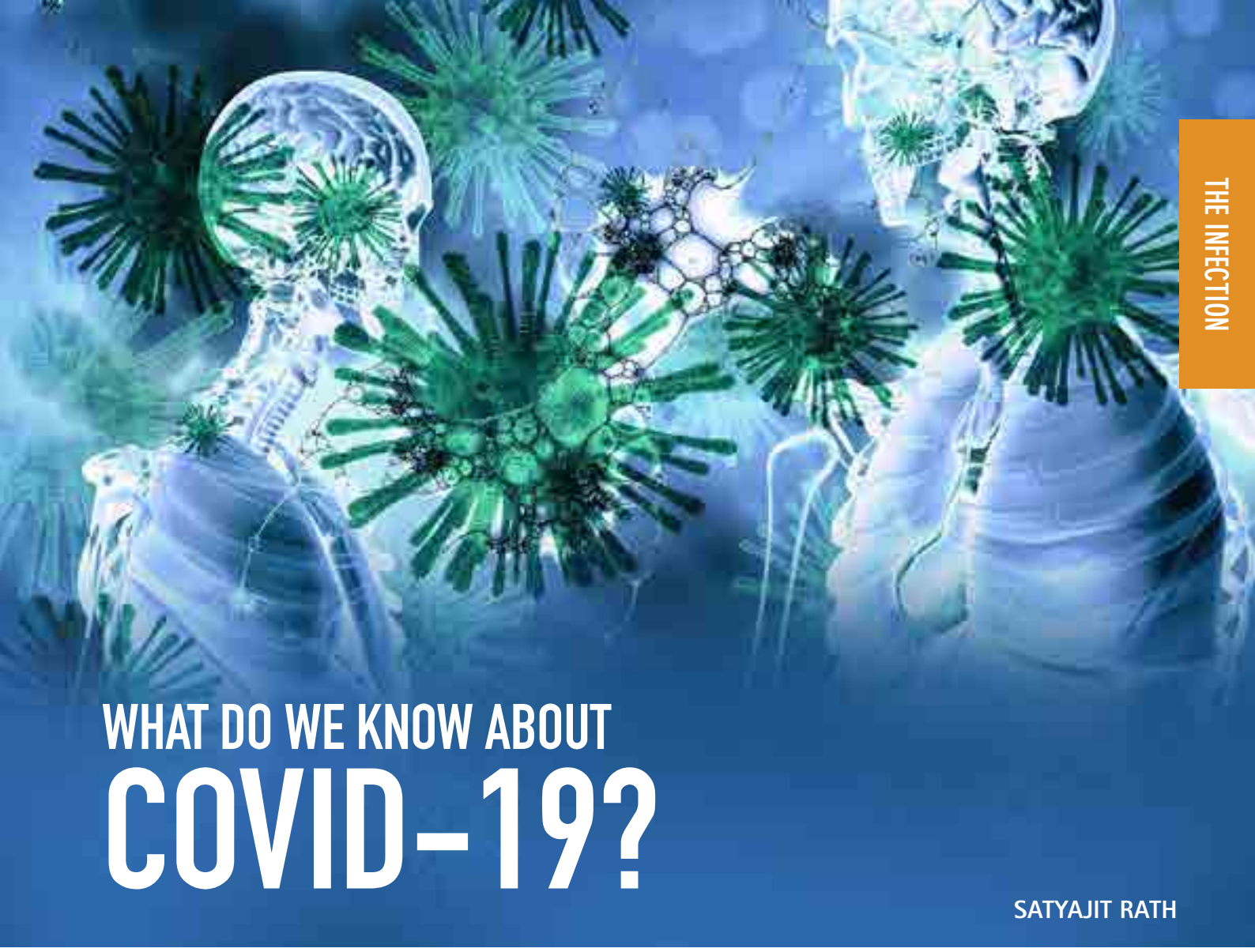

WHAT DO WE KNOW ABOUT COVID-19?

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How does SARS-CoV-2 infect the human body? What factors help or hamper infection? Why do we see such wide variation in the symptoms and signs of the disease? Does SARS-CoV-2 affect children? And how deadly is COVID-19?

SARS-CoV-2 is a virus. Viruses are very, very small particles that can stick to the surfaces of certain cells (called **host cells**) in our body. This sticking can only happen if the shape of a part of the virus surface matches the shape of a part of the cell surface. Only when this sticking happens efficiently can the virus particle get into the cell. Once inside, the genetic information in the virus particle (like the RNA in SARS-CoV-2) is brought into operation by the biochemical processes of the cell. This results in redirection of these processes towards making and assembling many copies of the virus particle. These copies can then emerge from the infected cell (which often dies) and drift around. They can stick to many more new cells, not only starting the cycle all over again, but enlarging it.

Establishing infection

SARS-CoV-2 particles enter the body, by and large, through the nose and mouth into the airways. So the first cells they meet and infect are the cells lining these airways. The immune response of the body limits and contains these spots of infection. Large numbers of these infection spots can cause problems for the functioning of the airways. The virus particles can also spill over from these spots into the rest of the body, infecting cells in other parts, and increasing the problem.

Two factors help the virus infect us. The virus particle's ability to stick very efficiently to target cells, and the usability of the virus RNA by the biochemical processes of many different cell types. The latter helps ensure that new virus particles will get made from

any cell type infected. Both are true of SARS-CoV-2 — it sticks very efficiently, and it can grow in most cell types. Two factors can hamper infection. The most obvious one is to prevent the virus from getting into the body. This is why measures like physical distancing, masks, and frequent hand-washing are recommended. Secondly, pre-existing immunity in the body, specifically against SARS-CoV-2, can prevent it, for example, from sticking efficiently to cells and entering them. This is what will happen, hopefully, with effective vaccination.

Infection symptoms and signs

Interestingly, most symptoms and signs of infection are, in fact, symptoms and signs of the body's response to the infection! Since SARS-CoV-2 enters through the airways, most (though not all) of the earliest symptoms will relate to the airways. Infection of cells of the airway lining causes irritation and cough. Depending on whether the upper airway remains extensively infected or not, there may or may not be a 'cold' (which simply means such a lot of fluid comes out from the airways that it drips out from the nose and throat!). One of the many ways the body responds to the virus is by resetting its temperature control system, meaning fever. Since this re-setting is quite variable, there may be differences in this symptom, ranging from mild to severe fever. Widespread growth of the virus in the airways and lungs as well as the body's response to it affect the normal functioning of the airways and cause breathlessness. When both spill over, beyond the airways and lungs, other symptoms appear (see **Fig. 1**). These symptoms will vary depending on where in the body the virus happens to establish a foothold, and how widespread the body's response is. In other words, the symptoms and signs of infection will then depend on which organs are most affected.

So far, there is no evidence that different genetic strains of the SARS-CoV-2 virus tend to cause more or less severe illness. Currently, most of the variation in illness seems to be due to differences between people rather than the virus. Two categories of people are at higher risk of severe illness. One of these appears mostly to be associated with the existence of pre-existing changes in the body's inflammatory responses. These are of the kind seen in obesity, type 2 diabetes, heart disease, hypertension, chronic kidney or liver diseases, in the elderly, and (in a double whammy) in people with pre-existing chronic airway-related illnesses. As of now, there is little evidence that asthma in particular predisposes to severe COVID-19 illness, although clinical researchers are looking for such associations. A second category is of people with poor immune responses, such as cancer patients under chemotherapy.

The general indication from evidence seems to be that COVID-19 affects children and young adults less severely than it affects the elderly, although the symptoms seem to be similar in all groups. (There are rare instances of a quite distinct illness pattern in children, which is not yet well understood.) However, this is not the same as 'children being at low risk'. They will and do get infected. Also, while their own illness may be mild, children can certainly spread the infection to other people, such as their grandparents, who are at higher risk. It is useful to keep in mind that a large proportion of SARS-CoV-2 infections are **'asymptomatic'**, meaning without any symptoms at all. Among the infected people who do develop symptoms, cough is the commonest; only about a fifth of such people show no cough at all. The next commonest is fever, although about a third of infected people with symptoms show little or no fever. Breathlessness is the commonest symptom in the severe form of COVID-19. Screening for fever at travel checkpoints is useful, but it is likely that the spread of the virus

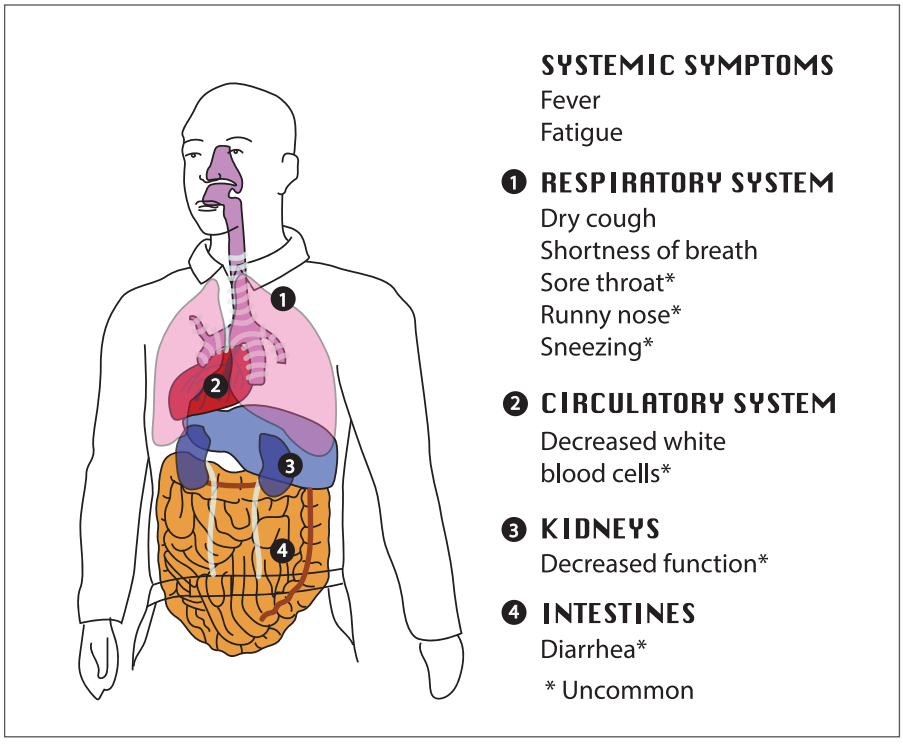

Fig. 1. The symptoms and signs of COVID-19 infection will vary depending on where in the body the virus happens to establish a foothold, and how widespread the body's response is.

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Box 1. How is COVID-19 different from other viral infections?

COVID-19 is likely more 'dangerous' than seasonal flu or influenza, in the sense that its 'infection fatality rate' is likely to turn out to be higher. While the viruses causing these infections are likely to be equally contagious, how 'contagious' a virus actually is will also depend on how susceptible the population is. Many of us are at least a little bit resistant to seasonal flu because of prior exposure to similar viruses, but that does not seem to be the case with COVID-19. This is likely to increase the actual rate of spread of SARS-CoV-2. Once again, this is why, even though COVID-19 infection does not put every individual who is infected at major risk of severe illness, it is a societal problem. If enough people get infected at the same time, then even the small proportion of severely ill people will be in large numbers and overwhelm hospitals.

Measles, chickenpox and mumps all enter the body through the nose and mouth, but they spread outside these areas of the body quite often. These viruses are all MUCH more contagious than either flu or COVID-19. Because they are so common, many adults tend to have met them and developed resistance. Therefore, most actual cases are in children. Measles can cause death about as frequently as seasonal flu does, while chickenpox and mumps are much less lethal than that.

from an infected individual starts a few days before that individual develops symptoms.

Fatality rates

Knowing exact numbers for measurements such as death rates for a pandemic is only possible when we look back at it. The so-called 'infection fatality rate' is the proportion of death amongst all infected people. Since so many SARS-CoV-2 infections are asymptomatic, this number is impossible to determine accurately at the moment. We need much more evidence of 'exposure' from surveys that will take a long time to collect. The so-called 'case fatality rate', which is widely discussed as being between 2-8%, is also quite inaccurate. This rate is the proportion of death amongst all infected and symptomatic 'cases', but what degree of severity is to be called a 'case' varies a lot from place to place and from time to time. Nonetheless, what we do know is that SARS-CoV-2 infection is not as dangerous as other coronaviruses we have met earlier, such as SARS-CoV or MERS-CoV (see **Box 1**). In fact, all the very approximate estimates and guesses of the infection fatality rate of SARS-CoV-2 put the number at much below 1%. Even among the categories of people at extremely high risk of severe COVID-19 illness, the eventual infection fatality rate is unlikely to exceed 5%.

However, nobody can predict, with absolute accuracy, what the course of illness will be in an individual. All our information is statistical and based on likelihoods, not guarantees. Good medical facilities will make the difference between life and death in people with severe illness. Severe illness is characterised by extensive lung involvement, with severe breathlessness and/or symptoms of other organs being affected. At such stages, if comparable medical-health facilities are available, the outcomes for severely ill COVID-19 patients are likely to be the same everywhere in the world. However, medical facilities are not comparable across the world and are, in fact, even less comparable between the well-off and the poor in the same place.

Parting thoughts

In this context, it is important to keep in mind that SARS-CoV-2 infection is not a major individual risk. In other words, every individual who is infected is not at major risk of severe illness, let alone of death. The spread of infection is a problem because if enough people get infected at the same time, then even the small proportion of severely ill people will be in large numbers and hospitals will be overwhelmed. This spread can be reduced by quickly identifying individual cases in communities, careful and rapid tracing of their contacts, providing every kind of support to infected/exposed individuals during their isolation, and increasing our public hospital capacity. Isolation needs to be seen as an action that infected or exposed individuals undertake for the good of the community, and not for their own sakes. This needs to be coupled with a cultural acceptance by society at large of a new norm of physical (NOT 'social'!) distancing along with the use of face-and-nose-coverings and frequent hand cleaning. Clearly, we — both the government and society — are failing miserably on most (if not all) of these fronts, and have simply been using versions of the so-called 'lockdown', including but not limited to keeping schools closed, as a (bad) substitute.

Key takeaways

- That SARS-CoV-2 sticks efficiently to target cells and grows in most cell types in the human body aids its ability to infect us.
- Preventing entry to the virus (through physical distancing, use of face masks, and hand hygiene), and developing immunity through effective vaccination can hamper SARS-CoV-2 infection.
- The symptoms and signs of COVID-19 infection vary depending on where in the body the virus happens to establish a foothold, and how widespread the body's response is.
- Most variations in illness seem to be due to differences between people rather than the virus. People with pre-existing changes in the body's inflammatory responses and poor immune responses are more susceptible to severe illness.
- Evidence suggests that COVID-19 affects children and young adults less severely than it affects the elderly. Children can spread the infection to people at risk, including their grandparents.
- It is difficult to know exact numbers for measurements such as death rates at this stage of the pandemic. But eventual infection fatality rates are unlikely to exceed 5% even among people at extremely high risk of severe COVID-19 illness.

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