COVID-19: Latest news of the world by IFGR

Diagnosis of Covid-19: a complex infectious disease - 05.04.2020

Mirdad Kazanji, Institut Pasteur of French Guyana

Covid-19 keeps surprising us. The disease manifests itself with varied and different symptoms depending on the patients. New symptoms affecting the cardiovascular system or the skin have recently been described. In addition to its contagiousness, the virus seems to be linked to a number of pathologies, making diagnosis complex. Only screening tests confirm the infection, but are they all reliable and available?

This week we asked Mirdad Kazanji, director of the Institut Pasteur of French Guyana, to give us his answers.

Photo credit : Ronan Liétar – IFGR

First of all, let's go back to the symptoms of Covid-19, because we are still discovering them, even though the virus has been circulating for 4 months. Is that specific to this viral infection?

This disease affects a large number of organs and manifests itself through various symptoms that may appear gradually, which makes it so complex and specific. One can think that China, overwhelmed by the flow of patients arriving in hospitals, has not been able to provide information on all the pathologies presented by patients. Today, in Europe, which is the area most affected by the pandemic, we are discovering these pathologies that had not been described previously. The most common in adults are the onset of nasopharyngeal irritation and cough one week after contact with a patient, followed by fever, muscle aches and pains, and possibly digestive problems. In the most severe cases, respiratory difficulties lead to hospitalization of the patient in case of acute respiratory distress syndrome. Very frequent occurrences of anosmia (loss of sense of smell) and loss of taste in PCR positive individuals as well as confusional state in the elderly have also been observed in Europe.

Recently, dermatological manifestations such as urticaria on the fingertips or erythema on the face have been discovered.

With the SARS-Cov-2 virus, the agent responsible for the infectious respiratory disease known as Covid-19, **we are therefore faced with a range of pathologies that we have not seen in other coronavirus epidemics such as SARS or MERS**, which manifest themselves mainly as influenza syndromes. **Its other specificity is the large number of asymptomatic people**, i.e. people who are PCR-test positive and therefore contaminating but who do not present any symptoms.

According to the sero-epidemiological study[1] carried out by the Institut Pasteur in a high school in Oise (one of the first French territories affected), the proportion of asymptomatic people during the study period was at least 17%; on the cruise ship Diamond Princess, it was 18% and reached 50% on the military aircraft carrier Charles de Gaulle!

Let's counterbalance these facts with another, positive one: 80% of infected people under 60 recover within a week. Complications mainly

[1] Cluster of COVID-19 in northern France: A retrospective closed cohort study - April 23, 2020

affect the elderly or people with existing pathologies (obesity, diabetes, etc.).

Most recently, medical authorities in the UK, Italy and France have alerted about cases of children with important heart problems. How can these unprecedented cases be apprehended?

We have to take this alert seriously. Since the beginning of the epidemic, the number of serious cases among children and adolescents has been very low. However, in Great Britain, Belgium, Italy, Spain and France, the authorities are now reporting a small but growing number of children hospitalised due to inflammatory syndrome. It remains to be seen whether cases are also appearing in the United States or Brazil, which are highly exposed to the epidemic. For many of the cases, these symptoms are close to a rare but well-known pathology, the Kawasaki disease, which affects the arteries. Its causes are generally unclear but its onset could be favoured by an infection by a pathogenic agent (virus or bacteria). **Without yet being proven, a link therefore seems to exist with Covid-19**. In France, the AP-HP[2] has confirmed that the 20 or so children affected in the Ile-de-France region had been in contact with the virus 3 to 4 weeks before. The inflammation is reminiscent of the "cytokine storm", the excessive immune response that strikes adults at the beginning of the second week after the first symptoms.

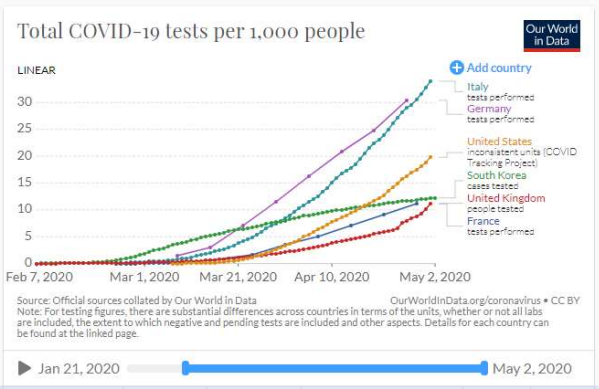
" It is a challenge to the initial finding that children are not affected or do not develop any pathology associated with Covid-19."

Why do children react later? It cannot be explained at this time but it is a challenge to the initial finding that children are not affected or do not develop any pathology associated with Covid -19.

I am worried at a time when schools are about to reopen in France and there are still cases. **I am also convinced that we will discover post-epidemic sequelae, particularly in asymptomatic people or in people who have been cured**, as is the case with this Kawazaki disease in children. General practitioners will have an important role to play in monitoring and detecting these sequelae.

Several countries are beginning to move out of containment. Among the necessary measures is the carrying out of tests. What tests are we talking about?

As early as mid-March, the WHO issued a call to all countries to test for suspected cases, so that they could isolate patients and break the chains of transmission. By that date, it announced that it had sent nearly 1.5 million tests to 120 countries. Since then, however, the strategies have varied greatly from country to country.



Number of tests per 1.000 people (with potentially different counting units depending on countries) - Source: Our world in data

Iceland, South Korea and Germany were early adopters of testing. France did not make this choice, apart from a logistical problem.

[2] Assistance Publique-Hôpitaux de Paris, the public health establishment of the Ile-de-France region.

Elsewhere in the world, other difficulties have arisen, such as the lack of suitable equipment to carry out these tests in laboratories or the impossible mobilization of financial resources for their purchase.

What is certain is that **these tests will be essential in the deconfinement phase, to avoid a second wave of virus spread.** The key indicator used is the R0, which is the basic reproductive rate of a virus. In the case of Covid-19, a highly contagious virus, it was initially 3 (one infected person can infect up to three others). The lockdown make it possible to limit its transmission and thus the number of reproduction. Reduced to 0.5, the R0 must not exceed 1 in France after 11 May, the date on which containment will be lifted, so as not to saturate the health systems. In Germany, it has already risen from 0.5 to 1, which shows how difficult the exercise is.

What tests should be used? We can say that there are two main types of diagnostic tests:

- **Molecular tests** (PCR for "*polymerase chain reaction*") that detect the genome[3] of the virus in the body and confirm a diagnosis of Covid-19.

Laboratory of virology – Institut Pasteur of French Guyana / Credit: IP – Ronan Liétar

Laboratory analysis of nasopharyngeal swabs is performed within a few hours.

- **Serological tests**, carried out on a blood sample, are designed to check for the presence of antibodies in the blood and thus to identify people who have been in contact with the virus and have developed immunity after recovery. The problem is that it is not yet known whether people who have contracted the new coronavirus are then protected against a new infection, and if there is a protective immunity, how long it lasts. In addition, a study[4] has shown that antibodies only begin to rise after 10 days of disease progression and that their intensity varies with that of clinical signs. **Serological tests are therefore not recommended for the early diagnosis of infection and for determining whether a person is contagious.** However, they are useful for epidemiological investigations or catch-up diagnosis, for example. Serological and molecular tests are complementary.

"Serological and molecular tests are complementary."

Are these tests reliable?

As of April 22, 2020, 278 PCR test kits and 233 serological tests, including 84 rapid tests, are produced and marketed worldwide and have been reported to the Foundation for Innovative New Diagnostics (FIND). However, there is now a reliability problem for serological tests. In Great Britain, two million serological tests to be done at home, bought for $20 million, will remain in their boxes because they are not reliable enough. In France, the minimum thresholds required by the High Authority of Health for a test to be approved

[3] The genome consists of a nucleic acid close to DNA called RNA.

[4] Severe Acute Respiratory Syndrome Coronavirus 2–Specific Antibody Responses in Coronavirus Disease 2019 Patients EID Journal

and placed on the market are not yet met for the available serological tests.

Molecular tests are currently the most reliable, even though they can have a 30% false negative rate when the sample is incorrectly collected. They will be used in France, at a rate of 700,000 per week for symptomatic people, paucisymptomatic people and contacts of confirmed cases. We are eagerly awaiting new automated serological tests being manufactured by major manufacturers (Roche, Siemens, Diasorin or Abbott) as they will be simpler, faster and less expensive. Abbott will supply France with 4.5 million tests by the end of May and 6 million per month thereafter.

Medical laboratory – Institut Pasteur of French Guyana / Credit : IP Guyane – Ronan Liétar

In French Guyana, the Institut Pasteur has ordered serological tests, as they are not yet available here. We are continuing the diagnosis with PCR tests and are going to set up a drive for patients who will be be tested in their car. By this way, we accompany the release from the containment and avoid the risk of contagion for the nursing staff. As part of our Epi-Covid study, which is studying the spread of the virus in family circles, we are also carrying out screening outside the Pasteur Institut, at the infected people' home, but we cannot generalize this system.

Interview conducted by Marie-Cécile Grisard