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COMMENTARY

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Should we be concerned about COVID-19 with nonhuman primates?

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Abstract

The coronavirus disease 2019 pandemic has radically changed the human activities worldwide. Although we are still learning about the disease, it is necessary that primatologists, veterinarians, and all that are living with nonhuman primates (NHP) be concerned about the probable health impacts as these animals face this new pandemic. We want to increase discussion with the scientific community that is directly involved with these animals, because preliminary studies report that NHP may become infected and develop symptoms similar to those in human beings.

KEYWORDS

coronavirus, disease, monkey, zoo

Coronavirus disease 2019 (COVID-19), also informally called the new coronavirus, is a severe acute respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, part of the *Coronaviridae* family (Gorbalenya, Baker, & Baric, 2020). Although research into the origins of COVID-19 is still being conducted, the first reports of infection in humans occurred in December 2019 in Wuhan, southern China, coming from infected animals sold in a popular market. Although debate continues about the zoonotic origin of the virus, it is currently thought that naturally infected bats (Zhou, Yang, & Wang, 2020) and pangolins (Zhang, Wu, & Zhang, 2020) transmitted the virus to people, and it then gained the capacity for human–human transmission (Andersen, Rambaut, Lipkin, Holmes, & Garry, 2020; Guo, Cao, & Hong, 2020).

Within a few weeks, the disease had spread to various regions of the world, with hundreds of thousands of cases reported in the first quarter of 2020, with thousands of deaths (WHO, 2020a). When more than 118,000 cases were registered in the world, the World Health Organization (WHO) declared, on March 11, COVID-19 as a pandemic (WHO, 2020b).

In humans, the virus incubation period occurs between 2 and 14 days, and it might be transmitting to other people even before the first symptoms appear; these symptoms are usually fever, tiredness, and dry cough (Rothan & Byrareddy, 2020; Singhal, 2020). The disease mainly affects the respiratory system and, in the most severe cases, can compromise the respiratory capacity, requiring intensive medical care. A variable percentage of people (between 50% and 80%) are asymptomatic or do not need medical treatment but can still spread the virus (Day Michael, 2020; Nishiura, Kobayashi, & Suzuki, 2020; WHO, 2020c).

Due to phylogenetic proximity, nonhuman primates (NHP) are excellent animal models to better understand the aspects related to the human biology, including the behavior of different diseases (Colman, 2018). Coronavirus can infect basically all mammals known so far. NHP were commonly used for research on previous related epidemics, such as SARS and Middle East respiratory syndrome (MERS; Haagmans, Kuiken, & Martina, 2004; Wang, Zheng, & Gai, 2017). NHP can be infected by the coronavirus and develop symptoms like those identified in humans, at least experimentally (de Wit, Feldmann, & Cronin, 2020).

Most of the current knowledge about the biology of COVID-19 in NHP is currently in pre-prints, published in online repositories, and consists of experimental inoculation studies. The animals targeted in these studies were primarily rhesus (*Macaca mulatta*) and cynomolgus macaques (*Macaca fascicularis*), widely used in clinical research worldwide. Preliminary data indicate that these monkeys, on the 1st day after infection, show changes in breathing pattern, being

accompanied by pulmonary infiltrate that remains for at least a week. Although fever is a common symptom in humans, in rhesus monkeys it appears to be a mild symptom (Munster, Feldmann, & Williamson, 2020) or not even observed (Bao, Deng, & Gao, 2020).

Hematological changes were detected in some NHP, such as leukocytosis and neutrophilia, but the values returned to a normal pattern in a few days. In addition, not all cynomolgus monkeys experimentally infected in the study of Rockx et al. (2020) showed symptoms of the disease, even though the virus was found from nasal swab collections early in the infection, lasting for at least a week. These results may resemble asymptomatic cases observed in humans, which can still participate in viral transmission (Mizumoto, Kagaya, Zarebski, & Chowell, 2020).

The route of infection also seems to be important, with an emphasis on conjunctival and intratracheal infection, in which rhesus had a detectable viral load days after inoculation, with weight loss for the animals. Despite the low number of animals studied (five, which were divided into three groups), the study indicates that the contact of the virus with the ocular mucosa can be an important route of infection (Deng, Bao, & Gao, 2020).

The positive results for viral RNA in the nasal and oropharyngeal swabs of these animals, especially in the 1st days of infection, is similar to what is observed in humans. This may indicate the high possibility of spread through close contact with infected animals. It is not yet possible to state that humans can directly infect the NHP, as well as the opposite, but these experimental studies that used viral cultures from human patients strongly indicates that SARS-CoV-2 can naturally infect these animals.

Many of these studies are still in development, have not been properly reviewed by the scientific community, and analyze a small sample size. However, previous knowledge of similar infections, such as the ones caused by SARS and MERS—both caused by viruses from the same family as COVID-19—point in the same direction and should not be overlooked (Rockx, Kuiken, & Herfst, 2020).

SARS was an epidemic disease caused by a coronavirus very similar to COVID-19 virus, which affected the world between 2002 and 2003, causing hundreds of deaths (Wilder-Smith, Chiew, & Lee, 2020). Experimental studies on the following years after the epidemic pointed out that NHP developed, in general, lighter versions of the symptoms than those detected in humans (Lawler, Endy, & Hensley, 2006). The animals normally presented pneumonia that peaked about 10 days after inoculation, with detectable pulmonary changes until 60 days, even though there were no meaningful changes in the rest of the laboratory tests.

Regarding MERS, the results tended to be similar. MERS is another disease caused by coronavirus that caused a major outbreak starting in 2012, with sporadic cases being reported up until today (WHO, 2020d; Zumla, Hui, & Perlman, 2015). Experimental studies with rhesus have shown few differences with SARS, characterized by fever, cough, and increased respiratory rate, with a mild picture of pneumonia. Marmosets (*Callithrix jacchus*) inoculated with MERS, on the other hand, presented more severe versions of the disease when compared to rhesus, including the virus being found in practically all tested tissues (Doremalen & Munster, 2015).

A lot of studies on SARS and MERS focus on NHP as good models to study vaccines (Gao, Tamin, & Soloff, 2003; Xu, Jia, & Zhou, 2007). These studies can guide the scientific community to the development of vaccines and drugs against the COVID-19. Our intention is precisely to alert the scientific community to the need for attention to NHP that are found in zoos within large urban centers. Even though many of those places were closed to visitors, the internal circulation of employees who work directly with these animals cannot be ignored, because there is at least a 50% chance that someone infected will be asymptomatic (Day Michael, 2020; Nishiura et al., 2020; WHO, 2020c). In addition, the participation of NHP in the maintenance of the virus in the environment is unknown so far, and whether only Old World primates are susceptible to be infected by COVID-19 (since they were the only animals used in these studies) or New World primates can also get infected and how the disease would develop on these animals are still unknown.

Filling in this knowledge of the subject would help the scientific community to understand other possible impacts related to NHP coronavirus infection. Conflicts and interactions between humans and monkeys are constantly reported in Africa and Asia (Karanth, Gupta, & Vanamamalai, 2018; Siljander, Kuronen, & Johansson, 2020), and tourists frequently interact with these animals (Sabbatini, Stammati, & Tavares, 2006). It is known that NHP are susceptible to several human diseases, such as measles (Jones-Engel et al., 2006) and this possible interaction can expose these animals to coronavirus, with chances of introducing it into its natural environment. Despite this, until more studies are developed focusing on coronavirus, mainly being published in peer-reviewed journals, we must extrapolate the previous data obtained with other diseases to the current situation.

Thus, it is necessary that primatologists, veterinarians and employees who work with NHP, mainly in zoos and places that receive visitors, stay alert and take protective measures, especially during the pandemic period, aiming at the health of the NHP. Although we do not know enough about the disease, they may need veterinary care during infection, in addition to the risk of infecting other NHP and also the management team.

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