



Placing the COVID-19 Pandemic in a Marine Ecological Context: Potential Risks for Conservation of Marine Air-Breathing Animals and Future Zoonotic Outbreaks

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INTRODUCTION

Viruses are key components of ecosystems. They regulate wildlife populations, and can spread to different species (French and Holmes, 2020). New human zoonotic diseases emerge periodically as a result of the interaction of humans with the environment, with microorganisms, or with their animal hosts (Morens and Fauci, 2020). The current pandemic disease COVID-19 is caused by SARS-CoV-2, a coronavirus (CoV) classified in the genus *Betacoronavirus* (Wu et al., 2020). The main animal sources for zoonotic CoVs are bats and birds (also seabirds), which potentiate viral evolution and dissemination (Woo et al., 2012, 2014; Alluwaimi et al., 2020; El-Sayed and Kamel, 2021). SARS-CoV-2 is thought to have jumped from bats to humans through an intermediate host that remains unknown. The presence of CoVs in aquatic organisms and in the marine environment has been barely studied (Mordecai and Hewson, 2020), which may lead to the erroneous conclusion that CoVs are scarce in marine ecosystems. In this opinion paper we highlight the importance of investigating and monitoring marine air-breathing animals (hereafter MA-BA) as reservoirs of CoVs, especially for seabirds and marine mammals, to control both human health and the health of MA-BA populations.

ZOONOTIC VIRUSES AND CoV RESERVOIRS IN MARINE AIR-BREATHING ANIMALS

In the oceans viruses can cause mass mortality events in MA-BA, well known examples are die-off events in dolphins caused by a morbillivirus (Rubio-Guerri et al., 2013). Marine mammals and birds are natural reservoirs for potential zoonotic pathogens (Bogomolni et al., 2008). The interaction of marine mammals with humans can derive in zoonotic events caused by viruses, including influenza A viruses (Waltzek et al., 2012). Although today human interaction with marine mammals is less frequent than in ancient times, a hunt directed to cetaceans still exists in some parts of the world (for example Faroe Islands in Denmark, and Taiji in Japan). In addition, thousands of marine mammal and sea turtle specimens are rescued annually by recovery centers around the world, mainly animals stranded on beaches through anthropogenic interactions, posing a real health risk for animal handlers.

Evidence is scarce but sufficient concerning natural reservoirs of CoVs in marine mammals and seabirds, though no evidence has yet been documented for CoVs of the genus *Betacoronavirus*

in which SARS-CoV-2 is classified. Marine mammals are infected by CoVs of the genus *Alfacoronavirus* (Bossart and Schwartz, 1990), and also by genus *Gammacoronavirus* (Mihindukulasuriya et al., 2008; Nollens et al., 2010; Woo et al., 2014). *Gammacoronavirus* and *Deltacoronavirus* are known to circulate among wild birds (Hepojoki et al., 2017; Canuti et al., 2019). Thus a hypothetical transmission of CoVs between wild birds and mammals in the marine environment may occur, as for influenza A virus (Runstadler and Puryear, 2020).

POTENTIAL TRANSMISSION OF SARS-CoV-2 BETWEEN HUMANS AND MARINE AIR-BREATHING ANIMALS

Molecular studies have raised concern in relation to transmission of SARS-CoV-2 from humans to MA-BA (Barbosa et al., 2021; Mathavarajah et al., 2021). Biophysical models raise awareness on vulnerable coastal areas where marine mammals can become exposed to SARS-CoV-2 via sewage (Guo et al., 2021). Productive SARS-CoV-2 infection of MA-BA requires not only the interaction between humans and animals, but also the entry of the virus into host cells through the binding of the S protein to angiotensin converting enzyme 2 (ACE-2) or alternative cell receptors (Masre et al., 2020). A study analyzing the structure of the S protein of SARS-CoV-2 and the receptor binding region of the ACE-2 receptor in higher vertebrates has concluded that cetaceans conserve most of the key residues for viral entry (Luan et al., 2020). The analysis of a fragment of ACE-2 has produced a list of species that includes 12 marine mammals with a high risk of being infected by human SARS-CoV-2 (Damas et al., 2020).

The mink (*Neovison vison*), a semiaquatic mustelid, has starred in the transmission of SARS-CoV-2 from humans to mammals, with infection documented from humans to mink and back to humans in farms (Hammer et al., 2021), raising questions about SARS-CoV-2 reservoir sustainability in wild mustelids (Fenollar et al., 2021). Occasional predation of bats has been reported for an aquatic mustelid that can be observed in the sea: the Eurasian otter (*Lutra lutra*) (Forman et al., 2004). Moreover, dolphin morbillivirus reservoirs were recently also detected in Eurasian otters along the Mediterranean Sea coast (Padalino et al., 2019). There is thus a dangerous link between bats-otters/cetaceans-humans, and therefore a hypothetical aquatic mammal intermediate host in

the emergence of the zoonotic COVID-19 disease should not be ignored.

PERSPECTIVE: GLOBAL NETWORK FOR EARLY CoV SURVEILLANCE IN MARINE AIR-BREATHING ANIMALS

The ecology and evolution of CoVs need to be refocused to understand the role of CoVs in global ecosystems rather than concentrating only on CoVs as pathogens that emerge following host jumping (French and Holmes, 2020). Early surveillance networks exist for diseases, such as the bubonic plague in mammals from USA (Biggins and Kosoy, 2001). CoV research in marine ecosystems faces an apparent challenge, the costly effort of exploration of seas and oceans for the collection of biological samples from MA-BA. Every year thousands of MA-BA are stranded on the beaches around the world (Alvarado-Rybak et al., 2020), and these animals are generally studied by different local scientific institutions and agencies. Moreover, a wide range of molecular and cellular tools for CoV detection is now available, either developed for COVID-19 diagnosis, or for CoVs (Woo et al., 2014). We suggest creating a new low-cost global network for early surveillance of marine CoVs with zoonotic potential through systematic biological sampling of stranded MA-BA, selecting only a routine number of specimens to be controlled globally, regardless of whether there are events that increase stranding probability. In conclusion, marine interdisciplinary science can contribute to answer questions concerning the COVID-19 pandemic and prepare us for future zoonotic disease epidemics by (1) identifying potential CoV reservoirs in the marine environment, and (2) evaluating CoV transmission from MA-BA to humans, from humans to MA-BA, and between MA-BA.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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