

## **Animal reservoir of SARS-CoV-2: a threat to humans?**

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As more and more animal species susceptible to SARS-CoV-2 infection had been identified under natural or experimental conditions from the onset of the pandemic [1], the risk of zoonosis was suspected by the French National Academy of Medicine and then confirmed when the Netherlands demonstrated human contamination by farmed minks.

Subsequently, several cases of animal contaminations by different human variants of SARS-CoV-2 were reported, affecting a wide range of species of which pets, livestock or wildlife (mustelids)[2]. Zoo animals (big felines, great apes, hippopotamus, otters) have been infected by their caretakers. In India, a leopard in the wild was infected with the Delta variant.

Although the cases of contamination of dogs and cats by humans are sporadic, the constitution of a virus reservoir in nomadic cats remains possible due to their contact with liminal wild fauna which is still little studied, and the sensitivity of felines to the different variants of SARS-CoV-2. Amongst new pets, a natural infection of two rabbits with SARS-CoV-2 was reported in France [3].

In Hong Kong, in January 2022, golden hamsters imported from the Czech Republic via the Netherlands were reported to have caused an outbreak of the Delta variant that started at a pet shop's worker before reaching 58 people. Since the farmed mink episode, this is the first time that a contamination of hamsters of human origin would be followed by a back transmission to humans, then by an epidemic spread with a human-to-human transmission. The high susceptibility of hamsters to SARS-CoV-2 makes them a potential reservoir. In addition, the investigation carried out around this outbreak revealed that pet international trade represents a risk of long-distance dissemination of SARS-CoV-2 [4].

In North America, white-tailed deer (*Odocoileus virginianus*) could constitute an animal reservoir of SARS-CoV-2. This hypothesis was reinforced in 2022 by noting that this overpopulated species is approaching urban or suburban areas, which has probably favored its contamination by humans. The seroprevalence of anti-SARS-CoV-2 antibodies has been estimated between 13.5 and 70% in these wild deer, with a peak of 82.5% during the hunting season in the USA [5]. It rises to 94.4% in captive animals, probably due to their close promiscuity. In Pennsylvania, where the white-tailed deer population is the densest (30 deer per square mile), the Alpha variant circulated simultaneously with the Delta variant during fall-winter 2021, while the Delta variant predominated in the human population. The dynamics of interspecies transmission were studied experimentally after intranasal inoculation of fawns by tracking contact animals [6]. Finally, a new and highly divergent lineage of SARS-CoV-2, discovered in Canada in white-tailed deer, was isolated from a human case in the same region, suggesting a possible transmission from deer to humans [7].

In Europe, the hypothesis of a reservoir in deer has not been confirmed, but other wildlife species are highly sensitive to SARS-CoV-2. This is the case for wild mustelids or ferrets found

to be seropositive: otters and minks in Spain [8], martens and badgers in France (Brittany) [9]. In our country, the epidemic spread of Covid-19 due to the Marseille-4 variant (B.1.160) in 2020 seems to have emerged from a mink farm in Eure-et-Loir [10]. Several species, classified as harmful in France due to their prolificacy, are also highly sensitive to SARS-CoV-2: the American mink, the raccoon dog and the red fox.

In their joint statement of 7 March 2022, the OIE, WHO and FAO emphasize the risk posed by the animal reservoir of SARS-CoV-2 and its potential role in the emergence of new variants through mutation or recombination [11]. Moreover, it should not be forgotten that the animal reservoir of coronavirus at the origin of the Covid-19 pandemic was probably a bat and that coronaviruses very close to SARS-CoV-2 have recently been identified in this species which from now must be particularly monitored [12].

Therefore, **the French National Academy of Medicine recommends:**

- to maintain continuous monitoring of the infections detected in domestic animals as well as in wild fauna sensitive to SARS-CoV-2;
- to carry out systematic sequencing for each case found positive in RT-PCR;
- to warn infected people, symptomatic or not, that they must also apply isolation measures with respect to animals living in their surroundings;
- to inform hunters, forestry workers and any person working in contact with wild and endangered animals (specialized care centers, zoos, etc.), as well as visitors to animal parks, about the zoonotic risks involved.

[1] Communiqué from the French National Academy of Medicine and the French Veterinary Academy "Do animals contaminated with SARS-CoV-2 represent a risk for humans?", July 23, 2020.

[2] Brugère-Picoux J et al. Report "Covid-19 and the animal world, from a still mysterious origin towards an always unpredictable future". Bull Acad Natl Med 2021; 205: 879 -90.

[3] Fritz M et al. First evidence of natural SARS-CoV-2 infection in domestic rabbits. Vet Sci 2022; 9, 49.

[4] Hui-Ling Y et al. Transmission of SARS-CoV-2 (Variant Delta) from Pet Hamsters to Humans and Onward Human Propagation of the Adapted Strain: A Case Study. Lancet 2022; 399: 1070-8.

[5] Kuchipudi SV et al. Multiple spillovers from humans and onward transmission of SARS-CoV-2 in white-tailed deer. Proc Natl Acad Sci USA 2022; 119:e2121644119.

[6] Martins M et al. From Deer-to-Deer: SARS-CoV-2 is efficiently transmitted and presents broad tissue tropism and replication sites in white-tailed deer. PLoS Pathog 2022; 18: e1010197.

[7] Pickering B et al. Highly divergent white-tailed deer SARS-CoV-2 with potential deer-to-human transmission. bioRxiv (preprint).

[8] Aguiló-Gisbert J et al. First Description of SARS-CoV-2 Infection in Two Feral American Mink (*Neovison vison*) Caught in the Wild. Animals (Basel). 2021; 1422.

- [9] Davoust B et al. Evidence of antibodies against SARS-CoV-2 in wild mustelids from Brittany (France). bioRxiv (preprint). <https://doi.org/10.1101/2022.01.20.477038>
- [10] Colson P et al. Analysis of SARS-CoV-2 variants from 24,181 patients exemplifies the role of globalization and zoonosis in pandemics. *Front Microbiol* 2022; 12: 786233.
- [11] OIE/WHO/FAO. Joint statement on the priority importance of surveillance for SARS-CoV-2 infection in wildlife and prevention of animal reservoir formation. March 18, 2022. <https://www.oie.int/fr/joint-statement-on-the-prioritization-of-monitoring-sars-cov-2-infection-in-wildlife-and-preventing-the-formation-of-animal-reservoirs/>
- [12] Temmam S, et al. Bat coronaviruses related to SARS-CoV-2 and infectious to human cells. *Nature* 2022. doi: 10.1038/s41586-022-04532-4. Epub ahead of print. PMID: 35172323.