

Covid-19: The Hypothesis of Cohabitation **Kamen F^{1*} and Bekkara A²**

Abstract

Researchers around the world have been working since January 2020 to better understand SARS-Cov2, the coronavirus responsible for the Covid-19 pandemic. The membrane structure of SARS Cov2, the characteristics of lung damage both pathophysiologically and radiologically, the categories of patients with severe forms, the prevalence of covid-19 smokers have raised questions and closeness with the toxicity of cadmium. Through a review of the literature on the toxicity of cadmium and the prevalence of cardiovascular and cardio-metabolic pathology, the hypothesis of a combined action SARS Cov2 and cadmium is discussed.

Keywords: SARS Cov2; Cardiovascular disease; Diabetes; Tobacco; Cadmium

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Introduction

The situation of the subject in the international context

Researchers around the world have been working since January 2020 to better understand SARS-Cov2, the coronavirus responsible for the Covid-19 pandemic. Knowledge about the SARS-Cov2 coronavirus is advancing rapidly. The main stages of human cell infection and virus replication are gradually being revealed, and with them potential targets for drug molecules.

SARS-Cov2 belongs to the large family of coronaviruses responsible for outbreaks of SARS (Severe Acute Respiratory Syndrome) 2003 and MERS (Middle East Respiratory Syndrome) 2013-2015. These viruses are characterized by their crown of proteins called "Spike" or S which earned them their coronavirus name. Like all viruses, they use human cells as hosts to reproduce.

The presence of the covid-19 receptor (ACE-2) in the nasal, pulmonary and vascular endothelium epithelium of other organs [1] explain the lung symptoms and affected symptoms of other organs. The other aspect of the cytokinetic storm is that the endothelium of various organs causing inflammation.

The biological roles of certain proteins in the new coronavirus provide a better understanding of the "hematological" role of SARS-Cov2 in pneumonia and acute respiratory distress. Two simultaneous actions: ORF8 and surface glycoprotein of the virus bind to porphyrin [2-9]. At the same time, the proteins orf1ab, ORF10 and ORF3a attack the heme on the 1-beta chain of hemoglobin to dissociate iron from porphyrin [10]. This action would be at the level of the synthesis of the heme. This disruption in heme synthesis results in a hemoglobin deficiency that causes

- 1 Occupational Physician, Faculty of medicine, University Oran, Algeria
- 2 Pharmacist, Private Sector

***Corresponding author:**
Kamen F

✉ fzkamen@gmail.com

Tel: +213797085602

Occupational Physician, Faculty of medicine,
University Oran1, Algeria

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a failure to transfer oxygen to the lung. Disturbed alveolo-capillary exchanges cause severe inflammation that results in characteristic radiological images of " ground glass opacities"

The latest studies from China as well as Europe or the USA report a prevalence of non-smoking men in less severe forms, however severe forms in intensive care unit are found much more frequently in smokers [5].

Clinically, benign forms that evolve towards spontaneous healing and severe forms that can have a fatal outcome.

On the radiological level, the « ground glass opacities » are in favor of a positive diagnosis of Covid-19.

Populations targeted by severe forms would be elderly subjects, smokers, comorbidities including individuals with diabetes, high blood pressure and people with obesity.

Two things that challenge us:

- The clinical and especially radiological signs reported (frosted glass) are similar to those of acute cadmium poisoning (respiratory distress but also anosmia and multivisceral disease by cytokinetic discharge)
- The hematotoxic action of SARS-Cov2 through the dissociation of the iron from the heme is similar in purpose to that of certain heavy metals.

Data from the Literature on Cadmium Toxicity

Tobacco and cadmium

In chronic smokers the kidneys may contain more than half of

the body load of cadmium [4]. The (ZIP8) is an avid carrier of zinc and cadmium in cells and is widely expressed in the lungs of smokers compared to non-smokers. Overexpression of ZIP8 (zinc transporter metalloprotein and Cd) resulted in an increase of pulmonary cadmium and lung damage in mice secondary to prolonged exposure to tobacco smoke by disturbance of zinc homeostasis [6].

Chemical pneumonia and cadmium

Acute Cd poisonings are accidental and rare clinical cases are reported in the literature, while the rest is animal experimentation. The so-called chemical cadmium lung disease is described in acute intoxications with radiologically "ground glass opacities". On the other hand, the chronic toxicity of Cd is better documented and repaired as an occupational disease while in environmental health it is less well known [11-16]. Environmental exposure through air pollution, food (phosphate fertilizers) and tobacco (would be made up of 50% Cd) is a current public health concern (WHO) [17]. Cadmium is a cumulative toxic in the human body and its elimination process is slow with an estimated biological half-life of 10 to 40 years.

Cardiovascular diseases and cadmium

Numerous epidemiological studies support the hypothesis of cadmium involvement in cardiovascular disease and myocardial infarction [7,9,11,14-16] including proatherogenic action of Cd [3].

On the experimental level there would be a direct toxic effect of cadmium on heart muscle cells and probably also on the cardiac conduction system [12-13].

Diabetes and cadmium

Although data on relationship between Cd exposure and diabetes mellitus have often been contradictory, a recent meta-analysis revisits this aspect of the issue by concluding that human and laboratory data support the role of Cd in diabetes. [2] Indeed; laboratory studies show that exposure to Cd causes adipose tissue dysfunction and that it is induced by Cd promotes insulin resistance without obesity.

Viral pulmonary diseases and cadmium

In terms of subchronic and chronic toxicity of Cd on pulmonary parenchyma, it is relatively well established that Cd has proinflammatory and immunosuppressive effects on inflammation of lung tissue and that immune reactivity accentuates complex immunomodulatory actions -metal [8].

It is also reported in the literature the potentializing role of Cd in respiratory syncytial virus [18].

Questions and suggestions

This ubiquitous damage by cadmium, and especially at the pulmonary level, may suggest that cadmium may potentiate the viral action of SARS-Cov2 on the pulmonary parenchyma.

Cd is reported in relation to cardiovascular and metabolic pathologies including high blood pressure, type 2 diabetes and obesity; could explain the prevalence of this category of patients among Covid-19 disease. Intimate mechanisms have yet to be determined, but we suggest some hypotheses:

The virus with its Spike protein (S) could interfere with Cd and zinc or even compete with Cd, causing a mobilization of cadmium stored in the body that may explain this complementary cytotoxicity at the lung level in addition to disruption of the synthesis of heme induced by the virus itself. This extra cytotoxicity would be exercised in all tissues where Cd is stored (kidney, liver, and probably nervous system).

This hypothesis of a combined action SARS Covid-2-Cadmium suggests some elements of responses.

- Cadmium present in large quantities in smokers and in the environment in particular through diet (phosphate fertilizers) and air pollution could play a role in this pandemic coronavirus SARS Covid-19?
- Metallothionein induced by prolonged tobacco use may be a form of protection against the virus in chronic smokers, explaining their low representativeness in benign forms?
- Like others respiratory viruses, SARS Cov2 could potentiate the action of cadmium on pulmonary parenchyma.
- Cadmium being a cumulative toxic could explain the severe forms found in intensive care unit given the cumulative amounts of Cd in the kidney and other tissues in patients with cardiovascular and cardiometabolic comorbidity.
- The disparity in the regions may be related to population exposure levels to cadmium and air pollution.
- The covid-19 virus because of its membrane structure could like metals behave like a complex immune? (the immune response of SARS Covid2 continues to be challenging).

Cadmium is an environmental toxic and certainly an underestimated scourge that perhaps the Covid-19 virus comes to reveal or mimic.

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