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Correspondence

Besides human booster doses: Could vaccinating highly susceptible animals to SARS-CoV-2 be the needed urgent strategic step?

Dear Editor

Animals are the source of all pathogenic human coronaviruses (CoVs) [1]. The emergence of multiple SARS-CoV-2 variants, including the mink-associated variant, and the Omicron variant with a probable mouse origin, poses a substantial danger to our attempts to contain the pandemic [2,3]. Domestic animals (dog, cat, and ferret), captive animals (tiger, lion, snow leopard, puma, otter, and gorilla), and wild and farmed minks have all been documented to have natural SARS-CoV-2 infections. Given the recently identified SARS-CoV-2 variants and the nature of coronavirus replication, other variants are likely to be circulating unnoticed in different parts of the globe. SARS-CoV-2 has emerged following cross-species jumping in animals, raising concerns about the possibility of reintroduction into human populations via interspecies transmission between people and animals [2]. Additionally, the ability of SARS-CoV-2 to infect animal populations raises concerns regarding alternate SARS-CoV-2 reservoirs in animals and the establishment of vaccine-resistant SARS-CoV-2 variants in animals.

There are currently no ongoing surveillance efforts to identify other animal species that may be vulnerable to the virus. We are currently unsure of the complete range of animals that can contract SARS-CoV-2 from people or other susceptible mammals in the absence of such attempts [4]. Banerjee et al. [4] have suggested a hierarchical model for prioritizing animal species for surveillance. Furthermore, the effects of SARS-CoV-2 infection in animals on their health are unknown. More crucially, we have no way of knowing if SARS-CoV-2 will re-emerge in certain animal species and infect humans who have been naturally exposed to or vaccinated against it [4]. The entry of SARS-CoV-2 into the feral population and subsequent transmission to wildlife may be avoided if domestic animals are vaccinated [2].

The vital step to prevent SARS-CoV-2 from re-emerging in the future and to achieve successful elimination of SARS-CoV-2 is to control transmission in all susceptible animal species. Contact with animals is of our nature and for many purposes (hunting, livelihood, …) [5] and it is unpreventable. Certain free-living wild animals have a high susceptibility to SARS-CoV-2, suggesting that SARS-CoV-2 reservoirs could emerge in the wild [6]. Besides free-ranging wild animals, human-to-animal transmission has been reported in pets, farmed animals, and zoo animals [7–11]. Moreover, interspecies transmission of SARS-CoV-2 has been reported like mink-to-cat transmission [12] and deer-to-deer transmission [13], which greatly raises the likelihood of onward spread [14].

Asian lions (*Panthera leo persica*) have been observed to be naturally infected with the lineage Delta (B.1.617.2) variant [15,16]. Three Malayan tigers at a Virginia Zoo (Norfolk, VA, USA) experienced respiratory symptoms and were infected with the Alpha (B.1.1.7) variant [17]. Adult white-tailed deer (*Odocoileus virginianus*) in the United States have been shown to be highly susceptible to SARS-CoV-2 infection, as well as to the Alpha (B.1.1.7) variant [18]. Doe deer can transfer the virus vertically to their foetus and through direct contact [19]. North American deer mice (*Peromyscus maniculatus*) are vulnerable to SARS-CoV-2 infection, with little or no clinical symptoms, when exposed to a human SARS-CoV-2 isolate. Furthermore, SARS-CoV-2 can be transmitted directly from deer mice to naive deer mice. The possibility of SARS-CoV-2 reverse zoonosis in deer mice and humans is still unknown. White-tailed deer, numbering 30 million in the United States, have been extensively infected with SARS-CoV-2 in several human-to-deer transmission events and efficient deer-to-deer transmission. The extensive widespread infection of white-tailed deer indicates that they have been established as potential SARS-CoV-2 reservoir hosts, significantly implicating the virus's ecology, long-term persistence, and evolution, as well as the risk of human spillover [20]. A recent study has reported infection of white-tailed deer with the Omicron variant in New York [21].

In Denmark, SARS-CoV-2 spillover from minks to people was linked to a reduced ability of pre-existing human antibodies to neutralize the mink variant [22], and the most dramatic scene is that at least 12.5% of all people being infected with dominated mink-derived SARS-CoV-2 variants in Denmark and the Netherlands were caused by human-to-human transmission [23]. Concerns about SARS-CoV-2 transmission via the fecal-oral route [24,25], which has been demonstrated in hamsters [26] and has the potential to cause respiratory infection. But, it has yet to be proven in people. Worryingly, researchers in Hong Kong have identified evidence that pet hamsters can transmit the SARS-CoV-2 Delta (AY. 127) variant to humans and have linked the animals to human infections in the city [27]. To date, pet hamsters are considered the second confirmed animal species able to transmit SARS-CoV-2 to humans, following farmed mink [28] found in Denmark, the Netherlands, and Poland [28–31]. Recently, the first evidence of a deer-to-human COVID-19 case has been reported in Canada [32]. They discovered a highly diverse SARS-CoV-2 lineage in a white-tailed deer that originated in humans. Interestingly, SARS-CoV-2 infection rates in white-tailed deer in North America have reached up to 70% with three distinct lineages (B.1.2, B.1.582, and B.1.596) discovered in several places [33], highlighting the risk of future variants originating from adaptation in other wild animals and transmitting to humans. Human has endless contact with animals for many purposes [5] and in many ways [1].

Owing to the worries about waning immunity and SARS-CoV-2 mutations after the advent of the Omicron variant, some governments have deployed booster doses of COVID-19 vaccines [34]. Worryingly, the waning immunity is a repeated reported issue that calls us to focus on immunosuppressed patients. However, wild, feral, and domestic

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animals that met the hierarchical model should not be underestimated. Therefore, active or passive surveillance frameworks for domestic, captive, and wild animals must be built to restrict the spread of SARS-CoV-2 in domestic and wild animal species. Ramping up vaccination of highly susceptible animals to SARS-CoV-2 that could be viral reservoirs is a strategy to prevent viral reintroduction into the human population. As a result, in-depth investigations of the interrelationships between animals and humans for disease transmission and spread, as well as adoption of appropriate preventative and control techniques using interdisciplinary and holistic approaches, are required. Indirectly, WHO should attempt to increase vaccine manufacturing regions, like in Africa, to aid in this regard.

Ethical approval

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The data in this correspondence article is not sensitive in nature and is accessible in the public domain. The data is therefore available and not of a confidential nature.

Declaration of competing interest

None.

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