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## Correspondence

## SARS, MERS, and COVID-19: What's next?



## ARTICLE INFO

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The three zoonotic coronaviruses (CoVs), namely, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome CoV (MERS-CoV), and Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), have resulted in major outbreaks in the past two decades [1]. We would like to compliment and add our analyses on the instances where we have come very close to the emergence of a novel CoV as the result of cross-species jumping.

The novel CoV that emerged in Wuhan, China, was given the name SARS-CoV-2 (previously, 2019-nCoV) due to the close genetic similarity with SARS-CoV. Whole-genome analysis identified 80.6–81.1% similarity between SARS-CoV-2 and SARS-CoV. However, only 51% similarity was observed with MERS-CoV at the nucleotide level [2]. Preliminary findings indicate bat as the most probable source of SARS-CoV-2 origin just like its predecessor, SARS-CoV, and MERS-CoV [3]. SARS-CoV-2 is suspected to have originated from *Rhinolophus* spp. bats [4]. Compared to the previous zoonotic CoV outbreaks, SARS-CoV-2 has very high transmission potential that is evident from the efficient human-to-human transmission [5]. In addition to that, SARS-CoV-2 has also exhibited cross-species transmission to companion and wild animal species such as dogs, cats, tigers, lions, and minks [6–9].

Our research experience with SARS-CoV and MERS-CoV has fuelled the initial search for SARS-CoV-2-specific vaccines and therapeutics [10, 11]. However, a great part of the efforts was directed at repurposing drugs to facilitate emergency use. Among the evaluated drugs, a few have shown promising results and might be beneficial for reducing the death rate among COVID-19 patients [12,13]. Immunotherapeutic strategies such as convalescent plasma and monoclonal antibodies will bridge the gap until suitable vaccine candidates are identified [26].

Compared to other viruses, CoVs are characterized by a high rate of mutation and recombination, which facilitates host adaptability and cross-species transmission [14]. Cross-species transmission can occur most commonly at the human-animal interface, where there is an increased chance of contact between different animal species and human beings. SARS-CoV-2 is the third zoonotic CoV affecting human

beings after SARS-CoV and MERS-CoV. These betacoronaviruses are believed to have originated from bats, the major reservoir host of CoVs. These CoVs are thought to have ‘spilled over’ from animals (intermediate host) to human beings [6]. During the 2003 SARS outbreak, SARS-CoV was isolated from the wild animals such as Himalayan palm civets (*Paguma larvata*) and raccoon dogs (*Nyctereutes procyonoides*) [15]. Further studies suggested palm civets to be an intermediate host that facilitated interspecies transmission to human beings [16]. Similarly, the dromedary camel played a major role in transmitting MERS-CoV infection to human beings [17].

During the year 2016, a novel HKU2-related bat coronavirus named swine acute diarrhoea syndrome coronavirus (SADS-CoV) emerged in Guangdong province of China, causing large-scale mortality in piglets across several farms [18]. This virus is suspected to have originated from the *Rhinolophus* spp. bats [18,19]. It is also interesting to note that the Guangdong province is approximately 100 km from the location where the index case of SARS was reported in China [18]. SADS-CoV may be considered as a potential risk to human health if it can get directly transmitted from pigs to human beings or through other potential intermediate hosts [20]. In vitro studies have identified broad species tropism as the virus can infect cell lines of species such as bats, rats, mice, gerbils, chickens, hamsters, pigs, non-human primates, and humans [20,21]. The potential destruction caused by SADS-CoV would have been much bigger if this novel virus was successful in adapting to human beings.

Porcine deltacoronavirus (PDCoV) is another example of a novel CoV that could have crossed the species barrier affecting human beings. PDCoV was first detected in United States in the year 2014. It is an enteropathogenic CoV that is currently affecting pigs across the United States and Asia, resulting in substantial economic losses in farming [22]. Sparrows are suspected to be the primary source of PDCoV in pigs due to the high genetic similarity of deltacoronaviruses between these species [23]. The peculiar ecological niche of pigs enables them to be in frequent contact with both human and wild animals at the same time. In addition to that, the lower interspecies hurdles in pigs would make it easy for

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novel CoVs to jump the species barrier, thereby acting as a potential mixing vessel for deltacoronaviruses such as PDCoV [23]. Thus, it is too early to consider deltacoronavirus safe as it still possesses the potential to be transmitted to more mammals, including humans.

Bats have been already linked to the emergence of several viruses, including Nipah virus, Ebola virus, Hendra virus, Marburg virus, Dengue, Influenza A, Equine Encephalitis viruses, Lyssaviruses, SARS-CoV, MERS-CoV, and most recently, SARS-CoV-2 [24,25]. Bats are considered the most important reservoirs for emerging viruses, especially CoVs, that can get subsequently transmitted to human beings via intermediate hosts [18]. Therefore, the striking similarities existing between the SARS-CoV, MERS-CoV, SARS-CoV-2, SADS-CoV, and other novel CoVs highlight the need to identify existing CoVs in the bat population and to study their diversity, distribution, and zoonotic potential to mitigate future outbreaks. This is only possible by facilitating the proactive discovery of viruses in wild animals and establishing targeted disease surveillance at the human-animal interface. We have to improve our understanding of how the CoVs circulate and transmit within the bat population without affecting them clinically.

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Khan Sharun, Division of Surgery, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, Uttar Pradesh, India Email: [sharunkhansk@gmail.com](mailto:sharunkhansk@gmail.com).

### Declaration of competing interest

All authors declare that there exist no commercial or financial relationships that could, in any way, lead to a potential conflict of interest.

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Khan Sharun

*Division of Surgery, ICAR-Indian Veterinary Research Institute, Izatnagar,  
Bareilly, 243 122, Uttar Pradesh, India*

*E-mail addresses: [sharunkhansk@gmail.com](mailto:sharunkhansk@gmail.com), [sharunkhan@ivri.res.in](mailto:sharunkhan@ivri.res.in).*