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► To cite this version:

Renaud Piarroux, Jean Gaudart, Stanislas Rebaudet. COVID-19 Pandemic: the story is not over yet. *Anaesthesia Critical Care & Pain Medicine*, 2021, 40 (1), pp.100802. 10.1016/j.accpm.2021.100802 . hal-03199467

HAL Id: hal-03199467

<https://hal.sorbonne-universite.fr/hal-03199467>

Submitted on 15 Apr 2021

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COVID-19 Pandemic: the story is not over yet

Renaud PIARROUX^{a,b*}, Jean GAUDART^c, Stanislas REBAUDET^{c,d}

^a Assistance Publique – Hôpitaux de Paris, Paris, France

^b IPLESP, Sorbonne Université, 27 rue Chaligny 75571 Paris Cedex 12, France

^c S Aix Marseille Univ, INSERM, IRD, AP-HM, SESSTIM, UMR1252, La Timone, BioSTIC, 27, Boulevard Jean Moulin, 13005, Marseille, France

^d Hôpital Européen, 6, rue Désirée Clary, 13003 Marseille, France

***Corresponding author:** Renaud Piarroux

Service de parasitologie et mycologie, CHU La Pitié Salpêtrière, 83 Boulevard de l'Hôpital,
75013 Paris

Email : renaud.piarroux@aphp.fr

Keywords: COVID-19; pandemic; epidemiology

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The scenario had been feared for decades: at the end of 2019 a new virus emerged, a coronavirus that can be transmitted from person to person, and since then we have been in the grip of a pandemic that we still cannot control. The first alert was given on the 31th of December 2019, when China notified the WHO of a pneumonia outbreak in the city of Wuhan, Hubei province [1], and a 61-year-old man seemed to be the first dead, the on 11th of January [2]. On the 7th of January, Chinese authorities confirmed the identification of a novel coronavirus (named 2019-nCoV then SARS-CoV-2) causing these pneumonia cases, before sharing its whole sequence on the 12th of January [1]. The outbreak was associated with exposures in a seafood market in Wuhan City [1], although the hypothesis of an accidental leak of SARS-CoV-2 from a laboratory has been questioned [3].

The first case outside China was diagnosed on the 13th of January in Thailand, followed by Japan (15th of January) and South Korea (20th of January) [4]. On the 24th of January, while China began taking drastic measures to combat the emerging epidemic, France was recording its first cases in Bordeaux and Paris, all returning from Wuhan [4,5], even though SARS-CoV-2 seemed to be already present in the country in late December 2019 [6]. On the 30th of January, the WHO classified the new epidemic as a public health emergency of international concern. Then everything followed within a few weeks. While China gradually regained control over the epidemic, cases and clusters were multiplying outside its borders with outbreaks in South Korea, then in Iran, Italy, Spain and France [7]. Among these five countries, South Korea was the only one able to control the situation before it escalated. On the 11th of March, the WHO finally declared a pandemic state. A few days later, the WHO recommended the “test trace isolate” strategy [8]. Caught unaware with hospitals reaching their saturation point, many countries were forced to confine their population. Since then, most industrialised and emerging countries have been engaged in a kind of "dance" with the virus, trying to find a balance between control measures needed to control the spread of the virus through the population and socio-economic concerns.

With the beginning of winter in the northern hemisphere, however, several elements have disrupted this precarious balance, which could lead us to a short-term worsening of the

epidemic situation and a hardening of the control measures. Some other elements allow considering an eagerly awaited long-term improvement.

The second epidemic wave has grown slowly since the end of July in France, but in October 2020, the increase of the COVID-19 incidence in France compelled the government to impose new containment measures such as a curfew, highlighting the failure of the French "test, trace, isolate" strategy. This strategy had quickly been identified as essential to achieve effective control of the pandemic. It has been successfully applied in several countries, as in China, where it has obviously succeeded in controlling all emerging outbreaks[9], or in South Korea, where it could stop an outbreak following the transmission of the virus during religious ceremonies [10]. Unfortunately, this French strategy proved unsuccessful, partly due to the delay between case suspicion, actual testing and result analysis, partly to the difficulties encountered in the search for contacts either through mobile phone apps or phone calls from the Health Insurance staff, and finally, to patients and contacts reluctance or difficulties in quarantining. This has led our society into a vicious circle, as the more we fail to effectively identify and isolate infectious patients, the higher the number of cases increase and the more difficult it gets to devote sufficient resources, staff and time to identify and isolate new patients.

The situation is now complicated by the arrival of winter. The relationship between the transmission of SARS-CoV-2 and weather conditions has been suspected since the beginning of the pandemic, and several studies showed that the winter temperatures can be particularly favourable to the transmission of the virus [11]. The epidemic situation in Europe has thus worsened since the beginning of autumn, and the coldest departments in eastern France have exhibited the highest COVID-19 incidence [12].

Mutations are a common phenomenon in the evolution of viruses and have already been observed since the beginning of the epidemic [13]. They can affect virulence, or lead to improved transmissibility of the disease, since selective pressure will favour more efficient variants over less competitive ones. The occurrence of a pandemic with millions of infected individuals every week has provided an excellent opportunity for SARS-CoV-2 to become increasingly adapted to humans. More transmissible variants appeared recently in the United Kingdom and in South Africa [14]. These SARS-CoV-2 variants, already sporadically

identified in France, may spread globally soon, contributing to the acceleration of the pandemic and further complicating its control. In addition to seasonal effects, such an improvement in the transmissibility of the virus could also explain the worsening of the situation in virtually all industrialised countries, including those that have so far well resisted the epidemic. Even South Korea is having more difficulty containing the expansion of the epidemic nowadays than in February 2020 [15].

A race against time is therefore underway to control the epidemic before the disease becomes even better adapted to human-to-human transmission. Population fatigue about non-pharmaceutical methods to prevent COVID-19 transmission is another problem that should not be overlooked. It is obvious from the messages on social networks and daily observations, even though the majority of the population surveyed by *Santé Publique France* still declares to respect the barrier and physical distancing measures [16]. This lassitude may also explain the disaffection of "massive" screening campaigns which, in France, have only finally drained a very small minority of the targeted people [17]. It is also accompanied by a generalised scepticism about the communication of health authorities, which risks compromising the vaccination campaigns.

In view of all these elements, it is reasonable to think that the situation will remain complicated throughout the winter and that major efforts will be required to avoid finding ourselves in an uncontrollable situation. Nevertheless, two elements raise the hope that in the medium-term, the most difficult phase of the crisis should give way to a slow return to normal. The first element is the continuously increasing immunity level in the population, resulting from natural immunisation and vaccination campaigns. Indeed, the first vaccine efficacy studies bring excellent news, even though the results announced so far – about 95% efficacy for two RNA vaccines [18,19] and 70% efficacy for a more "classical" vaccine [20] – mostly concern the vaccine's short-term protection against non-severe symptomatic forms and not its efficacy on most-at-risk populations or its ability to prevent virus transmission. The second factor that could accelerate the epidemic decline next spring is the return of good weather and the increase in outside temperature leading to less virus transmission. It should be noted, however, that the seasonal effect did not prevent outbreaks in Florida last summer or in South Africa in December. Improvement in the spring is therefore not

guaranteed if the population turns away from the vaccine and begins to reject the barrier measures massively.

The ordeal we are going through is particularly destabilising for individual citizens as well as whole societies. It highlights our vulnerability and weaknesses facing an "enemy" we were poorly prepared to fight. This situation is all the more destabilising as the epidemic has split the world into countries that have brought the epidemic under control, mainly in Asia and Oceania, and those that are sinking into an increasingly deep health, economic and social crisis, mostly in Europe and the Americas. Such a dichotomy may lead us to question our lifestyles and values. At least, it should push us to rethink our healthcare systems, their place in our society, and the logic – financial or health-related – underlying their management and structure, as well as the importance that should be given to preventive aspects in modern medicine. Healthcare covers a much broader field of activity than curative medicine, and health management shall not be guided by market logic only.

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