

# How to Further Reduce the Risk of Serious COVID-19 Infections:

*Exploiting the Fragile Viral Envelope and the Self-Cleaning Mechanisms of Our Respiratory System*

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## Abstract

*Social distancing, washing hands and good hygiene are essential and currently the most potent methods available to curb down the unprecedented speed by which the new coronavirus is spreading across the globe. Even under lockdown, which is necessary to significantly reduce the number of people that get infected by an ill person, are there additional measures that each of us can embrace to even further reduce the risk of infection and the severity of the COVID-19 disease? Given the lack of licensed drugs that target SARS-CoV-2 specifically, we have to look into additional non-specific defense mechanisms that animals and humans evolved to protect themselves from pathogen invasions. The goal of this article is to describe how various of our non-specific defense mechanisms work, which actually precede the inflammatory response, and to discuss whether we can exploit the unique features of the coronavirus envelope and the self-cleaning machinery of the human respiratory tract to strengthen our self-defense. The challenge is to actively interfere with supportive measures during the short time window between getting exposed and before an inflammatory response gets initiated.*

**Keywords:** *coronavirus; self-defense mechanisms of the human body*

Since time is pressing as our health care system has already reached the limit of its capacity, are there additional measures that we ought to consider to reduce the risk of infection and perhaps even the severity of the COVID-19 disease and thus patients that require hospitalization? A closer look at the protective envelope of coronaviruses, as well as at the human physiology of the respiratory tract suggests several levels at which we might actively interfere: first, to pay conscious attention to taking care of our nasal cavity, mouth and throat. Second, to take measures to support the self-cleaning powers of the respiratory tract, and third, to think about how to best support our scavenger cells (alveolar macrophages) that are sitting in the dead ends of the highly branched lungs whose task is to gobble up the nanoparticles that arrive there. The more the new coronavirus spreads in our environment, the harder it will become to avoid coming into contact with it. Our body copes with the constant exposure to pathogens entering our nose or mouth in several stages, first by various non-specific defense mechanisms as discussed here, followed by the specific defense that is associated with an inflammatory response. Once viruses have invaded our body through the nose or mouth, it is increasingly important that each of us takes additional supplementary measures to ensure that as few of them as possible reach our lungs, where they infect host cells and can then cause the life-threatening inflammatory reactions. Since our respiratory tract is covered with a protective mucus layer, that is enriched with antiviral peptides [1], a look at the journey of a virus, from the mouth to the inner lungs, suggests that there might be a short time window of opportunity to act before an inflammatory response gets staged.

## Targeting the viral envelope

Some viruses have protective envelopes, including the coronavirus, that contain lipids (fatty substances originating from the host cell membrane), as well as viral glycoproteins. The many little spikes seen on the surface of a coronavirus are CoV-specific spike-proteins and give this virus its name “corona”. This spike protein contains the docking site by which the coronavirus specifically recognizes a host cell and infects it. Efforts to develop SARS-CoV or MERS-CoV specific vaccines thus focused mostly on the spike-protein [2-4]. Most recent reports suggest that a human monoclonal antibody specific to the first SARS-CoV virus, binds potently to the new SARS-CoV-2 too [5]. Despite intensive research on vaccines, mostly conducted in Asia since the first break-out of SARS in 2003, a licensed vaccine is still not available.

What else can be tried and why is the washing of hands with soap so effective? In contrast to vaccines that typically block the specific virus-host recognition, lipid membranes can be destroyed by detergents. Substances that destroy lipid membranes thus have the potency to destroy viral envelopes too – and in this case have an antiviral effect. Soap molecules have this ability, which makes the careful washing of our hands with soap so effective. Toothpaste also contains detergents which are able to destroy lipid membranes. It could therefore be effective if we gargle with available mouth washes, or the toothpaste foam that fills our mouth after brushing our teeth. However, I am not aware of any scientific literature on this.

Furthermore, plants synthesize a number of substances to protect themselves from microbes and viral attacks [6], such as ginger, which is known for its phenolic compounds [7, 8]. Since phenolic compounds like both water and fatty environments [9], they preferentially deposit at the interface of membranes with the surrounding water and thereby perturb or dissolve lipid rich membranes. Since the Influenza virus contains lipids in its viral envelope too, herbal compounds that are already used to relieve the early sore throat symptoms of Influenza may also help us in early stages - and this is speculation - to damage the envelope of the coronavirus while it is still attached to the mucus layer of the throat.

## The journey of the virus from the mouth into the lung

Our body not only fights viruses with specific antibodies, but also deploys an arsenal of other, non-specific defense mechanisms when it comes into contact with pathogens. Biology shows us how we can reinforce these endogenous safeguards to our benefit: When a coronavirus travels through our body, what happens on its journey before it infects one of our cells? And how does the virus actually get from our mouth or throat into our lungs?

What we know so far is that the coronavirus spreads mainly via droplets. This happens when an infected person exhales virus particles embedded in tiny water droplets and another person close by inhales them: thus social distancing is crucial. Upon entry into our respiratory system, incoming particles bind non-specifically to the walls of the airways, and it is well known today that the location where they get stuck depends primarily on the particle size [8-10]. While naked viruses are nanoparticles that can directly fly into the deepest pockets of our lungs as we inhale, the new coronavirus is transmitted embedded in droplets, and luckily for us, they are micrometers in size. This is good news as it provides us with more options to fight them. The virus-laden droplets settle on the mucous membranes in the nasal cavity or throat, or on the walls of the trachea and bronchial tubes.

For the virus to multiply, it must infect a cell close by – which takes time since the inner cell linings of our airways are covered up by a thin layer of mucus. Once inside the host cell, the host cell replicates the genetic information of the virus and produces a large amount of new virus particles which are finally released. Over several replication cycles, the virus spreads further into the respiratory tract until it reaches the last branches of the lungs.

## Conveyor belt cleans the respiratory tract

Since lungs, like manmade air filters, get dirty very quickly as they ventilate air, our respiratory tract possesses extremely effective and natural self-cleaning mechanisms by which the airways get regularly cleaned of dirt, spores and pathogens: the airway walls consist of cells that expose tiny cilia, which are covered by a thin layer of mucus (Figure 1). In analogy to a conveyor belt, the cilia all move in synchrony in a circular pattern to transport the mucus slowly from the bronchial tubes up into the throat [10-13]. In this process, particles deposited on the mucosal lining are removed from the respiratory tract [10, 11, 13]. However, when the mucus becomes too viscous, or the mucus layer gets too thick, this cell-driven conveyor belt begins to stall.

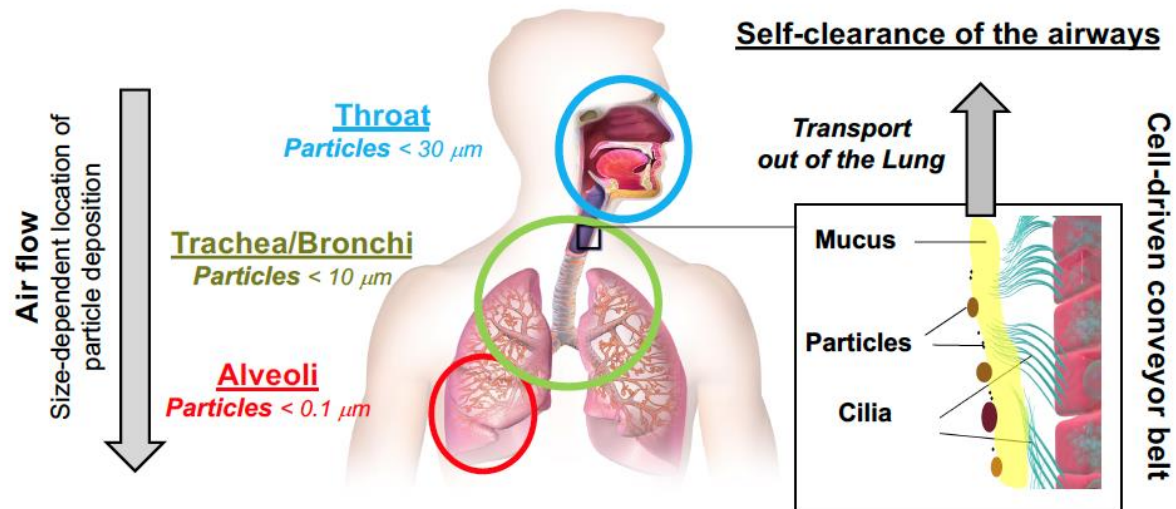


Figure 1: Self-Clearance Mechanism of the Lung. Environmental particles and pathogens are carried into the lungs as we inhale air. Nature developed a powerful mechanism to self-clean the airways as their cellular linings operate as conveyor belts. Inhaled particles collide with the airway walls where they get stuck on slimy surfaces, whereby the prevalent location where they get deposited along the airways depends on the particle size. The particle-enriched slime, including virus particles, is transported towards the mouth through synchronized circular movements of cilia (adapted from Blausen / Wikipedia / CC BY 3.0)

## Alveolar macrophages gobble up (virus) nanoparticles that reach the alveoli

In the lungs, a final, non-specific defense mechanism against viruses is provided by macrophages, specialized immune cells, which are found in the alveoli. These cells are responsible for keeping the lungs clean [14-16]; in doing so, they do not distinguish between pathogens and pollutants from the environment. But their capacity to gobble up particles is limited as evidenced by a smoker's lung gradually turning black. The more time alveolar macrophages spend removing fine dust and other particles from the alveoli, the less efficient they are at reducing the number of viruses. Once a virus has been given sufficient time to infect host cells in the alveoli, an inflammatory reaction gets started and additional macrophages get recruited.

## Multitude of measures to reduce the number of invading viruses

It is important to recognize that we do not necessarily become infected as soon as we inhale a first virus (even though our highest priority needs to be to prevent this), as we are equipped with a number of non-specific and specific defense mechanisms. The probability of the onset of an infection increases with the number of viruses that enter our body, which means that the dose of viruses is critical. The minimum dose of virus particles that can initiate infection, however, depends on the virus type as each of them uses different molecules to bind to and then penetrate the host cell [17]. Breathing only through the nose already reduces the number of viruses that enter the mouth region. Once they have entered into our body, there might be a window of opportunity for us to act as it takes some time for a virus to get in close proximity to a host cell and penetrate. At least some of the viruses that get nonspecifically stuck to the mucus linings of the nose, mouth and throat might get removed when using nose washes of which a wide variety is available. Since the Influenza virus also has a lipid-rich envelope as well, common home remedies that we typically use to fight the very early symptoms of influenza infections, such as gargling and drinking hot ginger tea, might be helpful too. Regular inhalation of warm water vapor further helps to keep the mucus layer in our respiratory tract more fluid, which in turn helps the conveyor belt to transport particle-enriched mucus towards our throat such that we can cough or rinse them out. Finally, to allow the macrophages in the alveoli to fight off viruses as efficiently as possible, it helps to avoid exposure to other environmental pollutants such as particulate matter, and to give up on smoking. Once the body starts to stage an inflammatory response, the measures discussed here how to strengthen our nonspecific defense mechanisms have little to no chance to cure a severely sick person as they are not specific to COVID-19.

The current situation is so serious that every possible option needs to be considered. Taking small, additional steps can help to further reduce the number of viruses that enter our lungs, and whether our alveolar macrophages have a chance to fight them successfully. Each of us might help the self-defense mechanisms of your body at several levels: from the nose, mouth, throat and bronchial tubes all the way to the alveoli. Please notice though that the viruses initially attach to the mucus linings of the airways. Those viral invaders that are not getting cleared by mechanisms discussed here will eventually infect host cells and this, as well as the subsequent immune response of our body, determines whether a severe lung infection might occur or not. We are not helpless against the coronavirus. Each and every one of us can do our bit to keep it in check.

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