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The scientific and technical aspects of the fight against the Covid-19 pandemic



2020, by addressing vaccine pharmacovigilance, opening up vaccination to children, and the debate on the lifting of patents on vaccines. It also covers other aspects of the fight against this disease such as monitoring the virus and the epidemic (monitoring SARS-CoV-2 variants and screening the asymptomatic population) as well as identifying and providing medical care for those affected by Covid-19 (long Covid syndrome, research into treatment strategies, etc.).

Recommendations have been made for each of these issues with the aim of finding a rapid way out of the crisis. By presenting a first look at how the health crisis has been managed, the report aims to provide guidelines for preparing France for the emergence of a new infectious disease.

More than a year after the first Covid-19 wave in France, and despite the introduction of vaccination from the beginning of 2021, the daily lives of the French people are still strongly affected by the circulation of the SARS-CoV-2 virus. In particular, the new variants have changed the dynamics of the epidemic, bringing a new risk and raising fears of a fourth wave.

Given this prolonged threat, the Office has been working on the fight against the pandemic and held a number of hearings between 9 March and 17 June 2021, three of which have been made public on the Assemblée nationale and Senate websites.

This study¹ builds on the "Vaccine strategy for the Covid-19 epidemic" report,² published in December

1 Report by Ms. Sonia de LA PROVÔTÉ and Ms. Florence LASSARADE, Senators, and Mr. Jean-François ELIAOU and Mr. Gérard LESEUL, MPs, on "The scientific and technical aspects of the fight against the Covid-19 pandemic", n° 4315 (XVth Term) Assemblée nationale – n° 741 (2020-2021) Senate.

2 Report by Ms. Sonia de LA PROVÔTÉ and Ms. Florence LASSARADE, Senators, and Mr. Jean-François ELIAOU and Mr. Gérard LESEUL, MPs, on "The vaccination strategy against Covid-19" - n° 3695 (XVth Term) Assemblée nationale – n° 234 (2020-2021) Senate.

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The pharmacovigilance plan for Covid-19 vaccines

Vaccines are subject to strict marketing rules. Pharmacovigilance involves continuously assessing the benefit/risk ratio of Covid-19 vaccines.

The French Agency for the Safety of Health Products (Agence Nationale de Sécurité du Médicament - ANSM) is responsible for pharmacovigilance in France, in conjunction with the European Medicines Agency (EMA). The ANSM relies on the Regional Pharmacovigilance

Centres (Centres régionaux de pharmacovigilance - CRPV) to monitor the adverse effects of vaccination.

The ANSM and the EMA have taken into account several pharmacovigilance alerts since the beginning of the vaccination campaign, and have reassessed the benefit/risk ratio of the vaccine and the recommendations for its use.

The data collected by the ANSM in June 2021 confirmed a favourable benefit/risk ratio for all the vaccines used throughout France in the populations targeted by the vaccination strategy.

Recommendations

- The Office believes that the pharmacovigilance plan for Covid vaccines is rigorously organised in France and in Europe. It commends the health authorities for their efforts to authorise their marketing rapidly, while rigorously respecting health safety rules.

Therefore, the Office recommends that data on adverse side effects continue to be reported in a transparent manner and that the public is clearly informed of the associated risks. It also recommends continuing efforts to simplify the procedures for reporting adverse reactions to vaccines.

Vaccinating minors against Covid-19

The available data shows that the Covid-19 vaccine is effective and - at least at present - safe for the young (non-adult) population. However, for this age group, the value and timing of vaccination is more debatable than for adults. Adolescents are less likely to develop severe forms of Covid-19 and the direct benefit of vaccination is therefore lower than for adults. On the other hand, they are not spared by the crisis, which mainly affects them indirectly. Furthermore, providing them with the vaccine would be of collective benefit to society as a whole by curbing the circulation of the virus.

Therefore, the benefit/risk ratio must be carefully considered. Strict pharmacovigilance monitoring should be carried out and any side effects should be investigated thoroughly. The roll-out of the vaccine should also be accompanied by specific information campaigns specifically for this age group and organised in a school environment, so that all social groups can benefit from it.

Finally, vaccinating adolescents should not be seen as a substitute for vaccinating the rest of the population. There is a particular need to encourage vaccination for adults who have not been able - or willing - to receive the vaccine, and to encourage the vaccination of vulnerable or at-risk people in low- and middle-income countries.

Recommendations

- Encourage adults, especially those most at risk, to be vaccinated against Covid-19 so that vaccination coverage does not stagnate at unsatisfactory levels.
- Continue to vaccinate minors against Covid-19 while strictly monitoring pharmacovigilance.
- Systematically carry out serological tests when adolescents are first vaccinated in order to avoid injecting a second dose of the vaccine if they have previously been found to have Covid-19.
- Roll out information campaigns tailored to the younger population to inform them about the importance of the Covid-19 vaccine.
- Plan to introduce school-based Covid-19 vaccination campaigns from autumn 2021.
- Implement an ambitious vaccine donation policy to enable at-risk populations in countries that do

not currently have access to Covid-19 vaccination to receive the vaccine at the same time as those who do have access.

Lifting patents on Covid-19 vaccines

Nations are divided over lifting intellectual property rights for Covid-19 vaccines. There is consensus on equal access to vaccines for all countries, although there is no agreement on the usefulness and legitimacy of "lifting patents" to achieve this.

There are a number of possible legal mechanisms to redress this global imbalance. Several countries have asked the WTO to encourage Covid-19 vaccine voluntary licensing because the agreement of the patent holder facilitates the transfer of technology which is in any case necessary, while rewarding innovation. The option to quickly help poorer nations set up by the WHO seems promising in this respect.

The use of compulsory licensing, already provided for by the WTO, should not be seen as illegitimate when negotiations for a voluntary licensing agreement fail. This possibility can obviously be used as an argument in these negotiations.

The "lifting of patents", although subject to debate at the WTO via the request for a waiver of certain provisions of the TRIPS Agreement submitted by India and South Africa in October 2020 and again in May 2021, does not appear to be a real solution in the face of the reluctance of certain Member States.

Whatever mechanism might be implemented, there are certain requirements: the government will need to identify and support companies that are likely to produce vaccines, while at the same time increasing production capacity for critical inputs and preventing export restrictions on them to avoid shortages, and local inspection bodies will need to be particularly vigilant about new production lines to avoid the risk of "sub-standard" vaccines that could create health hazards.

Increasing production capacity will only provide a medium-term solution. The efforts to achieve this must therefore be accompanied by an ambitious dose donation policy in order to vaccinate vulnerable and high-risk populations in countries that have so far been under-resourced as quickly as possible.

Recommendations

- France must work within the WTO to encourage the widest possible use of the possibilities already offered by the TRIPS Agreement, to strengthen the Covid-19 Technology Access Pool in order to make it easier to conclude voluntary licensing agreements, and to prevent measures restricting exports of vaccines or their ingredients.
- At the same time, France must work to ensure that all countries have rapid access to Covid-19 vaccines, notably by making an ambitious contribution to initiatives aimed at providing doses to countries that still have limited access to Covid-19 vaccines, by strengthening their health infrastructures and by supporting local health authorities in charge of monitoring production

chains to avoid the risk of producing “sub-standard” products.

Monitoring SARS-CoV-2 variants

As long as the virus is circulating and the population is not immune, new variants will appear. Those with a higher transmission potential or immune escape are likely to overtake the others, due to selection pressure.

In France, the increase in sequencing capacity and the significant increase of sequence sharing with the international scientific community should be commended.

PCR screening is an interesting technique for monitoring the most concerning mutations; their list will need to be regularly updated as mutations emerge that are associated with new features of epidemiological and clinical concern.

International scientific collaboration is crucial to monitor the emergence of new variants, which, as we have seen, are not stopped by borders.

Recommendations

- Maintain an ambitious policy of sequencing on randomly selected samples in order to monitor variants in circulation without selection bias.
- Request that the WHO set up a network for monitoring variants in developing countries that do not have the capacity to do so and in which the virus is still circulating. Boost the virological surveillance network set up by the ANRS-MIE in France by allocating adequate resources.
- Anticipate the emergence of new variants with different characteristics from those currently known, and plan to adapt screening, health and vaccination protocols to reflect these characteristics.

Screening the asymptomatic population

Although the scope of individual self-testing is limited, these tests appear to be essential for the deployment of an effective screening strategy in the asymptomatic population - a strategy in which their disadvantages are largely offset by their advantages (low cost, ease of use, low level of invasiveness, etc.).

Models show their effectiveness in controlling viral circulation within schools, and these findings can be extended to hospitals and businesses. In the work place, they can be used to prevent the occurrence of clusters in places where employees are not sufficiently vaccinated when they return to work.

In schools and universities, where vaccination is likely to be less likely than in older age groups, because of a lower expected individual benefit and because vaccination has only recently been opened up to those over 12 years old, self-testing is likely to be needed to control the spread of the epidemic.

However, the actual deployment of this strategy is very far from meeting the identified conditions of effectiveness, which suggests a lack of effect at the

beginning of the next school year, which is a critical period.

Recommendations

- Re-launch the self-testing roll-out strategy in time for the start of the next school year, sufficiently in advance for industry to fulfil orders and for all schools and universities to be able to offer these tests to students.
- Accompany this with a communication campaign aimed at the general public to inform them of the usefulness of population-based screening campaigns in schools, universities and workplaces.

Long Covid syndrome: a somatic reality and medical enigma

Long Covid is a reality. Its various symptoms are not just a figment of the patient’s imagination and are distinct from depressive symptoms, although there are still strong questions about the mechanisms of this syndrome.

Long Covid is a complex condition that is still largely unknown and requires a systemic approach. Medical specialists need to communicate with general practitioners and patients, both to facilitate individual diagnosis and to determine the best treatment and research approach. The strong involvement of patients, their indispensable role in describing the disease and the relevance of their suggestions make them extremely valuable in researching and treating long Covid.

The lack of certainty about the causes and treatments of long Covid calls for pragmatic responses. Health professionals must work towards better training for practitioners and establishing regional interdisciplinary consultations, with the well-being of suffering patients as their main concern.

The administrative and financial arrangements for the coverage of long Covid are not satisfactory: it is not included in the list of major or long-term conditions that are fully reimbursable by the French social security system, it is too often not covered by the major or long-term conditions that are not exempted, and it is too difficult to have it recognised as an occupational disease.

It is therefore deemed necessary to provide research on long Covid with sufficient means to obtain rapid and effective answers.

Recommendations

- Relax the criteria for recognition of long Covid as an occupational disease, in line with the recommendations of the French Health Authority (HAS).
- Include long Covid in the list of major or long-term conditions that are fully reimbursable by the social security system, in order to avoid the social exclusion of patients.
- Make it easier for general practitioners to deal with long Covid and organise multidisciplinary care in relevant areas by identifying long Covid coordinating doctors.

- Implement specific communication on long Covid for the general public and doctors to minimise misunderstandings when a patient is affected by this syndrome.
- Accelerate and fund research into the causes of long Covid, including the establishment of cohorts, with the aim of developing appropriate specialist treatments.

Researching treatment strategies for Covid-19

Despite the high quality and diversity of French research, the development of treatment strategies for Covid-19 has only produced mixed results over the past year, with most of the molecules tested proving ineffective. In the rest of the world, only the monoclonal antibodies, developed by Roche and Eli Lilly, and dexamethasone have so far proven effective against Covid-19 (for the viral and inflammatory phases of the disease respectively).

The exceptional commitment of all those involved in research has made it possible to set up a number of initiatives in record time, with the aim of finding treatments for Covid-19. However, this effort, remarkable as it is, has been hampered by significant structural and strategic unpreparedness. With no national coordination and no preliminary results on SARS-CoV-1, the various projects, which were launched

in a hurry, led to a dispersion of efforts and a waste of time.

It will therefore be essential to draw conclusions from this pandemic and the various shortcomings that have been observed in order to improve the organisation of our medical research system and prepare it as well as possible for epidemics that may arise in the future.

Recommendations

- Provide the ANRS-MIE with strong guidelines and sufficient resources to enable it to prepare and coordinate research efforts against emerging infectious diseases.
- Encourage and provide funding for basic research in order to conduct relevant and effective pre-clinical and clinical research in emergency situations.
- Develop antiviral research in order to obtain a wide range of molecules that can be used in the event of a new viral epidemic.
- Review the initiatives put in place (in particular the Discovery and Coverage platforms) in order to be able to deploy similar platforms more effectively in the event of a new pandemic.
- Develop the evaluation system for researchers to reduce the importance of quantitative indicators and better value the real contribution of research to scientific knowledge.

To view the report:

www.assemblee-nationale.fr/commissions/opicst-index.asp
www.senat.fr/opicst