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The presumed receptivity and susceptibility to monkeypox of European animal species

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Abbreviations

CB Congo Basin
NHP Non-human primates
NP New pets
MPXV Monkeypox virus
WA West Africa

The Monkeypox virus belongs to the Orthopoxvirus genus, as does the specifically human smallpox virus. It is zoonotic and had never previously been considered as capable of human-to-human transmission over more than nine viral generation cycles. While relevant animal reservoirs have yet to be identified, non-human primates (NHP) are only accidental hosts. The potentially high number of current human shedders during the clinical phase (3 weeks maximum) raises the question of a risk in our countries of animals being contaminated by infected humans (reverse zoonosis). Cats as well as cows are susceptible to the Cowpox virus, another zoonotic Orthopoxvirus, which they transmit to humans. Dogs are much less susceptible to this virus and seem only receptive to Vaccinia virus (also belonging to the Orthopoxvirus genus). On the other hand, one study has demonstrated the pronounced susceptibility of the adult albino rabbit and of young animals of several rodent species to Monkeypox virus (MPXV). Given the susceptibility to MPXV of prairie dogs, which are American Sciuridae, the potential for infection of European squirrels cannot be ruled out.

While the animal reservoirs of MPXV have not been identified, it is now known that non-human primates (NHP) are only accidental hosts. On the other hand, different rodents and African squirrels are strongly suspected of being the main if not exclusive reservoirs of the virus [3,4].

That said, MPXV (WA lineage) had previously, albeit rarely, managed to extract itself from its African “cradle”. In fact, it was in Denmark, in 1958, that the virus was discovered, following the importation of cynomolgus macaques for experiments. Other imported cases were subsequently reported in laboratories in different parts of the world [5]. The most spectacular animal outbreak occurred in 2003 in the USA following the importation from Ghana of savanna cricetoma (Gambian pouched rats) as new pets (NP) [6]. They contaminated autochthonous pet prairie dogs, which were the source of 72 human zoonotic cases in six states (47 were confirmed). Interestingly, prairie dogs are Sciuridae, just like squirrels.

The first human cases outside of Africa (apart from the very particular outbreak of 2003 in the USA) were reported in 2018 but up until the unprecedented emergence in 2022, they remained sporadic (Fig. 1); only mild increases in numbers seem to have occurred. All of these cases were travellers coming or returning from Nigeria, plus one case of nosocomial transmission and one family cluster [7]. They were the secondary consequence of the abrupt reemergence of the WA lineage in Nigeria from 2017. While this increase in cases in historic foci, with increased human-to-human transmission are considered as resulting from
the discontinuation of smallpox vaccination, other anthropic factors (deforestation, population growth...) have likewise strongly contributed [8,9].

The current large number of potential human shedders, occasioning during the clinical phase (3 weeks maximum) either direct contagiousness through skin and/or mucosal contact and emission in the air of infectious droplets, or indirect contagiousness through contamination of the patient’s environment by secretions and scabs, raises the possibility of a risk of contamination not of humans by animals (as in Africa, or the USA in 2003), but rather of animals by humans (reverse zoonosis). This transmission could potentially concern pets, production animals and/or wild animals [10].

Not only are we largely unaware of their receptivity and susceptibility, but the animals contributing to the MPXV epidemiological cycle in Africa have yet to be formally identified. Only limited indications are presently available. What can we cautiously hypothesize, in this specific context, when we know that transmission from humans to animals presupposes:

- virus emission by humans (demonstrated);
- animal receptivity/susceptibility (unknown);
- and a possibility of transmission of the virus (which probability will vary according to species categories)?

Since domestic animals evolve in close proximity to their owners, they would seem to be the most at risk of being contaminated by humans. While cats as well as cows are susceptible to the Cowpox virus, another zoonotic Orthopoxvirus, which can be transmitted by them to humans, not a single case of monkeypox attributable to a cat has been reported in Africa, and a serological survey failed to identify any seropositive cats (or domesticated ruminants). For dogs and ferrets, no data are available for MPXV to date. However, dogs have proven to be weakly susceptible to Cowpox virus and receptive to Vaccinia virus (also belonging to the Orthopoxvirus genus).

As regards new pets, the rabbit is the most frequent species, and a study has shown a high susceptibility of the adult albino rabbit through “natural” routes of infection. The rat and the mouse as pets belong to Rat spp. and Mus musculus domesticus species respectively, neither of which is experimentally susceptible through “natural” routes of infection. However, under experimental conditions, the neonates of these species are highly susceptible to MPXV [11]. Regarding hamsters and guinea pigs, data are scarce. As for the Siberia chipmunk, since 2017 they cannot legally be kept as pets, at least in France.

Since synanthropic rats and mice belong to the same species as pet rats and mice, the same reasoning can apply. What is more, any contamination by infected humans could only occur indirectly, rendering even lower the likelihood of infection.

Lastly, as regards non-synanthropic wild species susceptible to infection, it is not sure that they exist, but were they to exist, they would most likely be rodents and squirrels. Given the susceptibility of prairie dogs (American Sciuridae), it cannot be ruled out that European squirrels could be infected. If the red squirrel has been found to be experimentally very susceptible, it does not approach humans, and there is no data for the gray squirrel, which can let humans feed it, but is apparently not present in France to date.

All in all, the risk of human-to-human transmission appears to be far greater than the risk of infection of animals by humans. That much said, a risk of transmission to domestic animals, particularly new pets (especially rabbits and neonates) cannot be ruled out. It also bears mentioning that while all Sciuridae potentially represent species at risk, they seldom approach humans.

Table 1 is an attempt at synthesis of the presumed levels of risk. The recommendations put forward are based on hypothetical levels.
Table 1
Available data on the receptivity and/or susceptibility of animal species to MPXV, presumed infection risk for certain species present in France and measures to recommend to prevent infection, be it theoretical, by a human case (according to [10], 2022).

| Order or Family | Data on their receptivity and/or susceptibility | Potential role as host? | Interactions with humans | Theoretical risk in France of contamination of animals by infected humans | Measures to recommend by the precautionary principle to prevent infection of animals in a human case is confirmed in France par |
|-----------------|-----------------------------------------------|-------------------------|--------------------------|------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Sciuridae       | African squirrels: One clinical MPXV+ case. At least very receptive (Ab+ prevalence in infected area) i.e. Laboratory*: susceptible to very susceptible Prairie dogs (USA) susceptible to very susceptible; (outbreak in the USA, 2003) i.e. Laboratory": very susceptible | Potential reservoir hosts | Rare (hunting and bush meat) | Exceptional and not with live animals (contact with/eating bush meat ) | N.A.                                                                                                                                |
|                 | Red squirrel: No field data. Laboratory*: very susceptible at high dose | N.A.                  | ++ (NP, essentially in the USA) | Exceptional (holding permit necessary) | N.A.                                                                                                                                |
|                 | Gray squirrel: No data | Non-African hosts with reservoir potential? | Almost nil (wild species) | Absent to exceptional | NP: no contact with the human patient and his environment for 21 days after symptom onset (left in cage in a dedicated room): paraenter Prohibit their possession Presumably none, because red squirrels avoid humans |
| Soricidae       | Wild African animals: Gambian pouched rat, African dormouse, jerboa, common rufous-nosed rat, African hedgehog, porcupine: MPXV+ and/or DNA and/or Ab. i.e. Laboratory*: | Potential reservoir hosts | Possible (hunting and bush meat) | Exceptional and not with live animals (contact with/eating bush meat) | Presumably none, because there are grey squirrels are not supposed to be present in France. Paraenter if they appear: don’t approach them, don’t feed them |
| Other small or medium-sized mammals, including rodents | | | | | |
| Order or Family | Data on their receptivity and/or susceptibility | Potential role as host? | Interactions with humans | Theoretical risk in France of contamination of animals by infected humans | Measures to recommend by the precautionary principle to prevent infection of animals in a human case is confirmed in France par |
|----------------|-----------------------------------------------|-------------------------|--------------------------|---------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Wild American mammals: common opossum, gray opossum, American woodchuck i.e. Laboratory*: thirteen-lined ground squirrel: very susceptible Rodents and lagomorpha present in Europe: no field data, i.e. Laboratory*: 1/ Rat, mice and rabbit: -Neonates: very susceptible. -Adults: not susceptible (except for rabbits, especially albino rabbits, and Asian house mice) 2/ Hamster and guinea pigs: not susceptible (neonates not tested) | Non-African hosts with reservoir potential? | N.A. | N.A. | Almost nil and only in America | NP: very important (direct and indirect) NP: potentially present NP: no contact with the human patient and his environment for 21 days after symptom onset (left in cage in a dedicated room) Draconian rat control program (rat-extermination, food resource reduction...) Rodent control program N.A. |
| African and Asian NHP: primary forests, zoos, experimental units: naturally susceptible to very susceptible i.e. Laboratory*: susceptible to very susceptible | Accidental hosts | Possible (hunting and bush meat) | Wild: absent or indirect | Wild: nil to practically nil and only indirect Limited by the fact that people shedding the virus are supposed to be on sick leave |
| Cat: no Abs in an infected African area, but only one study (67 cats) Dog and ferret: no data | No role? Accidental host? Potential spillover host? | Important (direct and indirect) | Very important (direct and indirect) | Nil to highly limited except if the cat is receptive and susceptible Probably: very limited to nil, except if dogs and/or ferrets are receptive and/or susceptible |
| Sheep and goats: no Ab in infected African area, but only one study (200 animals) Bovines: no data | No role? Accidental hosts? | Important (direct and indirect) | Important | Probably minimal to nil Isolation of the breeder if infected |

Ab: antibodies; +: positive; -: no data; N.A: not applicable; NP: new pets; NHP = non-human primates

* Routes compatible with natural infection
of risk, and more generally on the precautionary principle, which should prevail when reasonable doubts appear. In any event, the best way to anticipate even a theoretical risk of transmission to animals would be to dry up this outbreak of human cases, by isolating them and vaccinating human contacts.

**Author’s contribution**

Nadia Haddad is the only author.

**Disclosure of interest**

The author declares that he has no competing interest.

**References**

[1] Nolen LD, Osadebe L, Katomba J, Likofata J, Mukadi D, et al. Extended human-to-human transmission during a monkeypox outbreak in the Democratic Republic of the Congo. Emerg Infect Dis 2016;22:1014–21.

[2] Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, et al. The changing epidemiology of human monkeypox: A potential threat? A systematic review. PLoS Negl Trop Dis 2022;16:e0010141, http://dx.doi.org/10.1371/journal.pntd.0001014.

[3] Khodakevich LS, Szczeniowski M, Nambu-ma-Disu, Jezek Z, Marennikova S, et al. Monkeypox virus in relation to the ecological features surrounding human settlements in Bumba zone, Zaire. Trop Geogr Med 1987;39:56–63.

[4] Tine MS, Harrigan RJ, Thomassen HA, Smith TB. Ghosts of infections past: using archival samples to understand a century of monkeypox virus prevalence among host communities across space and time. R Soc Open Sci 2018;5:171089, http://dx.doi.org/10.1098/rsos.171089.

[5] Arita I, Henderson DA. Smallpox and monkeypox in non-human primates. Bull World Health Organ 1968;39:277–83.

[6] Reed KD, Melki JW, Graham MB, Regnery RL, Sotir MJ, et al. The detection of monkeypox in humans in the Western Hemisphere. N Engl J Med 2004;350:342–50.

[7] Mauldin MR, McCollum AM, Nakazawa YJ, Mandra A, Whitehouse ER, et al. Exportation of monkeypox virus from the african continent. J Infect Dis 2022;225:1367–76, http://dx.doi.org/10.3406/jid.2022.70989.

[8] Nakazawa Y, Lash RR, Carroll DS, Damon JK, Kareem KL, et al. Mapping monkeypox transmission risk through time and space in the Congo Basin. PLoS One 2013;8:e74816, http://dx.doi.org/10.1371/journal.pone.0074816.

[9] Nguyen PY, Ajisegiri WS, Costantino V, Chughtai AA, Macintyre CR. Reemergence of human monkeypox and declining population immunity in the context of urbanization, Nigeria, 2017-2020. Emerg Infect Dis 2021;27:1007–14, http://dx.doi.org/10.3201/eid2704.203569.

[10] Haddad N. Les animaux hors d’Afrique peuvent-ils être concernés par la flambée de monkeypox en cours, voire en devenir des acteurs importants ? Bull Acad Vét. France, https://academie-veterinaire-defrance.org/publications/bulletins-de-lavf. doi.org/10.3406/bavf.2022.70989.

[11] Parker S, Buller RM. A review of experimental and natural infections of animals with monkeypox virus between 1958 and 2012. Future Virol 2013;8:129–57, http://dx.doi.org/10.2217/fvl.12.130.