Virology FAQ to understand COVID-19

Pierre Sonigo. March 31st, 2020

I have gathered here the answers to questions I am often asked. Although there is no certainty about this new virus, it can be better understood using the general knowledge of virology accumulated on other viral infections.

Can viral testing be effective in protecting the public?

The issue of the shortage of tests is a complex subject. This is not just a question of placing orders on time. Not only PCR kits are needed, but also extraction kits, instruments and swabs. This concerns a whole chain of actors, the place of national health industries, public-private cooperation, the weight of standards and regulations that hinder market access to research results or the authorization of analytical laboratories to receive COVID-19 patients or to analyze samples safely.

Second, it should be remembered that in the event of infection, current tests (PCR) that detect the presence of the virus provide a "snapshot" of a rapidly changing situation. In the event of an active epidemic and without strict protection, one may test negative one day and become infected the next. Conversely, you can have a negative test when you were previously positive, since the tests become negative no later than two to three weeks after recovery, and probably much earlier in most cases. In addition, tests performed on a large scale on a nasal-pharyngeal swab may miss the virus because there is little virus outside the lung or the swab has not been used properly.

As a result, the tests are very useful, but they do not provide an absolute protective barrier to contain the epidemic. A strategy of targeted isolation of carriers identified by PCR testing would require frequent and repeated testing to keep pace with the dynamics of the epidemic. This may be possible at the very beginning to follow the chains of transmission, but when the epidemic is launched, it becomes untenable as things move so rapidly.

However, it is then possible to trace infections that are cured, even late, by tests that do not measure the virus directly, but the antibodies that the immune system produces in response to the infection. These are called serological tests. A positive result from such a test is called seropositivity.

Serological tests may therefore be used to find out if you are immune after an infection is cured. But does a positive test result (seropositivity) mean that you are still infected and contagious, like in AIDS?

The case of AIDS is more the exception than the rule. In the case of AIDS, typical of chronic viral infections, the immune response is ineffective. There is no spontaneous recovery from the infection, the virus persists along with the antibodies that define seropositivity.

On the contrary, in an acute viral infection, such as influenza or COVID-19, everything is different. The appearance of antibodies produced by the host's immune response accompanies the disappearance of the virus and healing. The virus disappears or is too low to be

contagious. In acute viral infections, seropositivity is therefore a good match for cure and protection.

What is a virus? What is the point of the virus to kill its host?

I see viruses as a ballet of crystals that grow, intertwine, combine and then break apart to grow again elsewhere in our body or someone else's body. They can be seen more classically as micromachines that copy themselves. Of course, the virus has no objectives. But it turns out that if the propagation stops, the matter is over, we don't talk about it anymore: the viruses that propagate efficiently are indeed the ones that concern us. It's hard to believe that they don't do it on purpose with a Machiavellian strategy and it's easier to describe them by talking about their interest!

The coronavirus can kill its host or be eliminated by its host's immune response, which makes a big difference for the host but is the same for the virus itself! In both cases, before this happens, the virus must have found a new host. So a virus that kills quickly or that is quickly eliminated must be highly contagious in order not to disappear. Contagiousness is promoted by rapid multiplication, especially in the upper respiratory airways. It is this scorched-earth viral strategy that corresponds to what is called acute viral infection.

Otherwise, the virus has to wait wisely in its host, without killing it too quickly and multiplying less so as not to activate the immune response too much. This is what the AIDS virus does, for example, and is a typical example of what is called chronic viral infection.

Are there healthy carriers of the SARS2 coronavirus?

In the classic pattern of acute viral infection such as influenza or COVID-19, the disease and its transmission result from a balance between virus production and the intensity of the immune response. In other words, the most severely ill patients are those with the most abundant virus, they are the most contagious and those with the lowest antibody secretion. Conversely, the less severely ill have more antibodies and less virus and are less contagious.

It would therefore be surprising if there were both healthy and contagious carriers, although this is observed with other infectious agents. However, some people have mild infections that are almost invisible. But these are not exactly healthy carriers because the infection is transient and is accompanied by an effective immune response. Remember that contagion requires sufficiently high viral levels and the production of aerosols through coughing. Of course, in the presence of viruses, the risk of transmission is not zero and asymptomatic infections can participate in the spread. But from anyone with few symptoms, no cough, and a low infectious load, transmission is much less effective. During periods of active circulation of the virus and in any case while waiting to learn more, symptoms or not, respect for barrier gestures remains essential.

If cases of long-term healthy carriers with no immune response are observed, as observed frequently with hepatitis B for example, this will soon become apparent. But, once again, available data do not support such possibility.

What about the children?

The data show that children are spared the severe forms, but also that they are less often carriers of the virus. As explained above, this fits the classic pattern of acute viral infection: less virus equals fewer symptoms and less severity. So the idea that it is children, and therefore the least sick part of the population, who are the most contagious is paradoxical and therefore needs to be verified.

Why are children protected?

No certainty, but the most likely hypothesis is that children have preexisting immunity. If this is true it is probably because of recent contacts with endemic coronaviruses that cause colds, flu syndromes or viral gastroenteritis, frequent in children. This would confirm that endemic coronaviruses are actively circulating in the the many countries where children appeared as protected. It must be said that coronaviruses are rarely sought by tests, if any, in the context of the common viral diseases that we encounter so often. If they circulate so much, we can also imagine that they are responsible for a significant portion of our excess winter mortality, generally attributed to influenza. Could it be that coronaviruses are already responsible for some of the 10,000 winter deaths (in France) that we have been attributing to influenza for years? It is highly likely. Research on the subject, which will no doubt unfold over the next few years, may confirm or disprove this hypothesis.

If coronaviruses are common in many countries and cause benign diseases, why is the new SARS-CoV-2 variant so dangerous?

To put it simply, it can be said that the dramatic severity of the infection by this emerging coronavirus is due more to the low prior immunity of the population than to any specific feature of the virus. SARS-CoV-2 is in fact what can be called a "big" variant that is too different from the coronaviruses previously encountered by the population. It is very similar to its cousins, which have been present for a long time, several types of which have been described. But this resemblance is too low for acquired immunity against endemic coronaviruses to be able to protect people who have too little or too old immunity.

Immunity declines over time, which is why we are doing booster shots in vaccination. That could also explain, at least in part, why older people are the most sensitive. The increase in severity with age would therefore not only reflect the fragility of older subjects, but also the loss of immunity acquired in childhood with endemic coronaviruses. Accordingly, it can be proposed that children are best protected because they have had recent contact with endemic coronaviruses and therefore still have a recent, thus stronger immune response. This would correspond to classical anti-viral immunology schemes but needs to be confirmed for this new and poorly known virus.

In relation to the controversy "Is COVID-19 just a flu?" the answer is "only for those with a fairly strong pre-existing immunity! " and this is unfortunately not the case for 20% of the population! One can hope that when the population is immunized, due to infections or vaccination, it will become a "simple" flu. However, let's remember that the "simple" flu remains very dangerous and that it is important to protect oneself and others through vaccination and barrier gestures. Let's hope that the current pandemic will teach us not to go outside when we are feverish or have a cold and that it is forbidden to cough anywhere other than in a cloth or mask, especially in densely populated areas. A small price to pay to allow

our dear bars and restaurants, concert halls, cinemas, etc. to reopen as soon as possible without any fear.

Antivirals are very effective for AIDS; can we expect the same success with COVID-19?

In acute viral infections (flu, polio, rabies for example), antivirals do not have a central role, unlike in chronic viral infections (hepatitis, AIDS, herpes). Indeed, in an acute viral infection, everything goes very fast. This poses problems for the use of tests (see above) but also for the use of antivirals. The virus multiplies in a few days. Then either immunity eliminates it or secondary complications arise. Antivirals are therefore difficult to use in practice: to be really useful, they have to be administered very quickly. To do this, you must already know the virus in question, because antivirals are specific. If we treat at the very beginning, before the symptoms develop, we should ideally also be sure that it is worth it, especially when there are side effects, knowing that the majority of patients recover without treatment. Of course, while waiting for vaccines and broad protection of the population, an effective antiviral would be a great relief. HIV research has led to an incredible expansion of our range of candidate molecules.

While waiting for vaccines, another interesting solution would be the old method used against rabies (passive serotherapy): injecting the serum of cured people or anti-viral antibodies capable of neutralizing the virus. Only for the most serious cases, trials have been carried out with encouraging results.

And the vaccines?

When most infected people recover spontaneously, it is because the immune response is able to efficiently control virus multiplication. It can be anticipated that vaccines will be relatively easy to design and will be effective: this is the best approach in terms of public health. However, we will have to wait until we can guarantee the safety of a product intended to be injected into millions of healthy people.

And in the very short term, immediately and urgently?

In this period of containment, I invite you to read about the miraculous "snake oils" of the American Far West. Or more recently, the story of AL721, a miracle antiviral extracted from peanut butter that everyone was eagerly looking for in 1987, because unfortunately there was nothing else to cure AIDS. These stories remind us that an extreme anxiety-provoking situation, where the deadly threat is felt or experienced, is a fertile ground for the emergence of manipulators of all kinds who exploit their authority or the fears of their interlocutors to build power and glory, or to enrich themselves. They excel in lies, which are difficult to dismantle because it mixes the true and the false in a cloud of smoke, turn the burden of proof back on their detractors or dare to claim the worst enormities, because there is no worse lie than the one that corresponds to what everyone wants to hear. Social networks and the wide sharing of information, which did not exist in the Far West, not even in 1987, can amplify the impact of such lies terribly. My dream, of course, is to be wrong and for the miracle cure to be quickly identified. But I do not believe in miracles. Except true miracles, of course.

Can the virus disappear when it contaminates an inert object? Or when summer comes?

I'd say the virus dries up or something similar. It looks like a microscopical doughnut stuffed with protein, fat and covered with sugar. If it's not at the right temperature and humidity its components will melt or detach from each other. Laboratory data on temperature and humidity favorable to coronaviruses are not consensual. Some have even invoked the disinfectant effect of ultraviolet rays on sunny days.

In tempered latitudes, it is clearly observed that the flu is taking a summer break. We can bet that this will be the case for the emergent coronavirus. But we don't really understand the reasons for this. Is it an effect on the virus or on the resistance of its host? In hot and dry weather, it is possible that our respiratory tracts are more resistant, that the aerosols necessary for contagion are more unstable or that viral multiplication is less efficient. This can be of great help, but it is not a certainty or an absolute barrier.

How and when do we get out of containment?

This is a difficult epidemiological question. The example of China could guide us. The criteria will obviously be the epidemiological numbers, the hope that the classic summer break in tempered latitudes will be respected by the new virus, the possibility of respecting the rules of social distancing and the information from test campaigns combining serology and PCR.

There is here an ambiguity to be removed about the role of testing in the exit from containment. Will tests be used as an individual pass to get out of the containment? In this case, everyone would have to be tested, and it is not that simple. We are not in the AIDS situation, where carrying is longterm and effective individual protection is possible. As mentioned above, the negativity of PCR on swabbing is not a reliable indication to protect one's contacts.

Furthermore, testing everyone will take time. In addition to the blocking points already exposed, the tests must also be available on high throughput automatic laboratory machines. This is the case in the USA where urgent registration procedures have been applied by the FDA. For serology, it also remains to specify the assay results (quantity or quality of the antibodies assayed) that really guarantee protection.

In the short term, the tests will serve above all to have a better vision of the pandemic, the presence of the virus and immunity in the population. In this case, a representative sample of the population would be enough to inform national decisions and trigger a relaxation of the lock down measures currently applied. At the end of the testing campaigns that have already been launched in many places, the percentage of infected or immunized persons will be a good or bad surprise that will condition the modalities of exit from containment.