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The zoonotic potential of mink farming

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Abstract: Minks can be infected and serve as a source of several zoonotic diseases, among which the recently gaining popularity SARS-CoV-2 and Highly Pathogenic Avian Influenza (HPAI). However, many others can be potentially dangerous to humans and other animals but have been neglected as rare. Nowadays mink farming has been widen its influence beyond the bars of cages and has become both an economical, ecological and ethical question. Economy lies in the heavy losses of many countries with developed mink industry during the COVID crisis and the need for welfare improvement in the sector. Ecology calls for attention on the invasive nature of the species and the effect of feral populations on native fauna. It is also ethical to ask do we really need to breed minks for their fur especially under conditions that do not answer their behavioral needs, definitely unsanitary and cruel, as well as being the cause of unprecedented exchange of pathogens between humans and a naturally solitary creature? This article is dedicated to the zoonotic potential of minks as a part of a wider problem that can shake the One Health concept.

Keywords: mink; zoonosis; SARS-CoV-2; avian influenza

INTRODUCTION

Fur farming began in North America in the 19th century and spread to Europe in the early years of the 20th century. In 2018, there were 5 000 fur farms in the European Union, which accounted for 63% of global mink production (International fur trade federation). The American mink (Neovison vison) is currently the most important species in the industry (Fenollar et al., 2021) and the main fur producing countries include Denmark, Finland, the Netherlands, Poland for Europe (Humane Society International) and China (Fenollar et al., 2021) on top of world statistics. European farmers produce around 40 million mink skins per year with value at auction prices of 1.2 billion Euro for 2016 (Hansen, 2017). Poland is the second largest producer of mink pelts in Europe after Denmark, with 354 active Polish mink farms and approximately 6.3 million mink (Rabalski et al., 2022). The annual production of Chinese mink was over 20 million in 2018 (Fenollar et al., 2021).

There is, however, no specific EU legislation providing detailed animal welfare requirements for this species except for the general minimum requirements covered by Council Directive 98/58/ EC (Humane Society International). According to "Code of practice for the care and handling of mink", the standard cage measurements in most Scandinavian countries are 90cm length x 30cm width x 45cm height with a nest box mounted outside. Cage size is similar in other European countries with minimal differences due to local legislation (Finley, 2012). However an article by Díez-León et al. (2017) states that mink cages in Europe must be at least 46 cm tall and argues if this is really necessary. On the other hand a minimum area of 25-30 m² is recommended for the captive breeding and husbandry of the European mink (Mustela lutreola) (Foundation LUTREO-LA, 2006). It is noted that cage size, complexity and stocking density may cause significant behavior changes most often expressed as stereotypies. For example, bite wounds can be estimated as an indicator of aggression and as a means for quantifying the social tolerance between individuals (Hansen et al., 2014).

Mink are highly territorial animals that mark the borders of their territory with secretions from the anal glands (Seremak et al., 2023). Under natural conditions they live close to streams and rivers with a range of about 2 km along the bank and a few hundred meters either side of it; when the water is frozen and when food is not plentiful they may range over greater distances (European Council, 1999). Observations show that distance varies between sexes with males wandering up to 5.8 km form the water source and females to 4.1 km (Haan and Halbrook, 2015). Adult mink are solitary, coming together briefly only at mating time (European Council, 1999). Male mink migrate to female territories during the breeding season, however, in farm rearing, the females are transferred to the male territory, i.e., the cage (Seremak et al., 2023). Of course, the territorial needs of the animals cannot be covered in the farm environment, within the limited space allowance of the cage. The high population size is not only a predisposing factor for behavioral deviation, but also for sanitary and health issues.

Another side of the problem is the escape and settling of farmed mink into the wild. The species is native to North America, but have expanded through Eurasia and South America with devastating effects on native fauna (Fraser et al., 2018). It has been reported in the wild in 24 EU Member States, while sustainable populations have been established in 19 of them (Ministerie van Landbouw, Natuur en Voedselkwaliteit, 2022). For example, in Spain the first feral animals were detected in the 1970s, and at present, there are stable populations distributed throughout the northwest and east of the Iberian Peninsula (Azami-Conesa et al., 2021).

According to biodiversity experts, there is a serious risk for mink raised on farms to quickly spread and reproduce in the wild, which will result in replacement and/or possible destruction of local species (Ministerie van Landbouw, Natuur en Voedselkwaliteit, 2022). Studies show that mink can have a significant negative impact on ground-nesting birds, rodents, amphibians and mustelids (Bonesi and Palazo, 2007). The effect is already visible in the populations of small and medium sized sea birds, while the influence in prey species is being indirect (Norwegian Directorate for Nature Mangement, 2011). The presence of *Neovison vison* on the banks of rivers leads to strong competition for resources with other aquatic carnivores, such as the European otter (*Lutra lutra*), or the endangered European mink (*Mustela lutreola*) (Azami-Conesa et al., 2021) due to population reduction from habitat degradation (Giner et al., 2022).

In 2013, the American mink farming was resumed in Bulgaria, and in 2019, there were four livestock farms with a total capacity of about 130,000 minks. During 2017-2019 a study in the area of the largest farm near the village of Madzherito (Stara Zagora District) (with a capacity of about 128,500) showed 54 records of a total of 108 escaped minks, of which 27 minks were found in the wild (Koshev, 2019). In 2022 the Ministry of Environment and Water prohibited the import and breeding of minks on the territory of Bulgaria for biosafety reasons (Ministry of Environment and Water, 2022). According to Koshev (2019), the reopening of mink farms on the territory of the country will lead to an increase in the number of escaped minks and will potentiate the establishment of a wildlife mink population.

Invasive species are now recognized as one of the major drivers of biodiversity change across the globe with serious environmental, economic, and human health impact (Keller et al., 2011). American mink is included in the invasive list for Europe and is subjected to control and eradication programs (Azami-Conesa et al., 2021).

Much has been written about the problems in mink farming; however, the question about the dangers to human and animal health has only recently been recognized (Peacock and Barclay, 2023). American mink in the wild can serve as a reservoir of zoonotic diseases (Azami-Conesa et al., 2021) that are difficult to predict or control. Epidemiological studies in mink farms are complicated enough to add the possibility of free roaming populations and their unexpected effect on other species. They can potentially become reservoirs of zoonotic pathogens and cause their spread during colonization, increasing the risk of zoonoses transmission to both wild hosts and humans (Kołodziej-Sobocińska et al., 2020).

MATERIALS AND METHODS

Structured database research was carried out in PubMed and Google Scholar to identify relevant articles that correspond to the set keywords (for example: mink, zoonosis, SARS-CoV-2, avian influenza). Only evidence-based and wellstructured studies were selected. Official documents of European and world public organizations were also included.

RESULTS AND DISCUSSION

Minks as reservoirs of zoonoses

Animal facilities constitute one of the most recent scenarios of the human-animal relationship (Martino and Stanchi, FAO). High-density environment allows for the rapid spread of infectious agents, especially viruses that can adapt to animals and sometimes to achieve pandemic potential (Peacock and Barclay, 2023).

A document published by FAO describes a long list of zoonotic diseases that can be transferred by mink. These include many viral conditions - spongiform encephalopathy (prion), rabies (rhabdovirus), Aleutian disease or viral plasmacytosis (parvovirus), rotaviruses. Among bacterial diseases several should be mentioned, like tuberculosis, hemorrhagic pneumonia due to *Pseudomonas aeruginosa*, ulcerative colitis due to *Campylobacter sp.*, tularemia, brucellosis, listeriosis, leptospirosis, staphylococcal dermatitis, etc. Potential parasitic invasion can be caused by *Toxocara canis, Echinococcus multilocularis, Ancyclostoma canium* and *Uncinaria stenocephala, Cheyletiella sp.* (Martino and Stanchi, FAO).

Transmissible mink encephalopathy (TME) is a progressive and fatal neurodegenerative disease, that seems to result from feeding contami-

nated food (Center for food security and public health, 2016). Recent evidence suggests these prions might be an atypical variant of the bovine spongiform encephalopathy agent and the two may be linked in some outbreaks in mink farms (Cassmann et al., 2020). Successful transmission of transmissible mink encephalopathy to cattle supports the bovine hypothesis of origin; furthermore, human and primate susceptibility to classical bovine spongiform encephalopathy (c-BSE) and the transmissibility of L-type BSE to macaques indicate a low cattle-to-primate species barrier and eventually the ability of the cattle-adapted agent to be transmitted (Comoy et al., 2013).

Rabies outbreaks have been confirmed due to vaccine viruses and consumption of viscera from affected animals (Bosgiraud and Nicolas, 1985).

Aleutian disease in adult mink presents as hypergammaglobulinemia, plasmacytosis, mesangial proliferative glomerulonephritis and severe interstitial nephritis, while in newborn mink it causes a fatal, acute interstitial pneumonitis (Bloom et al., 1994). Reports of a possible relationship to human infection are rare. However, two mink farmers with vascular disease and microangiopathy were found to have Aleutian mink disease virus (AMDV) specific antibodies and AMDV DNA (Jepsen et al., 2009). Furthermore, the same agent may be the cause for the serious decline in the populations of native European mink (Mustela lutreola) due to the introduction of the exotic American mink (Mustela vison) (Mañas et al., 2001). Data from France (Fournier-Chambrillon et al., 2004) and Spain (Sánchez-Migallón Guzmán et al., 2008; Mañas et al., 2016) confirmed seroprevalence in the European species; therefore, measures to avoid introduction or spread of the infection to native animals should be urgently overtaken (Fournier-Chambrillon et al., 2004).

Rotaviruses are able to cause severe enteric syndrome in both minks and humans; common serotypes are characterized by a fecal-oral route of transmission (Acha and Szifres, 1986).

There are several reports about tuberculosis in Mustelides (Hejlícek et al., 1973; Turkebaevaet al., 1975; Schaudien et al., 2013). The species can also suffer from ulcerative colitis caused by *Campylobacter jejuni* and *Campylobacter coli* (Hunter et al., 1986).

Hemorrhagic pneumonia due to *Pseudomonas aeruginosa* can be a major cause of diseases in mink farms during the fall with mortality rates reaching up to 75% (Salomonsen et al., 2013a; Salomonsen et al., 2013b). Animals are usually found dead with few prodromal signs; however, there is severe hemorrhagic pneumonia and consolidation of one or more lobes (Turner, 2022). Another causative agent of the same condition can be *E. coli* (Turner, 2022; Salomonsen et al., 2013a)

Potentially dangerous bacterial diseases in mink also include tularemia (Center for food security and public health, 2017; Henson at al., 1978), brucellosis (Jamil at al., 2022; Lupanov, 1970), and listeriosis (Bogachev, 1968).

A research from Chile warns for the possible reservoir potential of mink as a host of *Leptospira sp.*, *Cryptosporidium sp.* and several parasitic species, while underlining the need of a thorough research (Ramírez-Pizarro et al., 2019). According to a study from the same country the infection with Leptospira can be associated to cattlefarming or the consumption of rodents (Alfaro et al., 2020). Neovison vison may act as important environmental contaminators with Leptospira, as they inhabit aquatic areas and predate on rodents (Barros et al., 2014).

Talking about bacterial diseases, it is worth noting that indiscriminate use of antimicrobial agents on mink farms in North America and in the EU has resulted in moderately high antimicrobial resistance (Turner, 2022).

American mink can also act as a carrier of protozoans such as *Toxoplasma gondii* (Azami-Conesa et al., 2021).

Leishmaniasis is a zoonotic disease caused by a protozoan parasite. *Leishmania infantum* is the most frequently reported species in the Mediterranean basin, causing a life threatening disease in humans and animals (Azami-Conesa et al., 2023). The disease has several forms, with the cutaneous (CL) and visceral (VL) forms being the most common. More than one billion people are

at risk of leishmaniasis in endemic areas around the world, and 30,000 new cases of VL are estimated every year (Azami-Conesa et al., 2021). To assess the exposure to Leishmania sp. infection in mink species in northern Spain, blood samples from 139 feral American mink and 42 native European mink from north Spain were evaluated for Leishmania sp. Infection, using enzyme-linked immunosorbent assays against Leishmania spp. antibodies, with 52.4% of American mink and 45.3% of European mink being found seropositive (Giner et al., 2022). According to another study the majority of analyzed animals (90.1%) were positive for Leishmania; authors underlined the fact that American mink may act as an incidental host of the disease for other mammals and should be further investigated (Azami-Conesa et al., 2021). A research from Greece revealed 20% Leishmania seroprevalence in minks (Tsakmakidis et al., 2019).

Free-living American mink are exposed to parasites and likely to be involved in the maintenance of both *Echinococcus spp.* and *Toxocara spp.* in the wild as paratenic hosts (Kołodziej-Sobocińska et al., 2020).

Minks and SARS-CoV-2

Mink pose a serious risk for the emergence of future disease outbreaks and the evolution of future pandemics; they can serve as an intermediate species in which dangerous adaptations toward human infection can evolve (Peacock and Barclay, 2023). The first mink SARS-CoV-2 report came from the Netherlands in April 2020; subsequently a mink farm worker was infected, and finally the possibility of a human-to-mink and mink-to-human transmission was established (European Centre for Disease Prevention and Control, 2020).

Countries that have reported SARS-CoV-2 infection in farmed minks include USA, the Netherlands, Sweden, Italy, Denmark, France, Canada, Greece, Lithuania, and Spain (Sharun et al., 2021). In October 2023 Bulgaria also confirmed an outbreak of SARS-CoV-2 on a mink farm in the village of Madzherito near Stara Zagora. Contagion in mink farms is facilitated by the close proximity of animals and their low genetic diversity. Such facilities can serve as a reservoir where the virus is able to mutate. Mink often remain asymptomatic, but can transmit the SARS-CoV-2 to humans or animals living near farms (Fenollar et al., 2021). Disease in mink can develop with respiratory or gastrointestinal signs (rarely); however, in most instances the only indication of virus circulation is the slight increase in mortality levels (FAO, WOAH, WHO. 2021). Acute interstitial pneumonia was the most characteristic postmortem finding reported (Sharun et al., 2021).

Human infection with variant mink viruses with spike mutations led to the culling in Denmark of all mink in the country (Fenollar et al., 2021). Data from Denmark and the Netherlands concerning SARS-CoV-2 variants related to mink indicates that these variants are able to circulate rapidly in mink farms and the human communities close to the farms; however, they do not appear to be more transmissible than other circulating SARS-CoV-2 variants (European Centre for Disease Prevention and Control, 2020).

Human and mink viral strain genome sequences, although slightly different by a few mutations, are able to cluster together (Fenollar et al., 2021). Nevertheless, the probability of infection with mink-related variant strains is assessed as low for the general population, moderate for populations in areas with a high concentration of mink farms and very high for individuals with occupational exposure; patients infected with minkrelated variants do not appear to develop more severe clinical symptoms than those infected with non-mink-related variants (European Centre for Disease Prevention and Control, 2020).

The spread of SARS-CoV-2 in mink farms impacts animal welfare and poses a risk of spillover to native wildlife which may affect the biodiversity of species (FAO, WOAH, WHO. 2021). Monitoring and surveillance of mink farms should be undertaken for as long as SARS-CoV-2 exposure from humans to mink cannot be excluded; isolated SARS-CoV-2 strains should be genotyped and genome sequences shared in order to assist the rapid identification of possible clusters and related variants (European Centre for Disease Prevention and Control, 2020).

The risk of introduction and spread of SARS-CoV-2, within fur farms has been accessed as high for Europe, due to the highest number of fur farms compared to other regions, the high variety of susceptible animal species and the high numbers of human cases of COVID-19 reported (FAO, WOAH, WHO. 2021). Scientific evidence suggest that a recently isolated, highly divergent lineage of SARS-CoV- 2 found in deer might have infected these animals via farmed mink as an intermediate host (Peacock and Barclay, 2023).

The spread of SARS-Cov2 to mink farms in Europe during the Covid-19 pandemic presents an actual example for the serious consequences that can be expected from viruses that develop the ability to overcome the interspecies barrier. According to Fur Free Alliance COVID-19 outbreaks have affected more than 450 mink fur farms in Europe and North America since April 2020, resulting in the culling of over 20 million animals (Fur Free Alliance, 2022).

The European Centre for Disease Prevention and Control (ECDC) has warned that "the continued transmission of SARS-CoV-2 in mink farms may eventually give rise to other variants of concern" that may compromise the efficacy of vaccines (European Centre for Disease Prevention and Control, 2020).

The high population size of farmed mink populations, as well as their wide geographical distribution, the established transmission pathways and the ability of SARS-CoV-2 to accumulate potentially harmful mutations rapidly, lead to increased risk to global public health. Furthermore, the formation of a permanent reservoir of SARS-CoV-2 in wildlife populations could result to spill-back events of animal-adapted lineages of the virus into the human population and other susceptible animals (Porter et al., 2023).

Minks and Avian influenza

Mustelids are known to be susceptible to influenza viruses (Peacock and Barclay, 2023). Farmed mink are commonly infected with human (H3N2, H1N1/pdm) and avian (H7N9, H5N6, H9N2) influenza A viruses; usually transmission of human influenza viruses occur from humans to mink, while avian influenza is distributed by feed - for example, raw poultry by-products (Sun et al., 2021).

The high mutation rate of influenza viruses allows them to rapidly and frequently adapt to new hosts, including mammals; the zoonotic potential may finally result in an efficient human-tohuman transmission and give rise to a pandemic situation (Peacock et al., 2023).

The official opinion of WHOA (World Organization for Animal Health), published on 13.02.2023, indicates the possibility for viral adaptation of avian influenza type H5N1 to mammals, including humans, and other animal species. Furthermore, some mammals, such as mink can act as reservoirs of infection and a source of new strains and subtypes of high pathogenic activity to animals and/or humans (WHOA, 2023).

Avian influenza viruses circulating in mink have frequently gained typical mammalian adaptations similar to those seen during human infections (Peacock and Barcley, 2023). Mink could be highly permissive "mixing vessels" for the reassortment of circulating human and avian influenza viruses; therefore epidemiological surveillance in farms should be implemented (Sun et al., 2021). Any situation in which an RNA virus is allowed to transmit among multiple densely housed animals, may lead to the evolution of virus with altered phenotypes, including those with enhanced pandemic potential (Peacock and Barcley, 2023).

In October 2022, an outbreak of the infection was confirmed in a Spanish mink farm and the genetic analysis found a mutation that enables the polymerase activity of the virus (H5N1) in mammals (European Food Safety Authority, 2022; Agüero et al., 2023).

In July 2023, an outbreak caused by highly pathogenic avian influenza A(H5N1) virus clade 2.3.4.4b genotype BB was confirmed among farmed animals in South and Central Ostrobothnia, Finland; infections in foxes, American minks and raccoon dogs have been reported on 20 farms (Lindh et al., 2023).

INSTEAD OF CONCLUSION

According to the official page of the European commission there are around 1 000 active fur farms in the European Union for mink, fox and racoon dogs, with approximately 7.7 million animals; however, there is no specific EU animal welfare legislation which covers animals kept for fur production at present (European commission, 2023).

Opinion polls from 2023, indicate that the majority of European citizens oppose to the farming of animals for fur in cages. For example, 91% of Italians disagree with activities linked to the production of fur and 85% of Belgians support a ban on keeping and breeding animals for fur production; 81% of Bulgarian people do not support the killing of animals solely for their fur (Eurogroup for Animals, 2023). The negative attitude towards the fur industry has become even more pronounces after the Covid crisis and the outbreaks in multiple mink facilities. According to Peacock and Barclay (2023) "mink farming poses risks for future viral pandemics". Jahid et al. (2024) conclude that the species presents a highly susceptible host harboring SARS-CoV-2 with or without clinical manifestations, furthering infection transmission as a hidden animal reservoir. The Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (WOAH) and the World Health Organization (WHO) have even published a common statement concerning SARS-CoV-2 in animals used for fur farming. However, it is not only COVID, nevertheless the wide media coverage. But it is not only COVID. It is also Avian influenza and a number of other infectious diseases that have been the topic of this article. A One Health approach is certainly needed to prevent the outbreak and spread of potentially dangerous agents both for animals and humans. Attention should be paid on surveillance and monitoring and all suspicious cases should be promptly investigated. Meanwhile, it is the duty of specialists to collect and analyze data in order to get advantage out of mistakes and not repeat them in the future. The question about the zoonotic potential of mink farming is still open and will remain a matter for discussion in the future.

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