

What unusual symptoms to seek for Covid-19?

Press release of the French National Academy of Medicine

June 17, 2020

Fever or respiratory signs are the main symptoms of Covid-19. However, the SARS-CoV-2 infection may affect other organs and be revealed by digestive disorders, pulmonary or peripheral arterial embolisms, or other less typical inaugural clinical pictures.

The Enhanced Prevention and Protection Plan defined by the Covid-19 Scientific Council [1] includes an intensification of the protocol for case detection and contact tracing. These new provisions should encourage the prescribing of screening tests at the slightest doubt. Thus, some less frequent clinical presentations should not be overlooked:

- **Neurological manifestations:** while agueusia and anosmia are common, other manifestations are exceptional such as ophthalmoplegia or Guillain-Barré syndrome. Confusion syndrome, memory disorders have also been reported, particularly in elderly subjects, as well as ischemic strokes related to the thrombogenic activity of CoV-2-SARS. Constrictive, erratic and lasting pain are probably neurological in origin.
- **Skin signs:** pseudo-freezing, sometimes painful, has been described since the beginning of the epidemic. More common in children and young adults, they usually evolve favorably within a week, but can recur. Dyshidrosis, vesicles, hives, exanthema, petechiae and livedo are rarer.
- Clinical pictures suggestive of **Kawasaki disease** have been described in children with initial digestive signs, including severe abdominal pain, followed by cardiogenic shock with a collapsed ejection fraction, grouped as Pediatric Multisystemic Inflammatory Syndrome (PIMS). Skin signs are present, with a rash, then desquamation. The age of the affected children, from 9 to 17 years, is higher than in the usual form of Kawasaki disease.

- **Endocrine and metabolic disorders** are likely to be related to the wide organic distribution of the angiotensin-converting enzyme 2 (ACE2), the SARS-CoV-2 receptor: testicle, ovary, hypothalamus, pituitary, thyroid and pancreas. Contributing to the state of deep fatigue and correlated with the severity of the disease, a deficit in testosterone production can be observed. Frequently reported hypokalemia is thought to result from virus binding to ACE2 and increased aldosterone synthesis. The lymphopenia observed in some severe forms of Covid-19 does not rule out situations of hypo-cortisolism, already documented in SARS. Cases of subacute thyroiditis have been reported. Hypocalcemia may be observed, as well as hyperglycemia promoted by increased insulin resistance and direct damage to the pancreatic gland with elevated amylase and lipase levels.

The National Academy of Medicine recommends

- to explore neurological, endocrine or metabolic manifestations occurring in a known or unknown context of Covid-19 infection;
- to analyze cognitive disorders, their severity, evolution and persistence with the help of specific explorations;
- to evoke a PIMS in cases of severe abdominal pain and/or cardiogenic shock in children or adolescents;
- to prescribe SARS-CoV-2 screening tests (RT-PCR and serology) at the slightest doubt about any limited, atypical or unusual clinical picture that may suggest Covid-19.

[1] Notice No. 7 of the French Covid-19 Scientific Council "4 scenarios for the post-confinement period; anticipate for better protection", 2 June 2020