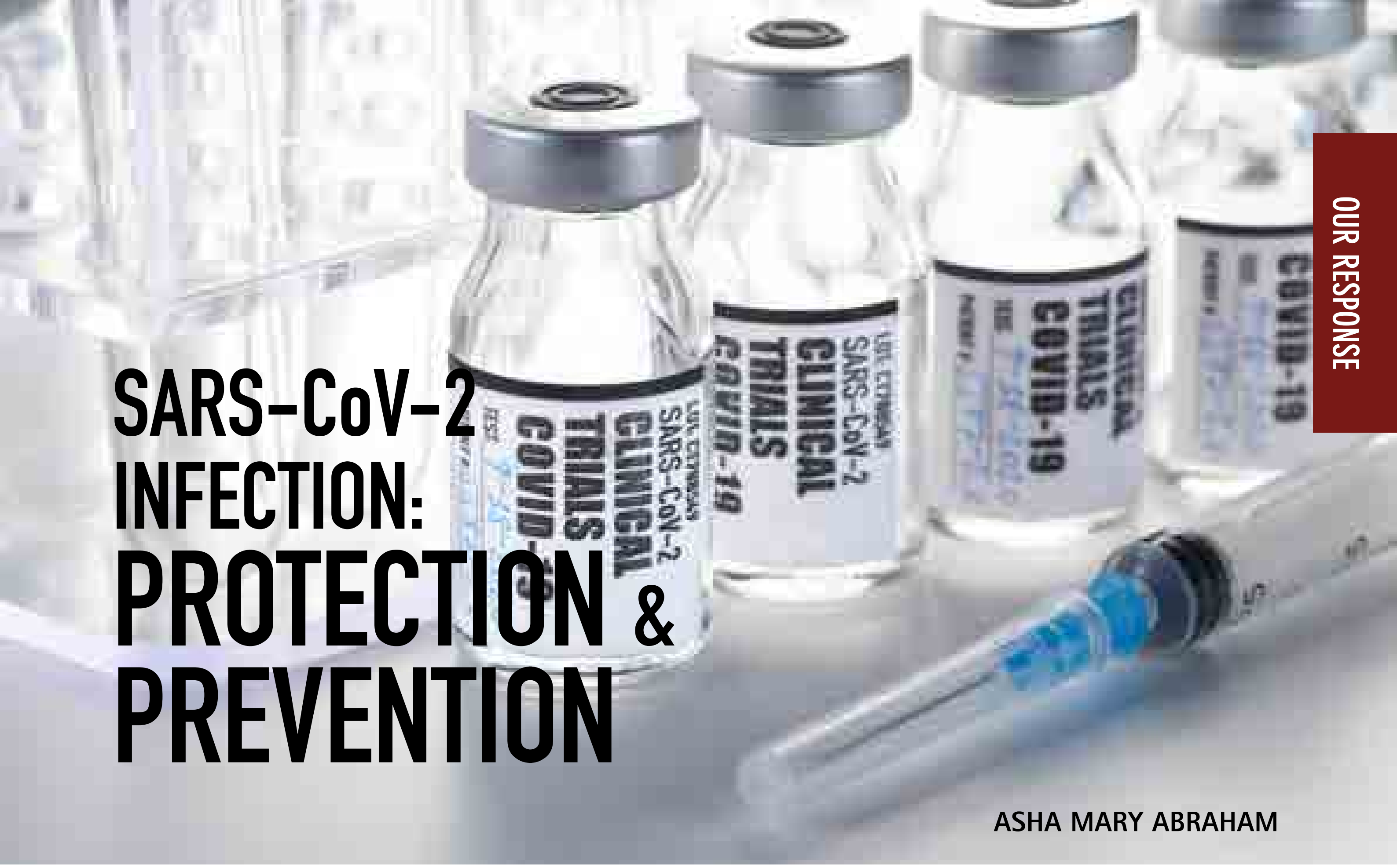

SARS-CoV-2 INFECTION: PROTECTION & PREVENTION

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How do vaccines protect us from infection? How are they developed? How quickly can a vaccine against COVID-19 be made widely available for use? What behavioural changes can help prevent infection? Do our general health and immunity impact our risk of developing severe disease?

The world has seen numerous pandemics in the course of human history. One of the most severe ones in recent history was the influenza pandemic of 1918 that infected a third of the world and killed between 20-50 million people.[1] Subsequent influenza outbreaks that occurred in 1957 and 1968 killed 2 million and 1 million people respectively.[2] The HIV/AIDS pandemic that began in 1981 has killed about 32 million people worldwide.[3] The Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) spread from 2002 to 2003, causing about 813 deaths, while the H1N1 influenza spread in 2009 led to about 575,000 deaths.[4] More recently, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), which was first identified in Saudi Arabia, has caused 858 deaths since 2012.[5] Currently, the world is in the grip of the COVID-19 pandemic caused by the SARS-CoV-2 virus. From its beginnings in December 2019 to mid-September 2020, there are over 29 million confirmed COVID-19 cases from around the world with about 900,000 reported deaths.[6] How do we protect ourselves and prevent infection?

Protection from SARS-CoV-2 infection

One of the most important methods of decreasing the burden of infectious diseases around the world is immunization. **Immunization** is a process by which we develop protection or immunity to the pathogen or infectious agent causing a disease through the administration of a vaccine. Vaccines are administered by injection, orally, or nasally via aerosol.

How does a vaccine protect us? It triggers antibody production and cell-mediated immunity against an infectious agent or pathogen inside the body. This is achieved by exposing our body to a killed or weakened pathogen, a toxin it produces, or a component (like a surface protein), called **antigen**, that can trigger such a response against the live, infectious pathogen. Often, adjuvants (like aluminum salts) are used to increase the immune response that the vaccine triggers. Which of these are used in vaccines against viruses? Some antiviral vaccines are in the form of an inactivated virus. Vaccines against polio, rabies, influenza, and Japanese encephalitis are examples of such vaccines that have led to the eradication of disease. Other antiviral vaccines can be in the form of live attenuated viruses. Examples include the oral polio vaccine, as well as vaccines against measles, mumps, rubella, yellow fever, influenza, and rotavirus. Live attenuated viral vaccines have low pathogenic ability but retain their ability to induce immunity. Yet other vaccines may be in the form of a component of the virus that confers immunity. For example, virus-like particles (empty protein shells of viruses) have also been used to make vaccines against the human papilloma-virus, rotavirus, and influenza virus. Newer vaccines, like the recombinant hepatitis B vaccine, have the viral gene of interest cloned and expressed in yeast cells to allow easy production. DNA vaccines can be in the form of genes of interest, which are delivered by direct injection into the individual. Some DNA vaccines against respiratory viruses are delivered nasally through aerosols, while others are delivered in edible forms. In contrast, RNA vaccines, delivered in lipid nanoparticles, induce antibody production by coding for proteins that resemble those of the pathogen.

As with any medical intervention, the general cycle of vaccine development and their routine approval for use involve multiple stages (see **Fig. 1**). The first stage, called the **exploratory** stage, is used to identify natural or synthetic antigens that may prevent disease. In the second stage, called the **preclinical** stage, cell or tissue culture systems and animals are used to determine if the vaccine candidate produces immunity or proves harmful. In the third stage, called the **clinical development** stage, institutions that receive approval from regulatory bodies conduct three phases of clinical trials:

- **Phase I** trials are aimed at determining safety of the vaccine in a small group of volunteers
- **Phase II** trials are aimed at determining safety, immunogenicity, immunization schedule, and dose size in a few hundred individuals, and
- **Phase III** trials where thousands or tens of thousands of test subjects are vaccinated to continue determining the safety and effectiveness of the candidate vaccine, perform regulatory review and approval, manufacturing, and quality control.[7]

The normal route to vaccine approval takes at least two decades. But these are not normal times. Over the past few months, many vaccine companies have stepped up to the task of developing an anti-COVID-19 vaccine in a matter of months rather than decades. For example, Oxford University has tied up with the Serum Institute of India and identified a vaccine candidate that has elicited a protective immune response in early trials. Meanwhile, Bharath Biotech's indigenously produced vaccine, Covaxin, has shown an encouraging safety profile in Phase I trials. The possibility of using a Controlled Human Infection Model (CHIM) is also being explored in this context. In this

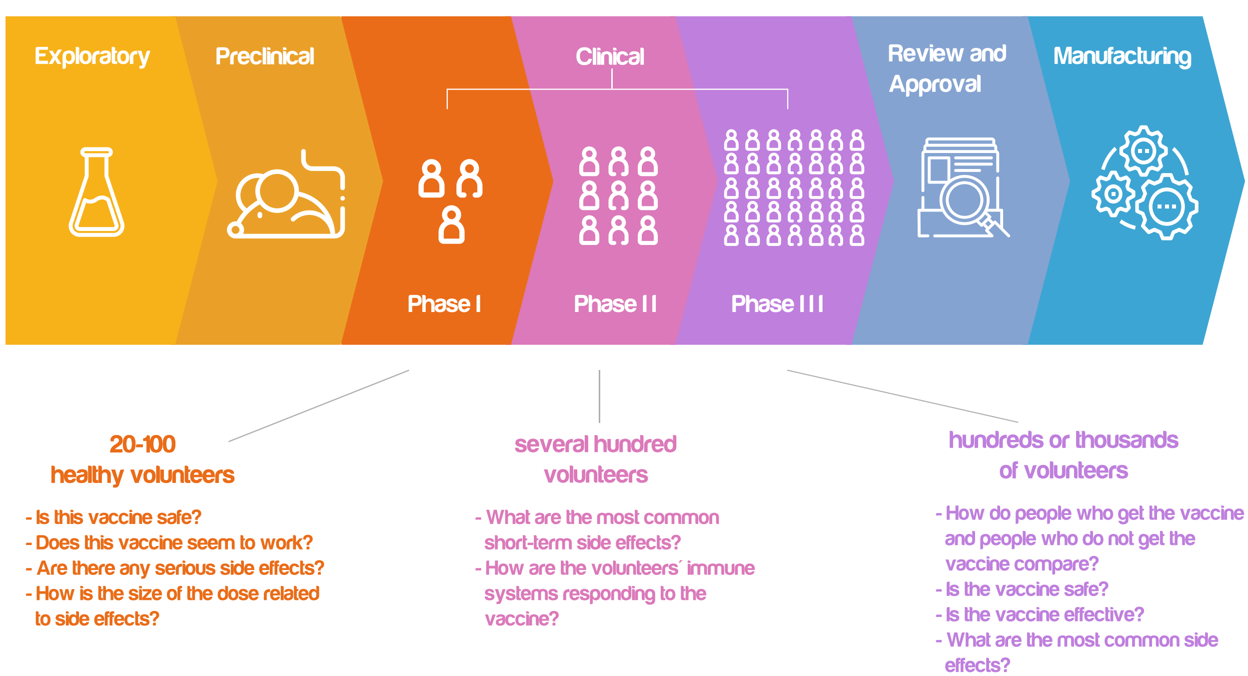

Fig. 1. How is a new vaccine developed, approved, and manufactured?

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model, healthy participants consent to being deliberately exposed to a well-characterized and weakened form of a pathogen under highly controlled conditions. This can help us gather more robust information on pathogenesis, potential vaccine candidates, duration of immunity post-vaccination, and the nature of protection in a healthy population.[8] The key challenge in vaccine development for COVID-19 is to achieve speed without compromising on the regulatory aspects built into the process to ensure safety, efficacy, and quality.

Prevention through behavioral change

That the SARS-CoV-2 infection is highly transmissible is evident by its current spread. This infection spreads through respiratory droplets released when an infected person coughs, sneezes, speaks loudly, or sings. Some of these droplets land on physical surfaces. An uninfected person catches the infection when they come into direct or indirect (touching a surface contaminated with the virus, and then touching one's nose or mouth) contact with these droplets. It is now believed that the infection can also spread by inhalation of aerosols that remain suspended in the air for a few minutes to a few hours. The risk of transmission increases in closed spaces. For example, a study showed the presence of the virus in the air up to 4 m away from infected patients in a hospital. While this is twice the distance recommended for physical distancing measures, the researchers involved in this study also cautioned that the small number of viruses found at this distance may not necessarily be infectious.[9]

Not everyone who is infected shows clearly identifiable symptoms of disease immediately after being infected. Once it enters the body, SARS-CoV-2 can go through an incubation period that ranges from 1-14 days. It usually lasts 3-7 days, but could extend to 24 days in some cases. During this presymptomatic stage, people continue to shed the virus. Other infected people show no symptoms at all, but can shed the virus and infect others. For example, in a study conducted in China, a small sample of asymptomatic individuals were found to show lower antibody levels and a weaker immune response. However, they were able to shed the virus over a longer duration of time.[10] Who would we be most likely to transmit the infection to? Spread is most likely to occur among close contacts (family, health care workers) at around 1.8 m distance.[9]

Simple behavioral changes can help prevent infection through:

- **Direct contact with droplets and aerosols:** Keeping a physical distance of up to 2 m (or 6 feet) from other people in public spaces is an important preventive measure. This can help protect us from close contact with infected people, and protect others from the risk of infection by direct contact with droplets released by us. Covering the mouth and nose with a cloth mask in public places is crucial, particularly when physical distancing is difficult to maintain. However, it's important to keep in mind that a mask is not a substitute for physical distancing. Other important ways of preventing infection include the practice of always covering the mouth and nose with a tissue when coughing or sneezing. If this is not available or possible, the inside of the elbow may be used instead. If a tissue is used, it must be disposed of immediately after use, and our hands must be washed well with soap and water. This will help prevent spread of any viruses on our hands to any surface or person one encounters next.
- **Indirect contact with fomites or contaminated surfaces:** Like other coronaviruses, SARS-CoV-2 is an enveloped RNA virus. It has been found to remain active on metal and plastic surfaces for up to three days, and on soft surfaces (like carpets and curtains) for shorter durations. For example, one study showed that the floors, computer surfaces, handrails, door knobs, and waste bins in Intensive Care Units (ICU's) can be contaminated with the virus shed by an infected person. How long the virus stays active on these surfaces depends on many factors. For example, SARS-CoV-2 is sensitive to ultraviolet rays and heat, but can resist the cold (even temperatures below 0°C). The phospholipid envelope of the virus can be effectively inactivated by solvents that dissolve lipids. These include ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid, and chloroform (except for chlorhexidine).[11] Soap can also effectively inactivate the lipid layer. This is why washing hands often with soap and water for at least 20 seconds (before touching one's face, eating, preparing food; and after using the restroom, coughing, sneezing, blowing one's nose, caring for the sick, and handling a face mask) is recommended. If soap and water are not available, then a hand sanitizer with at least 60% alcohol must be used.[11] Surfaces that are frequently touched should be cleaned and disinfected daily with household disinfectants.[12]

Some categories of individuals **are** at higher risk for severe COVID-19 illness. Risk factors in these categories include age (with the highest risk in individuals above 85 years) and underlying medical conditions (like cancer, chronic kidney disease, chronic obstructive pulmonary disease, obesity, serious heart conditions, and Type 2 diabetes mellitus). Other individuals who **might** be at risk for severe COVID-19 include those with moderate to severe asthma, cerebrovascular diseases, high blood pressure, immunocompromised states (from transplants, immune deficiencies, HIV, steroid use), dementia, pregnancy, liver disease, lung fibrosis, smokers, and Type 1 diabetes mellitus.[13] For individuals with these risk factors, the best way to prevent COVID-19 is to avoid contact with infected individuals. This is particularly important till COVID-19-specific drugs and vaccines become widely available. People with mild symptoms who are otherwise healthy are advised to manage their symptoms at home so that hospital facilities are available for more severely ill patients.

Parting thoughts

Maintaining a healthy lifestyle (eating a balanced diet, getting adequate sleep, being physically active, and refraining from smoking) is important in keeping the immune system healthy to reduce episodes and duration of disease. However, some supplements are essential to proper functioning of the immune system, and have been shown in various well-conducted studies to lower the risk and/or duration of respiratory infections. These include vitamin D, zinc, vitamin C and vitamin B complex. Other less rigorously studied supplements are garlic and curcumin (found in turmeric). However, no supplement is currently known to actually protect against COVID-19 per se.

Key takeaways

- Immunization is one of the most important methods of decreasing the burden of infectious diseases around the world.
- Vaccines protect us by triggering antibody production and cell-mediated immunity against an infectious agent or pathogen that is subsequently encountered inside the body.
- The general cycle of vaccine development involves three stages — exploratory, preclinical, and clinical development.
- The clinical development stage involves three phases of clinical trials to test the safety, efficacy, and quality of the vaccine.
- Many companies have risen to the challenge of developing a vaccine for COVID-19 through processes that combine speed with safety, efficacy, and quality.
- Infection can be prevented through simple behavioural changes like physical distancing, the use of face masks, frequent washing of hands with soap and water, as well as disinfecting frequently used surfaces.
- Maintaining a healthy lifestyle is important in keeping the immune system healthy enough to reduce episodes and duration of disease.

Note: Source of the image used in the background of the article title: https://media.istockphoto.com/photos/clinical-trial-vaccine-covid19-coronavirus-in-vial-with-syringe-on-picture-id1215846334. Credits: Bill Oxford.

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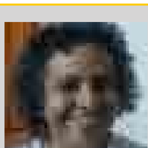

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