

Medical sequelae of Covid-19

Position statement of the National academy of medicine

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The Covid-19 epidemic is clearly decreasing in France. In the most severely affected patients, the medical sequelae are a real threat whose importance remains poorly assessed (1). Caregivers and patients will also face psychic medical sequelae that should not be underestimated.

The medical sequelae of Covid-19 can be separated into two groups. The first group includes those following the organ damage in the acute phase, which are not or only slightly reversible. The second includes complex poorly qualified disorders occurring a few weeks after recovery, the origin and fate of which remain unknown. Because of the spread of the pandemic, even a small percentage of medical sequelae represent a nationwide public health problem.

1- Medical sequelae of organ damage during the acute phase

- Residual respiratory damage (2)

The lung is the most frequently affected organ in the acute phase of the disease, and epidemics due to other coronaviruses such as Sars CoV and Mer CoV have shown that pulmonary fibrosis can persist after the initial infection.

Interstitial pulmonary fibrosis is a frequent consequence of respiratory distress observed in the acute phase of the disease. It may also result from an acute phase that appeared to be mild. It is mainly attributed to the increased production of pro-inflammatory cytokines, an indirect consequence of the viral infection. Other factors may be involved, such as airway hyper pressure following artificial ventilation and anoxia due to an imbalance between oxygen requirements and oxygen supply.

Fibrosis is characterized by a progressive decline in respiratory function, an extension of the lesions visible on the chest tomography, an increased susceptibility to respiratory infections. Even a low degree of residual fibrosis can increase mortality in the elderly.

- Cardiac damage (3).

Inflammatory myocarditis proven by elevation of troponin and BNP ("B-type natriuretic peptide") is frequently found in patients treated in intensive care units and may lead to left ventricular failure. Myocardial infarction may occur in connection with plaque rupture promoted by infection or prolonged anoxia. Right ventricular failure secondary to pulmonary arterial hypertension resulting from respiratory fibrosis and/or acute pulmonary embolisms is also possible. Arrhythmia is sometimes observed, including extrasystoles, ventricular tachyarrhythmia and atrial fibrillation. Heart failure, myocardial necrosis, and arrhythmia persist after the acute phase and require a prolonged monitoring and an appropriate treatment.

-Kidney damage (4)

Proteinuria, microscopic hematuria, and moderate elevation of plasma creatinine are common in the acute phase, indicative of renal impairment. Since creatinine measurement is a marker of decreased glomerular filtration rather than tubular injury, more specific markers such as KIM-1 ("kidney injury molecule-1") and NGAL ("neutrophil gelatinase associated lipocain") should be used. Reversible acute renal failure related to fluid and electrolyte disorders has been observed. Direct virus-related damage results in inconsistently reversible tubular epithelial cell necrosis leading to chronic end-stage renal disease. As the progression to chronic renal failure is always silent, patients with this disease should be monitored over a long period of time.

- Direct or indirect damage to the central nervous system (5)

Brain damage may be directly related to the virus or more often the consequence of prolonged anoxia in patients on artificial ventilation, strokes, or an autoimmune syndrome such as an acute disseminated encephalomyelitis which, if accompanied by peripheral disorders and affecting the diaphragm, can aggravate respiratory disorders. Brain stem damage has also been described contributing to breathing difficulties.

- **Sarcopenia** is almost constant in patients who are immobilized for several weeks in intensive care units, requiring prolonged rehabilitation during convalescence.

2- Poorly qualified disorders prolonging convalescence or occurring later (6)

Patients apparently recovering from the acute episode have been found to require prolonged convalescence or to complain of new symptoms after a period of remission. The initial infection was often short and healed spontaneously. Negative virus tests rule out a reinfection and the presence of IgG specific for Sars CoV-2 confirms the previous infection. The disorders complained of by these subjects are general discomfort or sometimes, attacks of tachycardia, muscular pain, arthralgia, fatigue at the slightest muscular or intellectual effort, memory loss. The clinical examination remains negative except often a loss of weight indicating undernutrition. These disorders are most often episodic, but are sometimes prolonged. Treatment is difficult, apart from the prescription of paracetamol, psychological support and correction of any undernutrition by a dietician. It is difficult to distinguish between the consequences of Covid-19 or other causes, as is the case in the post-borreliosis syndrome of Lyme disease.

3- Psychic sequelae (7)

Psychic after-effects are to be feared in patients, caregivers and victims of confinement.

- In patients

Those coming out of intensive care units with assisted ventilation and deep sedation, and then from a long convalescence, are intensely marked. In addition to the functional recovery of the affected organs, they need psychological support to enable them to return to work and a normal social life. Those who have recovered spontaneously also sometimes need this support, when they suffer from the various and poorly qualified disorders considered above.

- Among health care workers

Whether they work in hospitals or residential institutions for the elderly dependent persons, whether they are doctors, nurses, orderlies, stretcher bearers, manipulators..., this staff has been subjected to extended work schedules associated with increased responsibilities, given the worrisome condition of the patients treated, leading to fatigue, anxiety and lack of sleep. Even if most of these symptoms disappear with the return to their usual activity and the possibility of leave, some of them remain tired, anxious and insomniac, what requires follow-up and psychological support.

-Among the victims of the containment

Although the entire population was subject to the rules of containment limiting leaving the home and social contact, some groups were particularly affected: children and young adults with disabilities who left their host institution; children deprived of school and of any contact with their pals; students who returned to their parents' homes and whose studies were interrupted. While these disorders are often spontaneously self-resolving, some may require psychological help.

To treat the medical sequelae, within the limits of our current knowledge, the French national academy of medicine recommends:

- the resumption of a physical activity as soon as possible, of which walking is the easiest.
- vigilance as to the functional quality of the organs most often affected (heart, brain, muscles and lungs);
- monitoring the long-term evolution of these after-effects by assembling a cohort of patients in a longitudinal study lasting several years;
- measures concerning the organisation of work in hospitals and residential institutions for the elderly dependent persons (recruitment of nursing staff, increase of remuneration), to reduce the risk of "burn out" and the psychological tensions linked to an excessive work;
- helping the parents of disabled children who, in the event of a new containment, would have to replace the host institutions.

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