Omicron variants

On November 11, 2021, Botswana discovered the Omicron variant (B.1.1.529) [1], and on November 24, The SARS-CoV-2 Omicron variant was notified to the World Health Organization (WHO) by South Africa. It was evident that the Omicron variant has existed in various countries around the world. The first genome sequence (EPI_ISL_6590782) of Omicron was released in GISAID on November 22, 2021 [2]. Patient zero, also known as the index case, arrived at Hong Kong International Airport on November 11th after flying in from South Africa through Doha, Qatar. The SARS-CoV-2 Omicron variant was classified as a new variant of concern (VOC) by WHO on November 26. Omicron possesses 50 mutations accumulated throughout the genome, and 26–32 mutations in the spike protein [3]. These (32) mutations were nonsynonymous, and this proportion was twice that of the Delta variant in the same region, suggesting a positive selection of this gene [2]. Among them, 15 mutations are located in the receptor-binding domain (RBD) [3, 4].

Strikingly, the Omicron variant can cause reinfection three times more than previous variants is attributed to the numerous mutations in the spike [10, 11]. The virus must adapt and evolve to survive, which is consistent with what was said by Heraclitus, a Greek philosopher “Change is the only constant in life” [12]. The Omicron variant differentiates itself from other variants by having 50 mutations in...
its genomic sequence, compared to the Delta variant’s 13 mutations (B.1.617.2) [5, 110], and through sharing multiple mutations with the preceding VOC Alpha, Beta, and Gamma variants. Notably, Q493R and Q498R mutations exist in Omicron, are uncommon in pre-Omicron mutations, implying that Omicron may have originated in mice, as their development in laboratories might also occur in nature [13].

Many studies have suggested that the wild-type of SARS-CoV-2 most probably came from a bat host [14–16]. Pangolins were initially assumed to be the origins of human infection, but other animal species could have infected them [17]. In the Spike protein and RBD region, the amino acid sequence divergence between the Omicron variant and Wuhan-Hu-1 (the early SARS-CoV-2 sequence) was similar to that between SARS-like coronavirus (Pangolin MP789, Bat BANAL-20-52, and Bat RaTG13) and Wuhan-Hu-1 [14, 18–20]. The majority of the mutations were found on the trimeric Spike protein’s surface, particularly in the RBD region. K417N, G446S, E484A, Q493R, G496S, Q498R, N501Y, and Y505H were all assumed to be critical for viral binding to the angiotensin-converting enzyme 2 (ACE2) host receptor [21]. Both K417N and N501Y mutations in the Beta variant have been reported to alter human ACE2 binding [22]. While N501Y increases the viral Spike protein’s affinity for ACE2 [23]. It’s yet unclear how other mutations affect humans’ and other animals’ affinity for ACE2.

Several nations have reported SARS-CoV-2 infections in animals since the COVID-19 pandemic. Besides free-ranging wild animals, human-to-animal transmission has been reported in pets, farmed animals, and zoo animals [24–32]. Surprisingly, there has been evidence of animal-to-human transfer on mink farms. (mink-to-human transmission) [33]. The origins of Omicron’s proximal beginnings have quickly become a source of debate among scientists and public health experts. However, the most widely recognized scenario for Omicron’s proximal origin states that Omicron might have evolved in a persistently infected COVID-19 patient, such as an immunocompromised person, who provided a favorable host environment for long-term intra-host viral adaptation [34–36].

**Omicron variant and mouse origin**

Rodents are the most numerous and diversified mammals, and they are known to host various alpha and beta-coronaviruses [37, 38]. Rats and mice coexist in close quarters with humans, their companion animals, and cattle, sharing living spaces and that’s why presenting numerous opportunities for transmission. The mouse might have played this role with the Omicron variant. Because they live in close proximity to humans, often in large numbers, infectious diseases which impair human health, such as plague, leptospirosis, and Lassa fever, are transmitted by rodents. Omicron has N501Y, a convergent change found in several SARS-CoV-2 lineages, as well as changes to basic amino acids at residues 493 and 498, as seen frequently in mouse-adapted strains, implying its ability to reproduce in mice [39]. Montagutelli et al. found that mice resistant to the SARS-CoV-2-wild type were tolerant of viral replication of the Alpha, Beta, and Gamma VOCs [40]. They also showed that Beta may passed from mouse to mouse through direct contact [40]. The genetic mutations in Omicron are numerous enough that they could have been obtained by circulation in an animal reservoir, which is a credible alternative explanation for the Omicron emergence process. Importantly, widespread circulation of an emerging virus in a new host results in the accumulation of amino acid changes, some of which signal adaptation to this new environment and could lead to the generation of variants with unanticipated human infection characteristics [39].

Sun et al. [41] used a phylogenetic tree comprising all known VOCs and variants of interest (VOIs) to identify evolutionary links by analyzing the mutational profiles of numerous variants, encompassing the per-site mutation rate. The Omicron variant was discovered to have a distinct mutation profile when compared to other SARS-CoV-2 variants, comprising changes that are unusual in clinical data. Strikingly, the Omicron variant was not found on any intermediate evolutionary branch, revealing that it may have developed in a non-human host. In addition, Omicron may have evolved in a mouse host, as evidenced by the presence of five mouse-adapted mutation sites. Wei et al. [13] have found that the Omicron spike protein sequence has greater positive selection than in any other SARS-CoV-2 variant known to evolve persistently in human hosts, implying that host jumping is possible. They investigated whether the reported mutations acquired by Omicron prior to its outbreak were compatible with the cellular environment of human hosts. Significant differences were found in the molecular spectrum of Omicron and a relatively comprehensive set of molecular spectra from variants known to have evolved in humans, including those of three isolates from chronic COVID-19 patients. Thereafter, Wei et al. [13] compared the molecular spectra of mutations derived from various host animals to that of Omicron. Using molecular docking-based analyses, they have concluded that molecular spectrum of mutations acquired by Omicron’s progenitor was noticeably different from that of viruses evolving in human patients, but it was similar to virus evolution in a mouse cellular environment. Furthermore, Omicron spike protein mutations were shown to overlap significantly with SARS-CoV-2 variants that improve adaptation to mouse hosts, specifically through increased spike protein binding.
affinity for the mouse cell entry receptor. Humans are the largest known reservoir of SARS-CoV-2 because they come in contact with other animals on a regular basis for various purposes. Given SARS-CoV-2 capacity to leap between species, it’s conceivable that more animal-derived variants (such as the SARS-CoV-2 Y453F mink variant) will be exposed to global populations [42] until the pandemic is well-controlled. Due to selective pressure and continued virus replication in the human population, variants of SARS-CoV-2 will continue to arise as the virus spreads over the world [43]. Collectively, Wei et al. [13] have suggested that the progenitor of Omicron migrated from humans to mice most likely in mid-2020, rapidly accumulated mutations for more than a year in a mouse host before leaping back to humans in late-2021, mostly in mid-October 2021 [2], demonstrating that the Omicron pandemic followed an interspecies evolutionary path (Fig. 1). Therefore, the Omicron variant is unlikely to have evolved through mutation or recombination from recently discovered variants [2]. Numerous differences show that the Omicron lineage was split from other lineages a long time ago and has never been sequenced since [2]. The closest sequences to the Omicron lineage in public databases are from lineage B.1.1 and were gathered between March and June 2020 [2].

Animals: the upstream sources and downstream receptacles for SARS-CoV-2

Although most of the scientific community argues that infection of immunocompromised people with SARS-CoV-2, which enables the virus to mutate under the shadow of impaired immunity, is the key factor underlying the emergence of VOC, as was originally presented as a theory to explain how the Alpha variant came to be [44, 45]. All efforts may go unheeded and leave us in imminent danger and worrying scenarios if it turns out that animals have played a role in the emergence of VOC (Fig. 2). Canine coronavirus-human pneumonia-2018 (CCoV-HuPn-2018) is a novel canine-feline recombinant alphacoronavirus that was recently identified. It was first identified in a human patient with pneumonia in Sarawak, Malaysia. [46]. It could be the eighth coronavirus to cause sickness in people, following SARS-CoV-2 [46, 47]. Despite the fact that influenza A (H7N2), an avian-lineage influenza A virus, has a limited human-to-human transmission rate [48]. Lee et al. [49] reported the first instance of H7N2 cat-to-human transmission during an outbreak among cats in New York City animal shelters. Although this risk is modest, its existence and the possibility of recurrence represent a health risk [50].
SARS-CoV-2 variants of concerns in animals: An unmonitored rising health threat

Variant featured mutations that were similar to human AY.3 genomic sequences, while certain mutations were unique to the cat. Additionally, it possesses a difference of 4 to 14 single nucleotide polymorphisms (SNPs) than to humans with the AY.3 sequence. Another cat in Virginia had been infected with the AY.3 Delta variant. Doerksen et al. [62] have discovered and sequenced a Delta variant (AY.3) in a 12-year-old Collie who lived with owners who had tested positive for SARS-CoV-2 before. In a study of 26 canine and feline patients with suspected myocarditis at a veterinary referral center in the United Kingdom, two cats and one dog were diagnosed to be positive for SARS-CoV-2 by RT-PCR, sequencing the Alpha (B.1.1.7 lineage) [63, 64].

In Spain, SARS-CoV-2 Alpha (B.1.1.7) VOC was found in an asymptomatic dog whose owners were SARS-CoV-2 afflicted [65]. The viral loads were high in the nasal and rectal swabs; however, no symptoms were present in the animal. Seroconversion took place 23 days following the initial sample. In Germany, Keller et al. [66] found SARS-CoV-2 Alpha variant in a cat with pneumonia that was brought to a veterinary clinic and its owner had a SARS-CoV-2 infection. Additionally, a human-to-cat transmission of the SARS-CoV-2 Alpha variant (lineage B.1.1.7) in Italy was reported [67]. The lineage B.1.1.7 infections in domestic cats and dogs suggest that the mutations that define this lineage are not restricted to a specific host range [64]. In Latin America, the Iota variant of SARS-CoV-2 caused

The occurrence of this scenario with SARS-CoV-2 in cats is plausible in the light of a recent study in Thailand describing a suspected zoonotic SARS-CoV-2 transmission from a cat to a human [111], putting us in need of a One Health surveillance effort. Studies and cases have reported the susceptibility of client-owned, domestic, and experimental cats [51–53], Zoo’s tiger [54], captive Malayan tigers, and lions [55] to infection by the original wild-type of SARS-CoV-2 coming from humans. The intensity of the COVID outbreak in northern Italy was believed that linked to the high rate of dog ownership in that section of the country [56]. Additionally, the recognized similarities in ACE2 receptor binding sites between humans and several common domestic pets and the limited evidence of SARS-CoV-2 infection in companion dogs and cats necessitates further investigation [57]. Infected domestic cats (Felis domesticus) can easily spread SARS-CoV and SARS-CoV-2 to previously uninfected animals in the same room with illnesses [58]. Because cats are common household pets, there is a risk of disease transmission to humans [59]. One of the VOCs, the SARS-CoV-2 Alpha (B.1.1.7) variant, was identified in a pet dog and cat from the same household in the USA [60]. In Pennsylvania, the USA, researchers have identified the first case of feline COVID-19 infection from the Delta (AY.3) variant through fecal samples [61]. The cat’s infection was linked to contact with a SARS-CoV-2-infected human. The cat’s AY.3 variant featured mutations that were similar to human AY.3 genomic sequences, while certain mutations were unique to the cat. Additionally, it possesses a difference of 4 to 14 single nucleotide polymorphisms (SNPs) than to humans with the AY.3 sequence. Another cat in Virginia had been infected with the AY.3 Delta variant. Doerksen et al., [62] have discovered and sequenced a Delta variant (AY.3) in a 12-year-old Collie who lived with owners who had tested positive for SARS-CoV-2 before. In a study of 26 canine and feline patients with suspected myocarditis at a veterinary referral center in the United Kingdom, two cats and one dog were diagnosed to be positive for SARS-CoV-2 by RT-PCR, sequencing the Alpha (B.1.1.7 lineage) [63, 64]. In Spain, SARS-CoV-2 Alpha (B.1.1.7) VOC was found in an asymptomatic dog whose owners were SARS-CoV-2 afflicted [65]. The viral loads were high in the nasal and rectal swabs; however, no symptoms were present in the animal. Seroconversion took place 23 days following the initial sample. In Germany, Keller et al. [66] found SARS-CoV-2 Alpha variant in a cat with pneumonia that was brought to a veterinary clinic and its owner had a SARS-CoV-2 infection. Additionally, a human-to-cat transmission of the SARS-CoV-2 Alpha variant (lineage B.1.1.7) in Italy was reported [67]. The lineage B.1.1.7 infections in domestic cats and dogs suggest that the mutations that define this lineage are not restricted to a specific host range [64]. In Latin America, the Iota variant of SARS-CoV-2 caused

Fig. 2 Examples of VOCs transmission among humans and other animals
Evidence of transmission of SARS-CoV-2 variants of concerns from humans to close animals like pets and zoo animals was reported. In addition, some animals were shown their ability to transmit SARS-CoV-2 and its variants to humans. Mark (?) refers to that the suspected animals in the transmission of wild-type SARS-CoV-2 and Omicron variant are pangolin and mice, respectively.
the first human-to-dog transmission [68]. In a similar vein, the Delta (B.1.617.2) VOC has been found in a cat residing with a COVID-19 positive owner in Spain [69] and two dogs in USA [70], notwithstanding the human being fully vaccinated against SARS-CoV-2. Bashor et al. [71] found a remarkable quick selection of SARS-CoV-2 variants in cell culture and following infection of non-human mammalian hosts, such as dogs and cats, indicating the danger of human reinfec tion with new virus variants developing in species that come into direct contact with humans. These results demonstrate how spillover from animal hosts living in COVID-19-infected households could speed the development of novel viral lineages. It could be a similar scenario with the emergence of the Omicron variant.

The higher susceptibility of certain free-living wild animals suggests the likelihood of spillover and establishment of SARS-CoV-2 viral reservoirs in the wild [72]. In addition to the possibility of human-to-animal transmission, interspecies transmission of SARS-CoV-2, such as mink-to-cat transmission and recently efficient deer-to-deer transmission [73], has been recorded, greatly raising the likelihood of onward spread [74]. It was shown that Asian lions (Panthera leo persica) were naturally infected with the Delta (B.1.617.2 lineage) VOC [26, 75]. At a Virginia Zoo (Norfolk, VA, USA), three Malayan tigers had shown respiratory symptoms and were reported to be infected with SARS-CoV-2 Alpha (B.1.1.7) variant [76]. Adult white-tailed deer (Odocoileus virginianus) in the United States have been found to be more susceptible to SARS-CoV-2 infection, as well as the alpha (B.1.1.7) VOC, as recorded in Illinois, Michigan, Pennsylvania, New York, and Texas [31, 77]. Additionally, they can transfer the virus vertically from the doe to the fetus and through direct contact [78]. North American deer mice (Peromyscus maniculatus) are vulnerable to SARS-CoV-2 infection when exposed to a human isolate, with little or no disease signs. Not only that, SARS-CoV-2 can be transmitted from deer mice to naive deer mice via direct contact. The potential for reverse zoonosis of SARS-CoV-2 among deer mice and humans is still unknown [79]. White-tailed deer have been substantially infected with SARS-CoV-2 following many human-to-deer transmission incidents and efficient deer-to-deer transfer. The extensive infection of white-tailed deer indicates that they have established as potential SARS-CoV-2 reservoir hosts, implying that the virus’s ecology, long-term persistence, evolution, and the risk of human spillover are all important factors to consider [80]. A recent study has reported infection of white-tailed deer, numbering 30 million in the United States, with the Omicron variant in New York [81]. Recently, the first evidence of a deer-to-human COVID-19 case in Canada was reported by Pickering et al. [82]. They have identified a highly divergent lineage of SARS-CoV-2 in white-tailed deer coming from 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 [83], indicating the possibility of Omicron or future variants arising from adaptability in other wild animals and being transferred onto humans. Worryingly, researchers in Hong Kong have discovered evidence that pet hamsters can transmit SARS-CoV-2 Delta (AY. 127) variant to humans and have linked the animals to human infections in the city [84]. To date, pet hamsters are considered the second confirmed animal species able to transmit SARS-CoV-2 to humans, following farmed mink [33], which record in Denmark, The Netherlands, and Poland [29, 33, 85, 86]. The ability of pre-existing human antibodies to neutralize the mink variant was found to be diminished in Denmark after SARS-CoV-2 spread from minks to people [87], and the most dramatic scene is that in Denmark and the Netherlands at least 12.5% of all people are infected with dominated mink-derived SARS-CoV-2 variants, caused by human-to-human transmission [88]. In China, raccoon dogs are raised for their fur, as in mink farms in Denmark, the Netherlands, and the USA. Therefore, SARS-CoV-2 could potentially spread from SARS-CoV-2-infected workers to enclosed susceptible raccoon dogs, with eventual dispersion and spillover to humans [89]. Concerns concerning SARS-CoV-2 transmission via the fecal-oral [90, 91], which has been demonstrated in hamsters [92] and can cause respiratory infection but has yet to be proven in humans.

VOCs are linked to higher transmissibility, increased virulence, and poorer efficiency of public health and social policies [93]. SARS-CoV-2 enter the host cell through the angiotensin-converting enzyme 2 (ACE2), which exist across mammals [94, 95]; therefore, can infect cells of multiple mammalian host species [96]. Mutations at Q498R and N501Y in combination increased the binding affinity to ACE2 as reported in the Delta variant [23, 97]. Increased transmissibility may be linked to mutations at H655Y, N679K, and P681H in the S1-S2 furin cleavage site of the Omicron, Alpha, and Delta variants [98]. The cell’s capacity to degrade viral components is thought to be compromised by deletions at L3674-, S3675-, and G3676- (Mutations at ORF1a (NSP6), which may facilitate innate immune evasion [98].

Animals should be under the microscope

SARS-CoV-2 has been confirmed in 31 species by researchers and veterinary diagnostic labs as of February 2022 [99]. Cross-species transmission usually causes the virus to adapt quickly to the new host, and repeated transmissions
can hasten viral evolution and the formation of new variants. As a nutshell, the current genome data cannot be used to reconstruct the Omicron lineage’s evolutionary trajectory [2]. There are some factors related to animals within the SARS-CoV-2 pandemic are among them (a) infection of animals with SARS-CoV-2 simply raises the viral concentration in the environment; additionally, (b) numerous animals that can tolerate infection, could act as a reservoir for the virus, allowing it to persist even when the number of human infections declines. This is especially alarming in suburban areas, where deer are in large numbers and potentially spread the virus to humans. As a result, antibodies act as a mild selective pressure on SARS-CoV-2 to adapt to changing the antibody environment, resulting in a never-ending cat-and-mouse game via adding new mutations. Additionally, COVID-19’s circulation in animal populations can have an impact on their health and may help new viral variants arise as well. The creation of viral reservoirs in wild animals would offer enormous obstacles to infection control in humans, as well as a threat to wildlife welfare and conservation [72].

| Table 1 | FAO, OIE and WHO-suggested measures |
|--------|------------------------------------|
| 1.     | Encourage collaboration between national veterinary services and national wildlife authorities, whose partnership is key to promoting animal health and safeguarding human and environmental health. |
| 2.     | Promote monitoring of wildlife and encourage sampling of wild animals known to be potentially susceptible to SARS-CoV-2. |
| 3.     | Share all genetic sequence data from animal surveillance studies through publicly available databases. |
| 4.     | Report confirmed animal cases of SARS-CoV-2 to the OIE through the World Animal Health Information System (OIE-WAHIS). |
| 5.     | Craft messages about SARS-CoV-2 in animals with care so that inaccurate public perceptions do not negatively impact conservation efforts. No animal found to be infected with SARS-CoV-2 should be abandoned, rejected, or killed without providing justification from a country- or event-specific risk assessment. |
| 6.     | Suspend the sale of captured live wild mammals in food markets as an emergency measure. |

Nowadays, calls for the fourth dose of COVID-19 vaccines are appearing for applying to induce antibodies against the SARS-CoV-2 variants [101]. On the other hand, VOCs have been linked to being a source of increased case rates of breakthrough COVID-19 infections among people who have been vaccinated [102], with reports on a decrease in vaccine efficacy or effectiveness beyond six months [103]. Others have gone so far as to focus boosters on the highest-risk groups and reinstate some degree of non-pharmaceutical interventions (NPIs), to reduce the worst effects of the Omicron variant, which has replaced the Delta variant [104]. The vital step to prevent SARS-CoV-2 from re-emerging in the future is controlling transmission in all susceptible animal species. Contact with animals is of our nature, for many purposes (hunting, livelihood, …) [105], and unpreventable. This pandemic has taught us that human, animal, and environmental health are all intertwined and interdependent. The emergence of VOCs and VOIs capable of aiding SARS-CoV-2 intra- and interspecies dissemination must be limited through animal vaccination [106–108, 112]. Active or passive surveillance frameworks for domestic, captive, and wild animals must be created to limit the spread of SARS-CoV-2 in domestic and wild animal species. As a result, in-depth studies of the interrelationships between animals and people in terms of disease transmission and spread are being conducted, as well as the adoption of appropriate preventative and control techniques using interdisciplinary and holistic approaches is required. Indirectly, WHO attempts to increase vaccine manufacturing regions, like Africa [105], could aid in this regard. SARS-CoV-2 is knocking on most hosts’ doors, and therefore, theoretically and in real, vaccinating humans isn’t the only way in containing this pandemic virus.

Conclusion

In summary, the collected results included in this paper highlight that SARS-CoV-2 Omicron has infected humans as a result of jumping back and forth (back-and-forth transmission), and the danger of re-infection in humans from novel viral strains discovered in animals. The presence of SARS-CoV-2 in the environment could be increased by diseased animal hosts, sustaining the infection and speeding the establishment of novel viral lineages. As a consequence, reducing viral spread and transmissibility between humans and close-contact animals is an urgent exigency. COVID-19 might spread unrestrained among deer, according to scientists. That could lead to COVID-19 variants that scientists aren’t expecting. For forecasting or preventing future pandemics, a greater knowledge of the human-animal molecular and ecological interaction, as well as its importance to
infection transmission patterns, is essential that can only be accomplished by a more proactive and rigorous “One Health” strategy that includes active surveillance and longitudinal investigations to better understand SARS-CoV-2 ecology and evolution in deer and other animal species. Pet owners, pet shops, farmers, animal traders, and veterinarians should comply with the hygienic rules. Continuing to monitor the animal-origin SARS-CoV-2, It’s also crucial to modify preventative and control efforts in the future to avoid large-scale community transmission caused by the virus leaping from animals to humans. The reliance on only developing vaccines with ignoring this strategy could cost us many lives. Here, we advocate the science community to seek viral genomic surveillance and sequencing in animals, especially those in close contact with humans, data sharing globally and reduce viral transmissibility in tandem to reduce its infectiousness, enhancing our capacity to recognize quickly and monitor the source of new variants. SARS-CoV-2 variants of concern in domestic cats should be regularly monitored for a better understanding of how animal and human health are interwoven in this global pandemic. The realistic reinforcements of coordinated surveillance efforts at the human-animal interface and its environment are critical for rodents in both high-density cities and rural regions. One of the strategic solutions is to begin “One Health education” earlier than postgraduate programs and extend beyond medical and veterinary students [109]. Ultimately, effective public health initiatives will require collaboration between the human, veterinary, and environmental health communities, especially as more people come into intimate contact with wild and domestic animals.

Author contribution AAS: Conceptualization, Data Curation, Visualization, Writing - Original Draft, Writing -review & editing, AAM; Writing -review & editing. AAS and AAM have critically reviewed and approved the final version of the manuscript.

Funding There is no funding source used for this paper.

Declarations

Conflict of interest The authors declare that no competing interests.

References

1. Saied AA, Metwally AA, Alobo M, Shah J, Sharun K, Dham A. Bovine-derived antibodies and camelid-derived nanobodies as biotherapeutic weapons against SARS-CoV-2 and its variants: A review article. Int J Surg Eng. 2022;98:106233. https://doi.org/10.1016/j.jsue.2022.106233.

2. Ma W, Yang J, Fu H, Su C, Yu C, Wang Q, et al. Genomic perspectives on the emerging SARS-CoV-2 Omicron variant. Genomics Proteom Bioinf. 2022. https://doi.org/10.1016/j.gpb.2022.01.001. (published online).

3. Tian D, Sun Y, Xu H, Ye Q. The emergence and epidemic characteristics of the highly mutated SARS-CoV-2 Omicron variant. J Med Virol. 2022;94:2376–83. https://doi.org/10.1002/jmv.27643.

4. Pulliam JRC, van Schalkwyk C, Govender N, von Gottberg A, Cohen C, Groome MJ, et al. Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa. Science. 2022;376(6593):eabn4947. https://doi.org/10.1126/science.abn4947.

5. Diseases TLI. Emerging SARS-CoV-2 variants: shooting the messenger. Lancet Infect Dis. 2022;22:1. https://doi.org/10.1016/S1473-3099(21)00770-2.

6. Hastie KM, Li H, Bedinger D, Schendel SL, Dennison SM, Li K, et al. Defining variant-resistant epitopes targeted by SARS-CoV-2 antibodies: A global consortium study. Science. 2021;374(6566):472–8. https://doi.org/10.1126/science.abb2315.

7. Cele S, Jackson L, Khoury DS, Khan K, Moyo-Gwete T, Tegally H, et al. Omicron extensively but incompletely escapes Pfizer BNT162b2 neutralization. Nature. 2022;602(7898):654–6. https://doi.org/10.1038/s41586-021-03824-5.

8. Wilhelm A, Widera M, Grikseikht K, Toptan T, Schenk B, Pallas C, et al. Reduced neutralization of SARS-CoV-2 omicron variant by vaccine sera and monoclonal antibodies. MedRxiv. 2021. https://doi.org/10.1101/2021.12.07.21267432.

9. Cao Y, Wang J, Jian F, Xiao T, Song W, Yismayi A, et al. Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. Nature. 2022;602:657–63. https://doi.org/10.1038/s41586-021-04385-3.

10. Ikemura N, Hoshino A, Higuchi Y, Taminishi S, Inaba T, Matoba S. SARS-CoV-2 Omicron variant escapes neutralization by vaccinated and convalescent sera and therapeutic monoclonal antibodies. Medrxiv. 2021. https://doi.org/10.1101/2021.12.13.21267761.

11. Viana R, Moya S, Amoako DG, Tegally H, Scheepers C, Althaus CL, et al. Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. Nature. 2022;603:679–86. https://doi.org/10.1038/s41586-022-04411-y.

12. Saied AA, Metwally AA, Mohamed HMA, Haridy MAM. The contribution of bovines to human health against viral infections. Environ Sci Pollut Res. 2021;28:46999–7023. https://doi.org/10.1007/s11356-021-14941-z.

13. Wei C, Shan K-J, Wang W, Zhang S, Huan Q, Qian W. Evidence for a mouse origin of the SARS-CoV-2 Omicron variant. J Genet Genomics. 2021;48:1111–21. https://doi.org/10.1016/j.jgg.2021.12.003.

14. Zhou P, Yang X-L, Hu X, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579:270–3. https://doi.org/10.1038/s41586-021-04297-6.

15. Lau SKP, Woo PCY, Li KSM, Huang Y, Tsui H-W, Wong BHL, et al. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. Proc Natl Acad Sci. 2005;102:14040–5.

16. Cui J, Li F, Shi Z-L. Origin and evolution of pathogenic coronaviruses. J Gen Virol. 1995;76:2699–709. https://doi.org/10.1099/0022-1287-76-12-2699.

17. Shi Z-L, Rambaut A, Lipkin W,et al. Severe acute respiratory syndrome coronavirus-like virus in bats. Science. 2003;300:1319–22. https://doi.org/10.1126/science.1084019.

18. Zhou P, Yang X-L, Wan Y, Hu Y, Li L, Zhuo J, et al. Are pangolins the intermediate host of the 2019 novel coronavirus (SARS-CoV-2)? PLoS Pathog. 2020;16:e1008421. https://doi.org/10.1371/journal.ppat.1008421.
SARS-CoV-2 variants of concerns in animals: An unmonitored rising health threat

35. Callaway E. Heavily mutated Omicron variant puts scientists on alert. Nature. 2021;600:201. https://doi.org/10.1038/d41586-021-03552-w.

36. Burki T. The origin of SARS-CoV-2 variants of concern. Lancet Infect Dis. 2022;22:174–5. https://doi.org/10.1016/S1473-3099(22)00015-9.

37. Ge X-Y, Yang W-H, Zhou J-H, Li B, Zhang W, Shi Z-L, et al. Detection of alpha- and betacoronaviruses in rodents from Yunnan, China. Virol. J. 2017;14:1–11. https://doi.org/10.1186/s12985-017-0766-9.

38. Tsoleridis T, Onianwa O, Horncastle E, Dayeman E, Zhu M, Danjijtrong T, et al. Discovery of novel alphacoronaviruses in European rodents and shrews. Viruses. 2016;8:84. https://doi.org/10.3390/v8030084.

39. Montagutelli X, van der Werf S, Rey FA, Simon-Loriere E. SARS-CoV-2 Omicron emergence urges for reinforced One-Health surveillance. EMBO Mol Med. 2022;14:e15558. https://doi.org/10.15252/emmm.202115558.

40. Montagutelli X, Prot M, Levillayer L, Salazar EB, Jouvin G, Conquet L, et al. Variants with the N501Y mutation extend SARS-CoV-2 host range to mice, with contact transmission. BioRxiv. 2021. https://doi.org/10.1101/2021.03.18.436013.

41. Sun Y, Lin W, Dong W, Xu J. Origin and evolutionary analysis of the SARS-CoV-2 Omicron variant. J Biosaf Biosecurity. 2021;4:33–7. https://doi.org/10.1080/01652176.2021.1921311.

42. Bayarri-Olmos R, Rosbjerg A, Johnsen LB, Helgstrand C, Bak-Thomsen T, Garred P, et al. The SARS-CoV-2 Y453F mink variant displays a pronounced increase in ACE-2 affinity but does not challenge antibody neutralization. J Biol Chem. 2021;296:100536. https://doi.org/10.1016/j.jbc.2021.100536.

43. Plante JA, Mitchell BM, Plante KS, Debink K, Weaver SC, Menachery VD. The variant Gambit: COVID’s next move. Cell Host Microbe. 2021;29:508–15. https://doi.org/10.1016/j.chom.2021.02.020.

44. Choi B, Choudhary MC, Regan J, Sparks JA, Padera RF, Qiu X, et al. Persistence and evolution of SARS-CoV-2 in an immunocompromised host. N Engl J Med. 2020;383:2291–3. https://doi.org/10.1056/NEJMc2031364.

45. Kemp SA, Collier DA, Datir RP, Ferreira IATM, Gayed S, Jahan A, et al. SARS-CoV-2 evolution during treatment of chronic infection. Nature. 2021;592:277–82. https://doi.org/10.1038/s41586-021-03291-y.

46. Vlasova AN, Diaz A, Damtie D, Xu L, Toh T-H, Lee JS-Y, et al. Infection and rapid transmission of SARS-CoV-2 in Asian lions of India. Transbound Emerg Dis. 2021;00:1–9.

47. Abdelgadir A, Vlasova AN, Gray GC. Susceptibility of different cell lines to the novel canine coronavirus CCoV-HuPn-2018. Influenza Other Respi Viruses. 2021;15:824–5.

48. Belser JA, Lash RR, Garg S, Tumpey TM, Maines TR. The eyes have it: influenza virus infection beyond the respiratory tract. Lancet Infect Dis. 2018;18:e220–7. https://doi.org/10.1016/S1473-3099(18)30102-6.

49. Lee CT, Slavinski S, Schiff C, Merlino M, Daskalakis D, Liu D, et al. Outbreak of influenza A (H7N2) among cats in an animal shelter with cat-to-human transmission—New York City, 2016. Clin Infect Dis. 2017;65:446–54. https://doi.org/10.1093/cid/cix456.

50. Jain S, Murray EL. The cat’s meow: using novel serological approaches to identify cat-to-Human influenza A (H7N2) transmission. J Infect Dis. 2019;219(11):1685–7. https://doi.org/10.1093/infdis/jiy596.

51. Sailleau C, Dumarest M, Vanhomwegen J, Delaplace M, Caro V, Kwasiborski A, et al. First detection and genome sequencing of SARS-CoV-2 in an infected cat in France. Transbound Emerg Dis. 2020;67:2324–8. https://doi.org/10.1111/bed.13659.

52. Chen H, Shi J, Wen Z, Zhong G, Yang H, Wang C, et al. Susceptibility of ferrets, cats, dogs, and different domestic animals to SARS-CoV-2 variants of concern. BioRxiv. 2021. https://doi.org/10.1101/2021.06.10.242451.
67. Zoccola R, Beltramo C, Magris G, Peletto S, Aucitp P, Bozzetta  
66. Keller M, Gatri P, Gallardo-Romo N, Staddard RA, et al. Transmission of SARS-CoV-2 Delta variant  
63. Ferasin L, Fritz M, Ferasin H, Becquart P, Corbet S, Ar Gouilh  
61. Lenz OC, Marques AD, Kelly BJ, Rodino KG, Cole SD, Perera  
59. Songserm T, Amonsin A, Jam-on R, Meemak N,  
57. Leroy EM, Ar Gouilh M, Brugère-Picoux J. The risk of SARS-CoV-2 transmission to pets and other wild and domestic animals strongly mandates a one-health strategy to control the COVID-19 pandemic. One Heal. 2020;10:100133. https://doi.org/10.1016/j.  
55. Bartlett SL, Diel DG, Wang L, Zec S, Laverack M, Martins M,  
54. Li X. Cats under the shadow of the SARS-CoV-2 pandemic. One Heal. 2021;5:733–44. https://doi.org/10.1638/2020-0171.  
53. Zhang Q, Zhang H, Huang K, Yang Y, Hui X, Gao J, et  
51.10111/j.onehlt.2021.100133.  
50. Gournemenou M, Spandidos DA, Tsatsakis A. Possibility of transmission through dogs being a contributing factor to the extreme Covid–19 outbreak in North Italy. Mol Med Rep. 2020;21:2293– 
4.  
49. LeroY EM, Ar Gouilh M, Brugère-Picoux J. The risk of SARS-CoV-2 transmission to pets and other wild and domestic animals strongly mandates a one-health strategy to control the COVID-19 pandemic. One Heal. 2020;10:100133. https://doi.org/10.1016/j.  
47. An, A. A. Metwally. SARS-CoV-2 neutralization by antibodies in cats: a serological investigation. BioRxiv. 2020. https://doi.  
45. Li X. Cats under the shadow of the SARS-CoV-2 pandemic. Transbound Emerg Dis. 2020;67:1416–7. https://doi.org/10.1111/ tbed.13599.  
43. Martina BEE, Haagmans BL, Kuiken T, Fouchier RAM, Rim  
41. Songserm T, Amonsin A, Jam-on R, Sae-Heng N, Meemak N,  
40. Lenz OC, Marques AD, Kelly BJ, Rodino KG, Cole SD, Perera  
39. Doerksen T, Lu A, Noll L, Almes K, Bai J, Upchurch D, et al. Near-Complete Genome of SARS-CoV-2 Delta (AY 3) Variant Identified in a Dog in Kansas, USA. Viruses. 2021;13:2104. https://doi.org/10.3390/  
37. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
36. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
35. Delahay RJ, de la Fuente J, Smith GC, Sharun K, Snary EL,  
33. LeraY EM, Ar Gouilh M, Brugère-Picoux J. The risk of SARS-CoV-2 transmission to pets and other wild and domestic animals strongly mandates a one-health strategy to control the COVID-19 pandemic. One Heal. 2020;10:100133. https://doi.org/10.1016/j.  
32. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
31. van Aart AE, Velkers FC, Fischer EAJ, Broens EM, Egberink H,  
30. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
29. Depner BM, et al. SARS-CoV-2 infection and longitudinal fecal screening of a Domestic Cat. Viruses. 2022;14:421.  
28. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
27. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
26. Mitchell PK, Martins M, Reilly T, Caserta LC, Anderson RR,  
25. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
24. van Aart AE, Velkers FC, Fischer EAJ, Broens EM, Egberink H,  
23. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
22. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
21. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
20. Mitchell PK, Martins M, Reilly T, Caserta LC, Anderson RR,  
19. Depner BM, et al. SARS-CoV-2 infection and longitudinal fecal screening of a Domestic Cat. Viruses. 2022;14:421.  
18. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
17. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
16. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
15. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
14. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
13. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
12. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
11. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
10. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
9. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
8. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
7. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
6. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
5. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
4. Mishra A, Kumar N, Bhatia S, Asaad A, Kannipan S, Sekhar  
3. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
2. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/  
1. Palermo PM, Orbegozo J, Watts DM, Morrill JC. SARS-CoV-2 neutralizing antibodies published in white-tailed deer. Front Vet Sci. 2022;9:841430. https://doi.org/10.3389/
SARS-CoV-2 variants of concerns in animals: An unmonitored rising health threat

Barnes CO, Jette CA, Abernathy ME, Dam K-MA, Esswein SR, Gristick HB, et al. SARS-CoV-2 neutralizing antibody structures inform therapeutic strategies. Nature. 2020;588:682–7. https://doi.org/10.1038/s41586-020-2852-1

Thakur V, Ratho RK. Omicron (B. 1. 5.29): a new SARS-CoV-2 variant of concern mounting worldwide fear. J Med Virol. 2022;94:1821–4. https://doi.org/10.1002/jmv.27541.

The Conversation. Deer, mink and hyenas have caught COVID-19 – animal virologists explain how to find the coronavirus in animals and why humans need to worry. https://theconversation.com/deer-mink-and-hyenas-have-caught-covid-19-animal-virologists-explain-how-to-find-the-coronavirus-in-animals-and-why-humans-need-to-worry-176666. 2022; accessed 10 June 2022.

WHO. Joint statement on the prioritization of monitoring SARS-CoV-2 infection in wildlife and preventing the formation of animal reservoirs. https://www.who.int/news/item/07-03-2022-joint-statement-on-the-prioritization-of-monitoring-sars-cov-2-infection-in-wildlife-and-preventing-the-formation-of-animal-reservoirs. 2022; accessed 10 June 2022.

Page 475
global outbreak. International Journal of Surgery 105106848-S1743919122006252 106848 https://doi.org/10.1016/j.ijsu.2022.106848.

Publisher’s Note  Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.