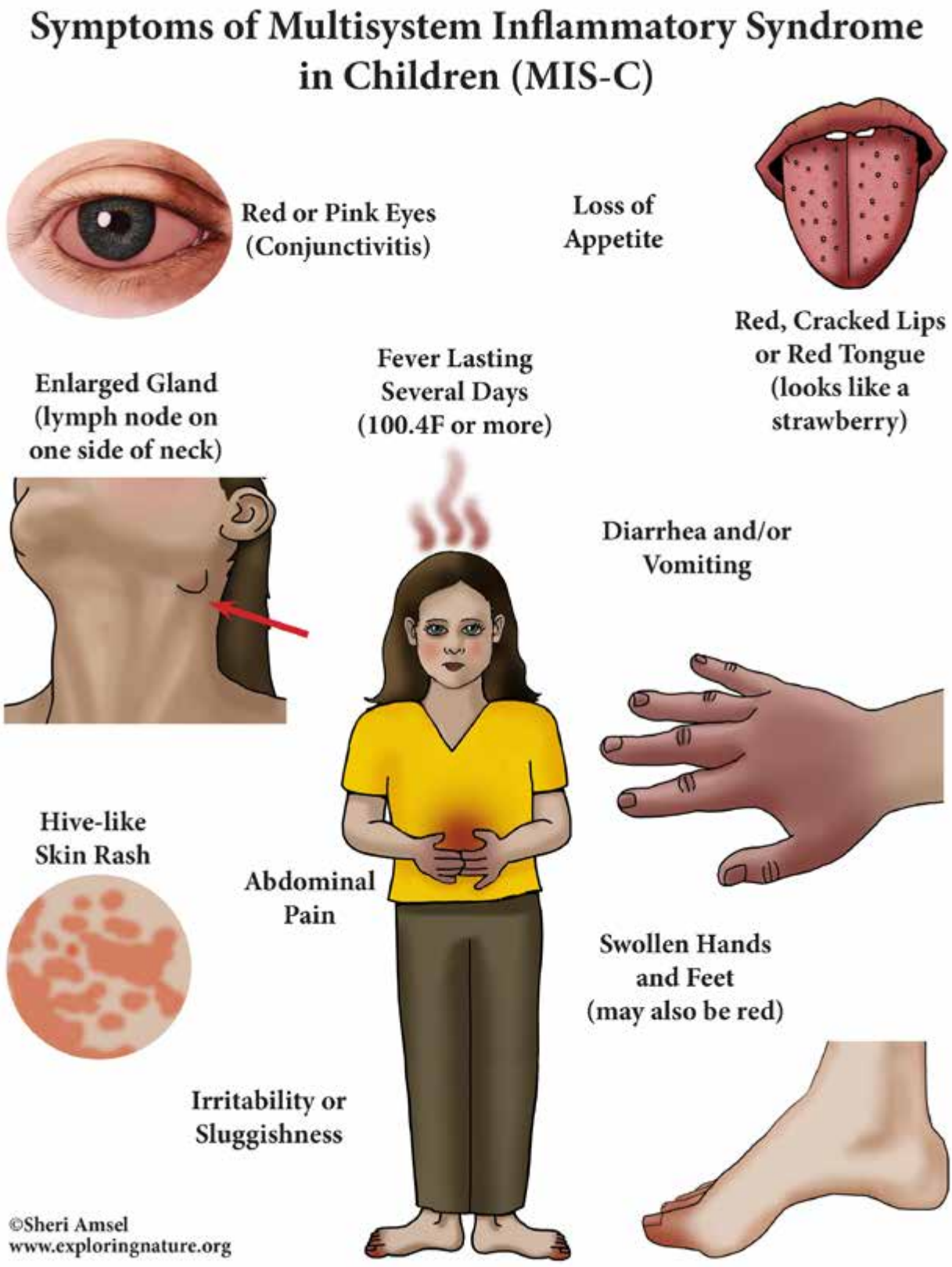

Symptoms of Multisystem Inflammatory Syndrome in Children (MIS-C)
Red or Pink Eyes (Conjunctivitis)
Loss of Appetite
Red, Cracked Lips or Red Tongue (looks like a strawberry)
Enlarged Gland (lymph node on one side of neck)
Fever Lasting Several Days (100.4F or more)
Diarrhea and/or Vomiting
Hive-like Skin Rash
Abdominal Pain
Swollen Hands and Feet (may also be red)
Irritability or Sluggishness
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Figure 7.12

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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.

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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