SARS-CoV-2 & THE INCREDIBLE TALE OF THE DYING MONKEYS

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Where did the SARS-CoV-2 come from? Did it appear suddenly, out of nowhere, fully equipped to infect us? Or is it a virus from a bat or pangolin that suddenly jumped species to infect us? How common is it for a microbe to jump host species? And why would a microbe make such a jump?

The story of the coronavirus causing the COVID-19 pandemic, technically called SARS-CoV-2, is yet to be fully unravelled. While our immediate impetus is to discover ways to treat and prevent the infection using drugs and vaccines, the pandemic has also raised many other questions. Where did this virus come from? Are there other unknown viruses and bacteria lurking somewhere, waiting to infect us? Where are they lurking, and why are they not known to us yet? Why, and how, do new diseases strike human beings? Do all new diseases have the potential to reach pandemic proportions? These questions are, today, of vital interest to everyone — from epidemiologists (who study patterns of disease spread) to the common man.

Did the virus know?

The earliest reports of COVID-19 infections came from China, sometime in late 2019.[1] Did the virus appear suddenly, out of nowhere, fully equipped to infect human beings?

Let us, for a moment, assume this to be true. If so, the virus would need to exist in a form that allowed it to pass the various barriers that the human body offers to infection. This includes hairs in the nasal passage and mucus in the upper respiratory tract, both of which could trap the virus before it reached its most common site of infection — the respiratory epithelium tissue, deep within our lungs.[2] Once it reaches this tissue, the virus would need to recognise and enter a cell with precision. Once inside a cell, the virus would need to reproduce, make copies of itself, and be released from the infected cell. It would also need to be expelled from our lungs in a sneeze or coughing bout, and remain active long enough to infect another host. How did the virus figure out that being suspended in droplets and aerosols was the best way to travel between individuals? How did the virus know, you may ask?

Neither did the virus know, nor was it 'designed' for humans. All that happened was that the virus combined the features it already possessed as an infectious agent in another animal with an opportunity to infect a human being. This happens all the time. We share homes and environments with many domestic and wild animals. These animals often harbour viruses and bacteria that may or may not cause diseases in them. We may not have encountered many of these microbes earlier, but sheer physical proximity increases opportunities for accidental contact with them. It is also very likely that a large number of microbes routinely come in contact with us, but not all of them are able to make the human body a home and cause disease.

Ever since the discovery, in 1907, that the tuberculosis bacterium could be passed from cows to humans through raw milk, we have known that animals can pass on pathogens to us.[3] Since then, many other discoveries have indicated the animal origins of some of the deadliest diseases ever known to us, including plague, AIDS, the 1918 influenza outbreak, and Ebola. All these diseases were initially **zoonoses.** This means that they were, at one time, exclusively diseases of wild or domestic animals that, at some point, started infecting human beings instead (see **Fig. 1**). The rest is history. For example, the plague, an old disease as far as zoonoses go, has killed millions of people in the past 2000 years.[3] But the frequency of new zoonoses has skyrocketed since the 20th century in comparison to any other point in history. To understand some reasons behind this, let us examine the case of a zoonosis closer home – the Kyasanur Forest Disease in the Western Ghats, India.

When does a virus jump species?

A mysterious new illness was first reported, in 1957, from the remote village of Kyasanur from the Shimoga district in Karnataka.[4] Around 500 people fell ill that year with very high fever, splitting headaches, drowsiness, and delirium. Since this was nothing like the diseases known at the time, malaria and typhoid were quickly ruled out. What was causing the disease? How did people acquire it?

In the initial years after the outbreak, studies by various groups of scientists on the area and the people infected with the disease revealed two interesting patterns linking them.[5] One, people with these symptoms had all spent a day in the forest, shortly before they fell sick. Since their symptoms were similar to that of Yellow Fever (a disease in Africa and South America that is transmitted from animals to humans by day-biting mosquitoes in tree canopies), scientists searched tree canopies for day-biting mosquitoes.[6] Not finding any, they had to eliminate the possibility of mosquitoes acting as transmission agents, or **vectors**, of this new disease. Two, often, people who were infected had been in the presence of dead monkeys in the days prior to developing symptoms. Residents of the village reported seeing hundreds of dead monkeys in the neighbouring forests. On investigation, scientists identified ticks on the dead monkeys as potential vectors and, soon after, discovered a new species of virus in the ticks as the cause of the mysterious illness (see **Fig. 2**). The disease came to be known as the Kyasanur Forest Disease (KFD) after the village where it was first discovered.

The science of putting together pieces of puzzles related to disease outbreaks and spread is called epidemiology. Often, some pieces of a jigsaw may be hard to find, but testing hypotheses through careful observation and reasoning can help epidemiologists take steps that lead to the missing pieces. For example, establishing the link between ticks and the dead monkeys helped explain why there were no reports of transmission of

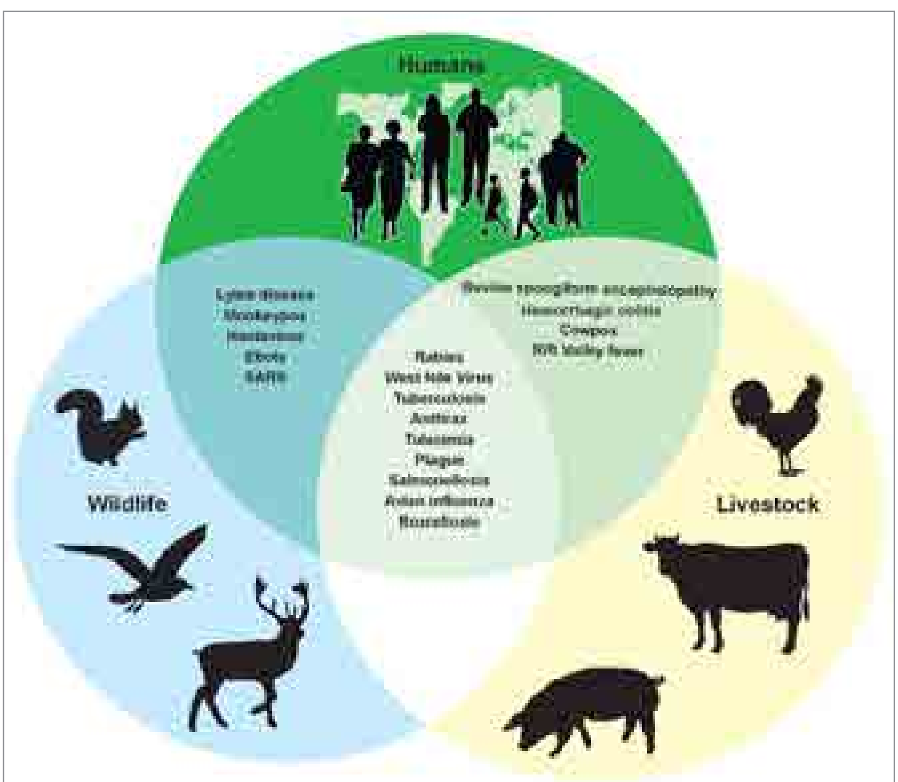

Fig. 1. Human history offers many examples of zoonoses.

Fig. 2. Like mosquitoes, ticks of domestic and wild animals can act as vectors or transmission agents of human pathogens.

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KFD between humans. In most cases, a tick bites a person once, lingers on long enough to get a full blood meal, then drops off without looking for another host (or person) to bite. Since the tick bite transmits the virus to the person it feeds on, this person develops symptoms of the disease. The only way in which the virus would be able to move out of the infected person's body is through their blood. Interestingly, mosquitoes can potentially transmit this virus quite effectively (since they bite many people), but seem not to do so.

So how does the virus reach humans in the first place? Many years of investigation by epidemiologists and virologists has revealed that the KFD virus can live, without causing symptoms of infection, in many wild mammals like Sambar and Bison, and domestic animals like goats and cattle.[5] It jumps species only when a tick that has had an incomplete meal jumps from an animal of one species to another. If the other species happens to be a monkey or human, the virus causes serious illness, even death. These linked patterns of movement of the virus are called **transmission cycles** (see **Fig. 3**). The transmission cycle of any zoonosis involves a primary host, a transmission agent or vector, and a secondary host. For a virus, the primary host is usually a wild or domestic animal or bird. The vector may be an insect, as in the KFD or Yellow Fever; or even just saliva droplets in the air, as in the case of Swine Flu or Bird Flu. Human beings are usually secondary hosts. Understanding the transmission cycle of a zoonosis can be quite challenging. For example, discovering it for the KFD virus took many years of investigation in remote and difficult terrain, limited equipment and intermittent funding, multiple twists, and wrong turns.[5]

When does a zoonosis become a pandemic?

Since there is no evidence that humans had been exposed to the KFD virus before 1957, it seems likely that this disease was caused when people encountered it for the first time. This is similar to what happened with SARS-CoV-2 last year. The KFD virus couldn't be transmitted from one human to another without a tick. By the time a tick that had taken a full blood meal from one human was ready to feed on another host, its chances of encountering another human, in a forest adjoining a remote village, were slim. In contrast, SARS-CoV-2 does not need a vector to move between humans. As we now know, it spreads through droplets and aerosols. This makes it much easier for the virus to be transmitted between people, and enables its rapid travel across the world through interconnected air routes between distant countries. Thus, the pandemic.

Parting thoughts

Zoonoses can be triggered by opportunities that bring humans, domestic animals, and wild animals closer to each other. Over the years, we have seen that the symptoms of KFD in humans are very similar to those caused by zoonotic viruses found in Russia and Saudi Arabia.[4] Similarly, SARS-CoV-2 has many close relatives in various animal hosts, including bats and pangolins. While we are yet to piece together the origins of this virus, the close proximity of these animals to humans is the only plausible reason for SARS-CoV-2 to have 'jumped' hosts.

The suspected source of the pandemic — a crowded market in China that sold wild animals, including bats and pangolins — would provide the virus with plenty of opportunities to make the jump to humans. Similar opportunities arise due to large-scale farming of pigs and chickens, the suspected sources of swine flu and bird flu respectively. Crowded conditions allow a virus to multiply and evolve,

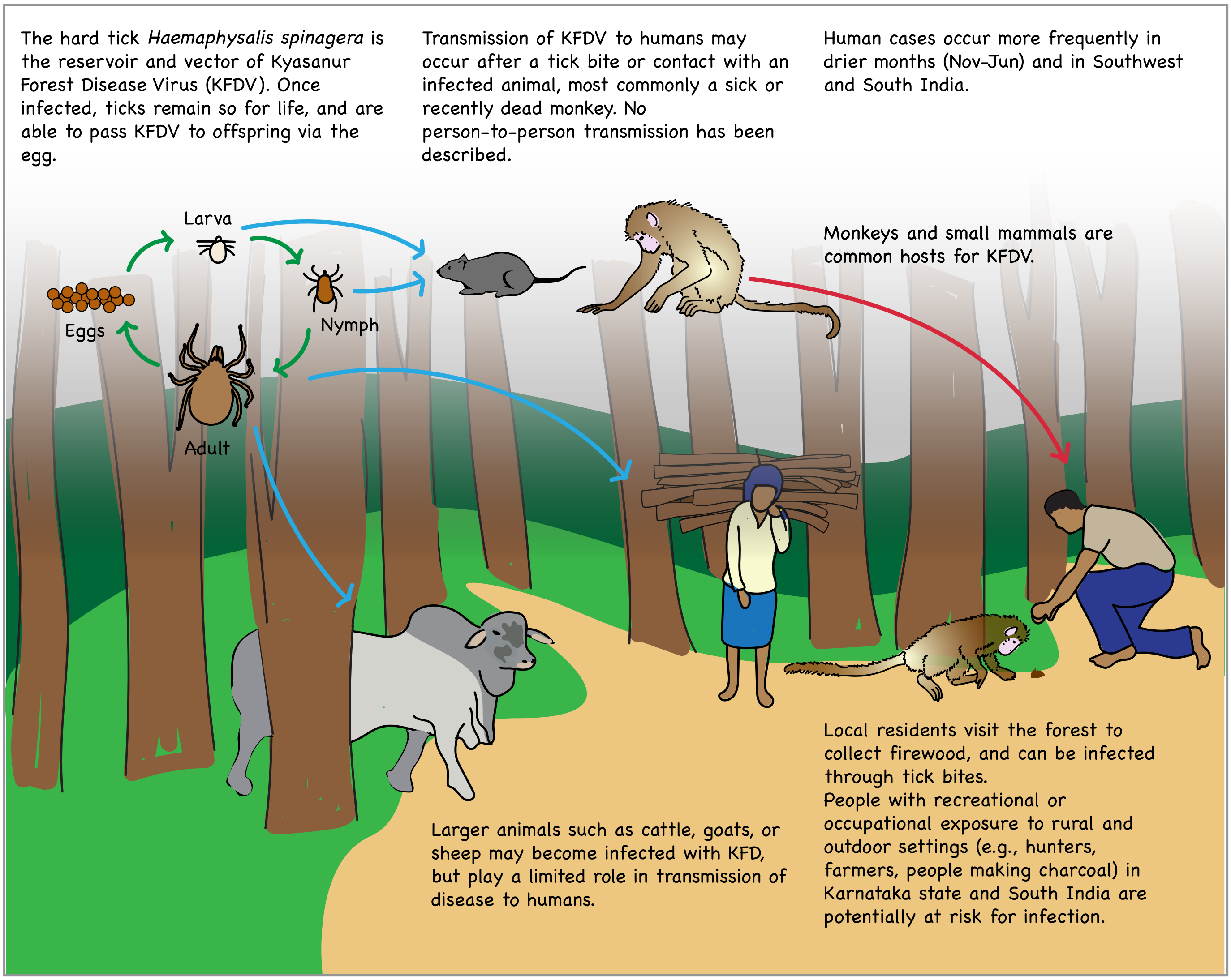

Fig. 3. The transmission cycle of the KFD virus.

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while also increasing opportunities for it to move between species. Moving deeper into forests, clearing them for agriculture, and settling in the neighbourhood of these forests increases our chances of contact with reservoirs of viruses found in wild animals. KFD as well as some of the most infamous and deadly diseases known to humans today, like HIV and Ebola, are zoonoses from wild animals. In one wide-ranging study, hundreds of new species of viruses were discovered across multiple species of animals in different parts of the world.[7] At present, we do not know if these have the potential to jump hosts and cause pandemics. However, the numbers indicate that increasing pressures of food production and land are likely to result in larger animal farms and further forest destruction. If the stories of zoonoses emerging in humans in the last century are anything to go by, this can only increase the potential for future pandemics like COVID-19.

Key takeaways

- The many zoonoses that have shaped human history were caused by microbes that were once exclusively found in wild or domestic animals.
- Sheer physical contact with wild or domestic animals increases the chances of the microbes they harbour jumping species to infect us.
- The capture and sale of wild animals, large-scale farming of livestock, and clearing of forests for human habitation can all increase our chances of contact with new microbes.
- Not all of the many microbes that we routinely come in contact with are able to make the human body a home and cause disease.
- Depending on its mode of transmission, a zoonosis can remain endemic to an area or become a pandemic by spreading simultaneously worldwide.
- Piecing together the transmission cycle (the primary host, vector, and secondary host) of a zoonosis can be quite challenging and time-intensive.
- Due to increasing pressures of food production and land, the frequency of new zoonoses has skyrocketed since the 20th century.

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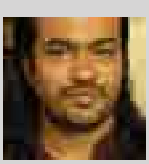

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