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Editorial

On-board toilets of long-haul flights: is sewage epidemiology effective for COVID-19 global surveillance?

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We can think of COVID-19 as a Camusian plague, as emblematically stated by Sansonetti [1] in his interesting editorial that discusses the current coronavirus global emergency in terms of an "expected pandemic." In fact, COVID-19 is the third coronavirus epidemic in less than 20 years, following the outbreaks of SARS and MERS. In 2015, WHO coordinated an expert workshop on the prioritization of emerging pathogens. Prioritization criteria included the severity of the disease; the pathogen's potential to originate a public health emergency in the near future; and the absence of preventive and therapeutic countermeasures. Seven pathogens were identified as requiring urgent R&D and, consistently, highly pathogenic emerging coronaviruses relevant to humans were on the list. SARS and MERS indeed showed their rapid and disruptive effects as emerging pathogens. Besides the invaluable insights they provided on beta-coronaviruses' cross-species transmission and their molecular pathogenesis mechanisms, their essential legacy was possibly that of recognizing the crucial importance of an orchestrated response in case of a rapidly disseminating global epidemic. However, despite major revisions of the International Health Regulations (IHR) and the many efforts made since then to improve surveillance networks, aspects of this coordination still leave much to be desired. Sensitive and flexible surveillance systems for early warning require further development [2].

The clinical detection of SARS-CoV-2 RNA in feces of infected people promptly lead to the idea of wastewater-based epidemiology (WBE) as a valuable strategy for COVID-19 environmental surveillance [3]. We have been personally working on COVID-19 WBE [4], so the idea of translating the concept from urban wastewater to aircraft toilet waste (ATW) of long-haul flights (i.e. $>$ 4000 Km) came up quite naturally. Current evidence suggests that detection in community sewage of one symptomatic/asymptomatic infected case per 100 to 2,000,000 non-infected people is theoretically possible [5]. Even more so, this should be feasible when sampling the excreta collected by "dry" vacuum on-board toilets of long-haul flights, with a capacity of more than 200 passengers.

If we recall the case of SARS-CoV-2 and how it spread in Europe, we could probably say that it was a business class passenger. A comprehensive pre-COVID-19 review [6] investigated the role of transport in the propagation of influenza and coronaviruses, highlighting how air transportation can supposedly accelerate the spreading of respiratory viruses in distinct geographical areas.

So, what is the point of considering an ATW-based surveillance activity for long-haul flights? Let's briefly consider the dramatic disruption of global travels. The European Union, for instance, banned all non-essential flights from March 17th to July 1st, 2020. Frontier barricades are now being dismantled and international arrivals are resuming, however some countries prefer to maintain a cautious approach. Indeed, Italy still demands a 14-day self-isolation and swab test upon arrival for all extra-Schengen passengers. Now, ATW-based surveillance possibly represents a reasonably time-saving and cost-benefit effective strategy for monitoring single flights, while obviating the need to swab all passengers.

Literature suggests that, as of today, ATW-based surveillance has been discussed - and, most notably, empirically tested - only by a couple of pioneering studies. In early 2019, with astonishing prescience, a Danish group applied a meta-genomic approach on ATW, targeting respiratory and enteric viruses [7]. A recent study reported the detection of SARS-CoV-2019 RNA in wastewater samples of a cruise ship and three passenger aircrafts [8].

Some details can be added to the hypothetical diagram of an ATW-based surveillance approach. Most likely, passengers allowed to board will either be not infected or asymptomatic/pauci-symptomatic/pre-symptomatic COVID-19 patients. Actually, recent publications support the presence and detectability of SARS-CoV-2 RNA in stools of such

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COVID-19 cases [9–11]. On a long-haul flight, they will probably avail themselves of the on-board toilet, thus enriching the content of the vacuum toilet septic tank. Of course, some passengers will not contribute to the common ATW sample but, intuitively, the rule is "the longer the flight, the greater the toilet usage and the representativeness of ATW". For long-haul routes, the general rule has toilet servicing being performed after landing of each individual flight. Minor exceptions could concern either airlines choosing to contract ground handling services under non-standard terms, or "empty leg" non-scheduled charter flights (i.e. aircraft flying with no passengers for repositioning). Nevertheless, such atypical situations can be identified *a priori* and their representativeness pondered. During servicing, a dedicated "honey truck" empties the aircraft septic tank(s), with the suction actually mixing the ATW quite thoroughly. An amount suitable for surveillance purposes (e.g. 0.5–1 L) could be sampled right from the truck or just before ATW is dumped in the disposal facility. The sample should then be processed as soon as possible. If SARS-CoV-2 RNA is detected, additional surveillance actions can be promptly extended to passengers. A passenger contact tracing protocol should be feasible thanks to the public health passenger-locator cards, as developed by the IHR.

Of course some practical aspects should be further scrutinized. For instance, we questioned the analytical suitability of ATW samples, due to the pre-filling of septic tanks with sanitation liquid during the ground toilet servicing. Although the precise composition (possibly nonylphenol ethoxylate or glutaraldehyde and benzalkonium chloride) of such liquids is not mentioned in ground operations manuals, toilet fluids are described as "corrosive" and could compromise the integrity of nucleic acids or other target biomolecules. Nevertheless, the above-mentioned investigations [7,8] actually support the feasibility of molecular methods. Moreover, air temperature at flight altitude (about −50 °C) could somehow help in keeping ATW refrigerated, thus preserving microbial genetic material.

In addition to technical aspects, we should also debate the near future of global travels. Unless a second massive COVID-19 wave occurs, air traffic will recover its pre-pandemic numbers in the coming months and years. In 2018, the global airline industry boarded more than 4 billion travelers, and this number was expected to double by 2037. The Asia-Pacific region is considered the biggest driver of demand in the airline industry. Before the COVID-19 pandemic, China accounted for about 600 million passengers per year, and was set to conquer the world's largest aviation market before 2025, thus displacing the US. Besides Asia, the other fastest-growing markets belong to Africa (e.g. Sierra Leone, Ivory Coast), so that by 2037 African countries will count 400 million passengers a year [12].

With the COVID-19 pandemic, the world has once more been forced to acknowledge that emerging pathogens can escape from their cage and then rapidly spread worldwide. After all, it appears to be an unavoidable, if undesired, consequence of the contraction of geographic and social lengths in this era of globalization. Advanced molecular techniques for the detection of novel pathogens and the monitoring of known ones should constitute a stronghold for the global surveillance of infectious diseases. Furthermore, the 360-degree potential of ATW samples could also be exploited by investigating the multitude of targets (e.g. illicit drugs, pharmaceuticals, xenobiotics) already realized by classic WBE, thus going even beyond the sole surveillance of communicable diseases.

The time has come for a revolutionary approach to be implemented and it urgently needs the joint efforts of the international community. Pandemics can be restrained to a certain extent, but ultimately the early identification of pathogens is our ace in the hole, together with the universality of science that should always prevail on politics, profits and fears.

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Declaration of competing interest

The authors declare no competing financial interest.

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