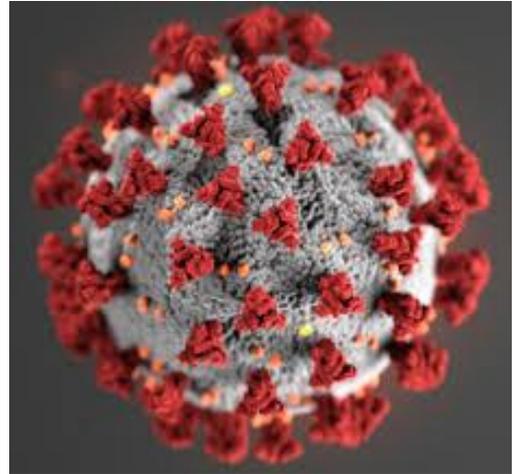


Hygiene habits for Covid-19 explained

To start, it is helpful to understand the differences between bacteria and viruses.

Bacteria are living cells that can divide and make more copies of themselves, and they do this in tissues, in the blood on the skin – it isn't necessary for them to be inside a human cell to divide, but they do borrow nutrients from the human body. Bacteria can be killed by various means, most often antibiotic drugs when a person or animal has a bacterial infection.

In contrast, viruses, such as SARS-CoV-2 that causes COVID-19 disease, are not living cells, but rather a piece of genetic material (RNA in this case) covered by a protective "envelope", which is a layer consisting of proteins and lipids (fats). A virus cannot divide and make more copies of itself on its own – it needs to get inside a cell of the infected host as it uses the cell's machinery to make more copies of itself. When a coronavirus such as SARS-CoV-2 enters the body through the nose, mouth or possibly the eye, the envelope uses protein "spikes" on its surface (shown in red on diagram) to bind to specific receptors on human cells and this allows the virus to enter those cells that carry that receptor. The receptor used for cell entry determines how many different tissues can be infected – some receptors are restricted to certain tissues and infection is thus limited to those tissues (for example influenza is mostly limited to the respiratory system), whereas in other cases, such as COVID-19, where the virus uses widely distributed ACE receptors, infection can involve a wide range of tissues throughout the body. Once in the cell, the virus uses the cell's machinery to make more copies of itself – these are then released from the cell and they can then go and infect additional cells.



Since the virus is not a living cell, in a literal sense it can't be "killed", but it can be destroyed. Outside the body, where it has no cells to infect and propagate itself, it will eventually disintegrate by itself. The speed of disintegration depends on temperature, humidity, the type of material on which it rests and other agents it is exposed to.

How do infected people spread virus? How do we reduce risk of transmission?

First and foremost, it is very important to recognize that infected people can spread virus during their asymptomatic incubation stage, which can last up to 2 weeks (or 4 weeks in rare circumstances). And some people will never develop symptoms yet can still spread virus for a number of days. Recent data suggests that about 50% of all infections are spread by asymptomatic people. It is for this reason that we all need to behave as if everyone, including ourselves, could be infected.

There are three main ways that an infected person spreads virus, two respiratory based, and one contact based. The respiratory routes involve virus being emitted into the air when a person breaths, talks, sings, coughs or sneezes – and in that order, more virus is expelled and the further it travels.

1. **Inhalation of large respiratory droplets** (5-1000 μm) are thought to be a primary method for spreading infection. These larger droplets are heavier so will not travel so far before settling with gravity onto surfaces. These can be inhaled if in close contact with an infected person and but are more likely to settle

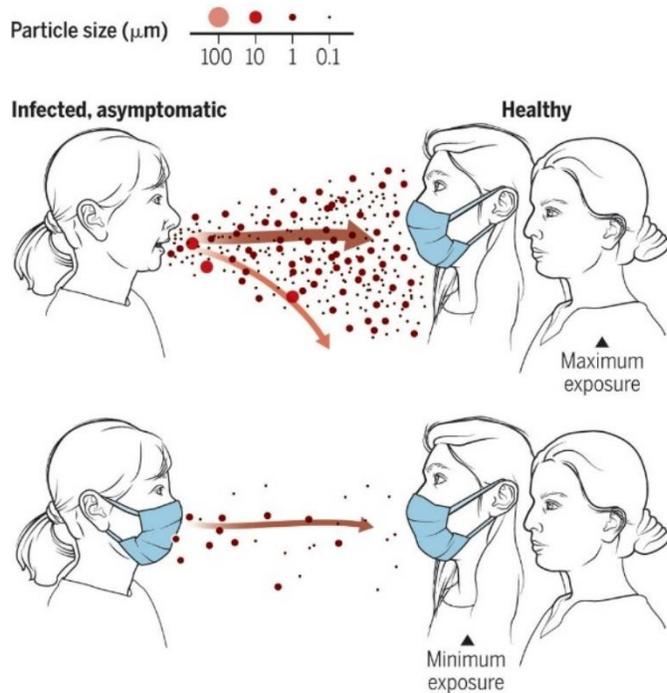
on surfaces and lead to contact transmission when another person touches those surfaces. The social distance guidance to stay apart at least 1.5 or 2 meters (depending on jurisdiction) is to reduce the risk of inhaling large respiratory droplets. Wearing a mask when social distancing can't be respected reduces the risk of transmission by large respiratory droplets

- Inhalation of smaller aerosols** ($<5 \mu\text{m}$) is thought also to be possible with this virus. It is estimated that 1 minute of loud speaking could generate more than 1000 virus-containing aerosols (V Stadnytski et al., PNAS, 2020). If aerosols are proven to be a possible mode of transmission, it does offer several concerns. First, aerosols don't settle quickly and can float in the air for several hours, and this means (i) virus aerosols can still be in the air after the infected person moves away, (ii) the aerosols can travel much greater distances than 2 meters by breezes or air currents (e.g., air conditioning), and (iii) the density can build up over time in an enclosed space (car, plane, small room). Second, inhaling small aerosols carries the virus much deeper into the lung, bypassing the main immune protective tissues in the nose and throat, and thus may result in a more severe disease outcome. For the reasons described above, the social distance guidance is less effective against small aerosols, especially inside buildings where the density of virus is less likely to be diluted into a large volume of air. Having everyone wear masks reduces but does not eliminate the risk of infection by aerosols since they can pass through cloth masks to some extent. One way to think about it is, if you are close enough to a smoker to smell cigarette smoke, or to a woman to smell her perfume, then you are close enough to be exposed to aerosols.

- Contact transmission** through touching a virus-contaminated surface. The most direct route would be to shake hands with an infected person who has covered a cough with their hand. Although few are shaking hands anymore, other surfaces can be contaminated with virus by an infected person touching them or by large respiratory droplets settling on them. If you touch a virus-contaminated surface, you can then infect yourself by putting your fingers in your nose or mouth, rubbing your eyes, or even just touching your face. This is the basis of the strong advice for frequent handwashing and use of alcohol gels when that isn't possible. It should be accompanied by sterilizing mobile phones, credit cards, car keys etc, if you may have touched them while your hands were contaminated. Mobile phones can be sterilized by rubbing with a cloth impregnated with rubbing alcohol (make-up removed pads work well).

Masks reduce airborne transmission

Infectious aerosol particles can be released during breathing and speaking by asymptomatic infected individuals. No masking maximizes exposure, whereas universal masking results in the least exposure.



GRAPHIC: V. ALTOUNIAN/SCIENCE

More about virus in the air

The likelihood of getting infected by sharing air with an infected person depends on several factors:

- **Viral load:** Some people put out much higher amounts of virus in their respiratory droplets than others; these are sometimes referred to as super-spreaders. Note that you need to inhale much more than one virus to get infected (if the number of viruses is low your immune system will take care of it) so being near a super-spreader is riskier than being near someone who sheds less virus.
- **Size of droplet:** This was discussed above – large particles may carry more virus but settle quicker and can be avoided with social distancing and masks. The smaller aerosols travel further, stay longer in the air and may be inhaled deeper into the lung, potentially causing a more serious infection.
- **Space:** This relates to viral density. The more limited the space, the higher the concentration of the virus and the greater likelihood of becoming infected. The more the space is open and ventilated, the more the concentration of the virus is reduced. Therefore, meeting people outside
- **Air currents:** These can spread the virus particles further, as was evidenced by a woman who infected 9 people in a Singapore restaurant – all 5 at her table but 4 at an adjacent table on the side that the air conditioner would blow her respiratory droplets or aerosols. On the other hand, air currents can also dilute the virus into a larger volume of air making it less infectious, especially when outside.

Virus on surfaces - how long does it last?

The most important factor for how long viable infectious virus lasts on a surface is the nature of the surface itself. A general rule of thumb for different surfaces:

- 3 hours on dust or another porous surface (fabric)
- 4 hours on copper (it is naturally antiseptic)
- 4 hours on wood (which dries it and prevents it from coming off easily)
- 24 hours on cardboard
- 42 hours on a metal
- 72 hours on plastic

Other factors that can affect how long the virus remains infectious on surfaces:

- **Temperature:** While heat destroys the virus, cold preserves it. Therefore, the risk of infection is greater in air-conditioned environments (e.g., building, car) and putting an infected item in the freezer will just preserve the virus until you take the item out (scientists keep viruses in freezers for years).
- **Moisture:** Some moisture is required for a virus to remain stable
- **Light:** Ultraviolet light (sunlight) can speed up viral decay by decomposing the protein of the envelope, regardless of the surface it is on. A UV lamp is a good way to disinfect a reusable mask.

Thus, a porous surface in a dry (dehumidified), warm and sunny environment is best. A shiny smooth surface in a cool, moist and dark environment is not so good.

How to destroy the virus on surfaces:

- **Soap or detergent** is the simplest but also one of the best approaches because foam disrupts the lipid (fatty) envelope layer and the virus falls apart. The more foam the better, which is why the instructions are to vigorously rub your soapy hands for 20 seconds or more. It is also possible to clean solid surfaces with soapy solutions; make sure you create foam.
- **Heat** is effective as it melts the fatty layer. It is good to use water above 30° C to wash your hands, clothes or anything else. In addition, hot water produces more foam, making it more efficient.
- **Alcohol** or any other mixture containing at least 65% alcohol (e.g., sanitizing hand gels) dissolves the outer lipid layer of the virus. Spirits such as gin or vodka are not effective as the alcohol content is too low (<50%). Listerine has 65% alcohol so can be used (except the alcohol-free version).
- **Bleach** dissolves the protein component of the virus envelope. Use a mixture of 1 part bleach mixed with 5 parts of water. This will dissolve the protein immediately and destroy the virus.
- **Hydrogen peroxide** (100%) will also dissolve the protein component of the virus envelope, but if used you should wear gloves as this high concentration is harmful to the skin.

What doesn't work? Bactericides and antibiotic are useless as the virus is not a living cell. Vinegar has no effect.

Other advice:

Never shake clothes (on their own or on worn clothing), sheets or clothing. If you shake a cloth or use a feather duster, the virus molecules can float in the air for 3 hours and sit in your nose.

The virus cannot pass through healthy intact skin, so it is okay to have virus on your hands, but make sure you wash them before you touch your face. However, by washing your hands a lot they may get dry and develop micro-abrasions where virus can enter – so make sure you use a hand moisturizer to keep the skin healthy. A thick glycerin-based moisturizer is best.

Always think about where your hands have been and what surfaces might be contaminated, then if there is a risk that your hands are contaminated, wash them before touching your face or anything in your home. You should wash your hands before and after touching mucous membranes, food, locks, door handles, buttons and switches (lights, lifts ...), telephones, remote controls, watches, computers, desks, televisions, etc.

Also keep your nails short, to prevent viruses from being trapped under the nails and not washed away.

When will it be safe to stop COVID-19 hygiene habits?

The short answer is not until there is herd immunity, and for you as an individual, not until you yourself have protective antibodies either because you were infected and recovered with adequate antibodies, or because you have been vaccinated.

Herd Immunity

Herd immunity means that a significant proportion of the population has protective immunity, in which case the virus can no longer spread easily within the community and it fizzles out. The proportion of population that needs to have protective immunity depends on the infectivity of the virus but is typically at least 50% of the population. For a highly infectious virus like measles, it needs to be closer to 95%. For COVID-19, it is estimated 60-70% may be required for herd immunity.

Today, herd immunity is always achieved through vaccination as this is the only safe way to ensure large proportions of the population are immune against a given disease. In theory, herd immunity could be achieved for COVID-19 through natural infection, but in practice it is an unacceptable approach. With Wave 1 of COVID-19 infections now past the peak in many countries, serology testing shows that only 2-5% of the population now have antibodies. This is a very far way from offering herd immunity and thinking of what would have to happen for more than 50% to have antibodies through natural infection is frankly unthinkable.

Vaccines – Let's be realistic

Enormous efforts are underway to develop a vaccine against COVID-19. Development of a new vaccine occurs in several different stages to ensure the vaccine is safe and effective and typically takes 5 to 10 years so the current efforts to develop one in 12-18 months is unprecedented, and while it is possible, is not guaranteed. Of the more than 100 vaccines currently under development, many will fail, but some should ultimately succeed. Here are some key points to keep in mind when you hear news about vaccine development for COVID-19

- While success for at least some of the vaccines is likely, it isn't guaranteed that a vaccine can be developed against COVID-19. To date no one has succeeded in developing an effective vaccine against HIV despite more than two decades of extensive effort.
- We currently don't know what type of immunity is required to be considered protective, and unfortunately it is different for every type of virus. This will be learned as late stage (Phase 3) clinical studies are undertaken where vaccinated people contact with virus and the outcome (protection from disease or not) can be correlated with the type of immune responses induced by the vaccine.
- It is important that all steps of vaccine development are respected to ensure the vaccine is safe and effective. Short cuts should not be permitted despite the urgent need. If the wrong type of immunity is induced it can actually make the disease worse than if the person was never vaccinated. This happened in the past with RSV and has also happened with a veterinary vaccine against a coronavirus in cats. Since we don't know the exact type of immunity required for COVID-19, this step cannot be skipped.
- When a company says they have "developed a vaccine" they can mean many different things. For those who announced it early, it means they have designed and constructed a molecule that could potentially be a vaccine. But this is very far from success as they have many steps to take, and there is a significant risk of failure at every step:
 - Prove that in animals the vaccine antigen elicits the types of immune responses thought to be protective against the virus. The spike protein is the target for most vaccines since that is how it

- enters cells, but the spike changes shape when it binds to cells, so if the vaccine is like the post-binding shape, rather than the pre-binding shape, it won't be effective.
- Prove that they can make it reliably – the antigen molecule needs to look the same with every batch. Depending on the platform, this can be sometimes challenging.
 - Develop all the assays needed to prove the manufacturing method is consistent – these assays must be done for every batch for the marketed vaccine.
 - Develop a formulation to deliver the antigen in. Sometimes this is just buffered water, but some vaccine platforms require lipid coats for delivery or adjuvants added to make them more effective.
 - Prove that the final vaccine combination (antigen + delivery system or adjuvant) is stable enough to permit distribution through the world. If it is falling apart within a few months, then it is not possible to manufacture and distribute within that time frame. Better stability can be achieved by freezing the vaccine, but that makes it very challenging to distribute, and virtually impossible in developing parts of the world.
 - Prove in Phase 1 studies in a small number of healthy people that the vaccine is safe (here safety only refers to reactions to vaccine administration) and induces the type of immunity thought to be required. This is also where the dose (amount of vaccine) may be selected as well as the number of administrations required –some vaccines work with a single shot but many require 2 or 3 spaced a month or so apart.
 - Prove in Phase 2 studies in a larger number of people of different ages, some with underlying health conditions, that the vaccine still appears safe (again just for reactions to administration) and induces desired immunity. It may be found here that older and less healthy people may require a higher dose or more injections.
 - Prove in very large Phase 3 studies (typically thousands of people in each study) who are at risk of being exposed to the virus (e.g., health care workers, or possibly the general community if there is a large outbreak) that the virus is safe (disease isn't worse than if they never had the vaccine) and effective (far fewer of them become infected, or become very ill if they become infected, compared to a control group who got placebo (water) vaccine. Phase 3 studies cannot be done in countries or communities where there is not a lot of virus circulating (due to lock-down measures for example). So companies need to be willing and able to go anywhere in the world that is appropriate to conduct Phase 3 trials at the time they are ready.
 - Prove that they can scale up the manufacturing to produce millions of doses. It can sometimes take years to work out how to scale up making some vaccines, especially if the approach used is novel, as is the case for many COVID-19 vaccines being developed today. This may require building new manufacturing plants, so for the desired timelines for COVID-19 (12-18 months) this has to start even before human trials start, when the company won't even know whether their vaccine candidate is safe and effective. So even if some of the vaccine have good clinical data, it

Expected outcomes if COVID-19 hygiene habits aren't maintained

This pandemic is not over, it is just getting going. One myth to address immediately is the concept of a second wave that won't come until November. That is influenza they are talking about – not COVID-19. Influenza is a seasonal virus and each year starts around November in the Northern Hemisphere. It is not known that COVID-19 is seasonal, plenty of virus are not. The fact that it spread quite effectively in Australia during its summer, as well as other hot countries (Singapore, Middle East) suggests that there may be no seasonality.

Many societies are starting to open up, not because it is completely safe to do so, but because there are competing needs to keeping people safe from the virus, for example the economy, mental health, employment and avoiding

starvation. As an individual, you should realize that if your government removes restrictions, it doesn't mean they can guarantee your safety from getting infected. No, it means they have enough empty hospital beds to be able to treat you if you get sick.

An important number to think about is the R value – R stands for “Reproduction Rate” and is the average number of people a single infected person infects. For some people who live alone and have early symptoms so they self-quarantined before they infected anyone, it could be 0 others infected. Or for the Biogen employee who attended a global work meeting in Cambridge MA in March, it was 60 others who ended up infected. But on average, most countries have shown R values of 2 to 4.

To understand what might happen next it is helpful to look at data that has been modelled by epidemiology experts. The data below was modelled by Adam Kleczkowski and was published in Science Alerts, 2 June 2020). The top row of the figure is R values over time (in all cases a R of 2.7 was used for the first wave – remember values around the world were typically between 2 and 4) and the bottom is the number of new cases over time.

Left Panel: If after the first wave, the country manages to keep the R value at 1 or less through adequate controls, then there will just be a long tail of infections but no second wave.

Middle Panel: If after the first wave, restrictions are eased until new infections reach a R value of only 1.2 then immediately introduces a new lockdown until R is 0.8, then eases restrictions again until R=1.2, and so on Then there will be a series of waves every 3 months or so, each almost the size of the first wave. This is feasible for countries that maintain strict social distancing rules even as they ease lockdown – if you are living in one of those you can be expecting your second wave by August (not November).

Right Panel: If after the first wave a country releases some control and the R value reaches just 1.2 and is held there, then they should expect a massive second wave, much bigger than the first. Truthfully, countries that remove restrictions too soon or too much will quickly achieve a R value higher than 1.2, in which case the second wave will be even more extreme than shown here. This is the likely fate for parts of the USA that opened too soon and do not have strict controls, especially now with all the groups of people assembling to protest, many without masks.

