

The end of the COVID-19 pandemic : 5 reasons to be optimistic with the arrival of 2021

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Scientists have made extraordinary progress in fighting the COVID-19 pandemic.

The year 2020 was marked by an unprecedented effort by the international scientific community to better understand the coronavirus responsible for the COVID-19 pandemic, to adapt drugs already available so that the mortality due to this disease decreases, while developing in parallel with vaccines and new therapeutic agents capable of neutralizing the virus and putting an end to the pandemic. An entire program ! But the good news is that science has achieved some real feats and there are at least 5 reasons to be optimistic about the year 2021.

1. AT THE TISSUE LEVEL: the mechanisms responsible for the aggressiveness of this virus have been identified



A worker at a hospital in Greater Noida, India, works with a patient infected with COVID-19 and placed on a ventilator in intensive care.

From the first months of the pandemic, it became apparent that COVID-19 presented an atypical clinical profile very different from common respiratory infections. Of course, the lungs are the main organs affected by the infection, but the virus also causes the appearance of extremely bizarre clinical disorders for this type of infections, including failures of several other vital organs (heart, kidney, brain). which greatly increase the risk of mortality.

One of the main factors responsible for these peripheral attacks is the very dangerous inflammation-coagulation duo. In some patients, the inflammatory response elicited by the infection becomes so disproportionate that it causes more harm than the virus itself: this is commonly referred to as the cytokine storm, a phenomenon characterized by the fact that immunity becomes anarchic and no longer manages to correctly distinguish the enemy to be fought (the virus) from the cells of the individual.

In addition to causing damage to the lungs and other organs, inflammatory shock can also lead to the formation of abnormal blood clots (thromboses) which block the flow of blood to vital organs (lungs, heart, brain, kidneys) and can cause several serious accidents (heart attack, stroke, pulmonary embolism, kidney failure) which increase the risk of death.

Good point: The importance of the inflammatory and coagulation reaction in the pathogenicity of the coronavirus means that the damage caused by the infection can be substantially reduced by specifically treating these disorders, even without effective drugs against the virus. It is for this reason that very common anti-inflammatory drugs like corticosteroids have been shown to be among the most effective in reducing mortality in patients with severe forms of COVID-19.

2. AT THE POPULATIONAL LEVEL: we better understand the risk factors for clinical complications of COVID-19



A door giving access to a "hot zone" of the CHSLD Fernand-Laroque, in Laval, an establishment which has been hard hit by the virus.

It is now clearly established that the severity of COVID-19 varies greatly from person to person and that certain factors can significantly accelerate the development of serious illness.

Age

Age is by far the main risk factor for severe COVID-19: in Quebec, 73% of deaths caused by COVID-19 have occurred in patients over 80 years old, while these deaths are extremely rare in young adults and children.

Only 0.5% of the deaths affected those under 50, or 45 people out of more than 8,000 deaths, for all of Quebec during the 9-month pandemic. Remember that cancer alone kills more than 60 people a day in Quebec.

The constant decrease in the effectiveness of the immune system as we age contributes greatly to this increased vulnerability of older people to the virus. This is especially true for men, whose immune response is weaker than that of women and also declines more rapidly with age. In Quebec, the data collected to date show that the standardized death rate is approximately 30% higher for men than for women.

Positive point: The effectiveness of basic non-pharmacological interventions (mask, ventilation, basic hygiene, social distancing) is now well demonstrated and these very simple actions are now adopted by the vast majority of the population. The arrival of a vaccine should not cause

relaxation, but on the contrary, encourage us to increase our efforts for a few more months to protect this vulnerable population.

Comorbidities and obesity

A recent analysis by the National Institute of Public Health of Quebec (INSPQ) reveals that 97% of deaths caused by COVID-19 occurred in patients with comorbidity, that is to say that they were already affected by a disease at the time of infection.

Since aging is often associated with a significant increase in the incidence of chronic diseases (diabetes, cancer, cardiovascular, respiratory and kidney diseases, among others), there is no doubt that these diseases contribute to the high mortality from COVID-19 observed in the very old.

These comorbidities also affect some younger people and can increase the risk of developing life-threatening complications of the disease. This is especially true when it comes to obesity: several studies carried out around the world indicate that obese people are more likely to be infected with the coronavirus, to be hospitalized to treat the infection and to die from the disease.

In adults under the age of 60, a segment of the population that should not normally be at high risk for complications, the risk of developing a severe form of COVID-19 is twice as high in obese people than in patients of normal weight.

Several factors explain this negative impact of being overweight: 1) the lungs of obese people do not function optimally (the rib cage of obese patients is compressed by excess fat), so they are more susceptible to lung infections; 2) obesity causes several metabolic imbalances (insulin resistance, hyperglycemia, chronic inflammation) which promote the development of pathologies (hypertension, dyslipidemias, type 2 diabetes, kidney and liver diseases) all important risk factors of mortality from COVID-19; 3) obesity disrupts the immune system and makes it less effective in fighting infection.

Positive point: The pandemic clearly shows that infectious diseases preferentially target the most fragile people and are therefore inseparable from the general state of health of the population. If there is one positive lesson that the coronavirus could teach us, it is that our society is surprisingly passive in the face of the alarming rise in obesity and several resulting chronic diseases that are hitting our population hard, including youth. Much more should be done to encourage the adoption of healthy lifestyles that can reduce obesity and improve healthy life expectancy, while reducing the disastrous impact of infectious diseases like COVID-19 on society.

Vitamin D deficiency

Several recent studies indicate that vitamin D deficiency is associated with an increased risk of developing severe forms of COVID-19 and of dying from it. This association is particularly problematic in winter, as shorter hours of sunshine cause an increase in the number of people deficient in vitamin D in the midst of a period when there is an increase in transmission of the coronavirus.

Good point: Taking supplements containing 1000 IU of vitamin D daily is certainly a simple way to decrease the risk of complications from this infectious disease, until the vaccine is widespread.

3. ON THE MOLECULAR LEVEL: our better knowledge of the biochemistry of the coronavirus makes it possible to neutralize it effectively



Science advances by accumulating a set of discoveries which, taken together, allow us to better understand a phenomenon and identify its main characteristics. In the case of the current coronavirus, it was the accumulation of these small advances on similar viruses that made it possible very quickly to make giant strides in understanding the main stages involved in its infectious action.

New drugs

Studies on the structures of two coronaviruses responsible for smaller epidemics (SARS in 2002 and MERS in 2012) had indeed shown that the peak-shaped structures on the surface of this family of viruses are absolutely essential to allow their entry into the cells.

It was quickly observed that an identical phenomenon was at work for the current coronavirus, that is to say that a protein present at its spicules (the S protein) has a very strong affinity for a receptor called ACE2 present on the surface of cells (especially those of the respiratory system and blood vessels) and that the interaction with this protein facilitates the translocation of the virus inside the cells where it can reproduce.

The very high-resolution molecular structures of the proteins involved in this interaction have already been determined by electron cryomicroscopy and, in the longer term, they should enable a whole new generation of antiviral drugs to be designed to block the entry of coronaviruses.

Positive point: Even though the virus was unknown only a year ago, we could immediately focus on what was to turn out to be the molecular Achilles heel of the virus, the S protein, without which it cannot succeed to infect and reproduce in our cells. The majority of vaccines target this virus protein, suggesting that other phase 3 vaccines will be just as effective.

4. IN THE IMMUNE LEVEL: the immune response to the virus is excellent



Canada has approved bamlanivimab to treat patients who have a mild or moderate form of COVID-19 but who could see the disease progress to a severe form due to their medical condition.

Globally, the death rate associated with COVID-19 is estimated to be around 1%, indicating that the immune system is successful in neutralizing the virus in the vast majority (99%) of cases.

This is also supported by several studies showing that the infection causes the production of antibodies capable of neutralizing the virus by blocking the S protein, which is absolutely essential for its entry into cells.

Pillars

The other pillars of the immune response, in particular the two types of T lymphocytes (CD4+ and CD8+) which eliminate infected cells, are also strongly activated, which allows a coordinated immune response and above all the development of a lasting memory that allows rapid neutralization of infection upon repeated exposure to the virus.

Moreover, although cases of reinfection have been reported, these situations seem extremely rare and are not associated with the development of severe forms of the disease.

Positive point 1: Very efficient antibodies, capable of neutralizing the virus even in very low concentrations, have been isolated from patients who have survived the virus. These antibodies have been used as a springboard for the manufacture of synthetic monoclonal antibodies, and one of these drugs (bamlanivimab) is now approved in Canada to treat patients with mild or moderate COVID-19 whose condition is health is at high risk of progressing to a severe form of the disease and / or leading to hospitalization.

Positive point 2: Research has also identified genetic variations (in interferon proteins, our first line of defense against viral infections) that decrease the immune response in 15% of severe cases of COVID-19. These people are at greater risk of being hospitalized, even if they do not have any apparent risk factors. Synthetic interferons that have been used for several years to treat other diseases (multiple sclerosis, hepatitis C) are already available and could be used to treat these very sick patients.

5. VACCINALLY: vaccines against the virus are extraordinarily effective



Gisèle Lévesque was the very first person to receive the COVID-19 vaccine in Canada. The 89-year-old woman lives at the CHSLD Saint-Antoine, in Quebec.

There are currently 61 different vaccines in development and 14 that have reached phase 3 clinical studies, the last step before approval.

Two of these vaccines, manufactured by Pfizer / BioNTech and Moderna, have already been approved in Canada and given to people considered most at risk. This is a mind-boggling scientific feat when you take into account that the virus was not even known just a year ago, and the structure of its genetic material was only determined last January.

Nanoparticles

These two vaccines consist of nanoparticles containing messenger RNA (mRNA) that dictate the synthesis of the virus's protein S. When injected into a patient, cells use this mRNA as a springboard to make a fragment of this protein, which allows immune cells to come into contact with this antigen and develop an immune response to neutralize it. Data collected during phase 3 clinical trials indicate robust immunity that results in a 95% reduction in the incidence of COVID-19, a remarkable protection on par with some well-established vaccines such as against measles.

It should also be mentioned that this viral RNA-based approach allows great flexibility if mutations in the virus modify the structure of the protein targeted by the vaccine and prevent it from inducing an effective immune response. The production of a new vaccine could then be quickly restarted simply by modifying the mRNA to produce the mutated form of the protein.

This possibility of rapidly counter-attacking in the event of an antigenic drift of the coronavirus therefore represents a huge advantage of this type of vaccine.

Obviously, vaccines will not immediately end the current pandemic. As a first step, the vaccination of the elderly, who are more vulnerable, should rapidly reduce the number of deaths (91% of deaths were over 70 years old); the vaccination of front-line staff should also ensure that we maintain our hospital response capacity.

As a second step, several million doses will be produced, circulated and administered to as many people as possible to achieve group immunity. It seems very likely that by 2021, enough people will have been vaccinated for the virus which will have difficulty finding a vulnerable host to infect.

In this case, even if the virus continues to circulate, the outbreaks will be very small and of short duration and a return to normal life can be anticipated.

CONCLUSION: WE CAN BE SERENE

2020 has been a very difficult year, but advances in science allow us to look to the future with serenity. What we have learned from this pandemic will be of use in the future battles against other viruses. Humanity is emerging from this ordeal and will be better prepared scientifically, but also at the pharmaceutical, political, decision-making and logistical levels. The year 2021 will mark the victory of human genius in overcoming the challenges it faces, as it has done so well throughout its development!