

Undetected and relatively sustained SARS-CoV-2 circulation
worldwide during the year 2019

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Althoff and colleagues interestingly reported that between January and March 2020, in a total of 24,079 All-of-Us study participants, seven individuals resulted seropositive prior to the first confirmed cases in Illinois, Massachusetts, Wisconsin, Pennsylvania, Mississippi [1].

The COVID-19 pandemic is presumptively originated in October-November 2019 in China, since symptom onset of the first identified patient occurred on 1 December 2019 [2]. Nevertheless, American and European data suggest earlier, undetected, and relatively sustained SARS-CoV-2 circulation. Indeed, in May 2019, in England, 2.97% (3/101) blood donors had high SARS-CoV-2 S-reactive IgG (two also had IgA and IgM suggesting recent infection), that did not react with other coronaviruses [3]. In November 2019, in France, 1.89% (42/2,218) individuals from a healthy cohort had high SARS-CoV-2 S1-reactive IgG levels [4]. In Italy, 2.22% (1/45) blood donors had high levels of IgG/IgM against the nucleocapsid protein in December 2019 [5], while 14.20% (23/162) individuals from a healthy cohort had detectable anti-RBD IgG/IgM in September 2019 [6]. In December 2019, in California, Oregon and Washington, 2.04% (39/1,912) blood donors had high S-reactive pan-Ig levels [7]. Importantly, specificity of antibody tests used in these studies was very high.

Two children, one from France (7.14%, 1/14) [8], another from Italy (2.56%, 1/39) [9], had oropharyngeal swabs collected in December 2019, retrospectively analysed with RT-PCR that tested positive for SARS-CoV-2 RNA. Remarkably, the French child's family did not leave France and had no contacts with Chinese or diseased individuals. In stored sewage samples from wastewater treatment plants, SARS-CoV-2 RNA was detected by RT-PCR starting from November 2019 in Brazil (3.1×10^5 genome copies/L) [10], December 2019 in Italy ($0.1-4.9 \times 10^4$ genome copies/L) [11], May 2019 in Spain ($6.4-8.3 \times 10^2$ genome copies/L) [12].

The distribution of COVID-19 mortality rates across European countries in May 2020 was correlated with the distribution of influenza mortality rates in the years 2016-2019, suggesting that in Spring 2020, SARS-CoV-2 circulation in Europe was already as sustained as the endemic influenza virus in previous years [13].

As correctly reported by Althoff and colleagues, their data corroborate the infectious disease epidemiology principle of pathogen circulation prior to the recognized outbreak. In addition, the present data suggest the hypothesis that in 2019, SARS-CoV-2 circulation was already relatively sustained in Europe and America. This eventuality is not astonishing, as

SARS-CoV-2 is mainly a respiratory pathogen that induces pneumonia. Each year, seven million hospitalizations due to community acquired pneumonia (CAP) occur among older adults –more than three million of them occur in industrialized countries. Case-fatality of these events is higher than 10%, and 20% in subjects older than 85 years [14]. In more than one half of these episodes, the causative organism is unknown. Therefore, each year three to four million CAP related hospitalizations with unknown causative agent occur [15].

In conclusion, a novel unknown respiratory virus, like SARS-CoV-2, that is responsible for severe pneumonia could circulate undetected for months or years, be responsible for many deaths, and even become pandemic, until peculiar characteristics of the disease are noticed that allow its identification.

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