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Covid-19's Origin: It wasn't the Wuhan Lab

By: Thomas Abraham

A leak from secret research into bats at a Chinese laboratory used to be suspected as the source of the Covid-19 virus. A careful assessment of evidence instead points to the virus jumping to humans from live animals in a Wuhan food market, eventually spreading across the world.

As our memories of Covid-19 fade and we try and put behind us the deaths, the lockdowns, the disruptions, and the fear, it remains important to understand how this extraordinary event happened. Did the virus that killed between 15 million and 20 million people from the end of 2019 to the end of 2022 leak out of a laboratory in the central Chinese city of Wuhan? Was Covid-19 a man-made tragedy, rather than an act of nature? Was it part of a Chinese plot to destabilise the world and lay the foundations for a global order dominated by China? Or, like every other pandemic so far, was it the natural transmission of a lethal animal virus to human beings?

The most attractive and easily understood explanation is that China was in some way responsible for Covid-19. By early 2020, as the virus spread across the globe, so did speculative theories of its origins. Wuhan is home to the Wuhan Institute of Virology, one of the world's leading coronavirus research centres. If a new coronavirus suddenly appears in a city where coronaviruses are stored and studied, it is reasonable to suspect a laboratory leak.

It also emerged that the closest known coronavirus to severe acute respiratory syndrome (SARS) Cov-2 was a bat coronavirus that had been collected by a team from the Wuhan Institute of Virology from a cave in Yunnan province in southeast China. What if that virus, dubbed RaTG13, had been manipulated at the institute to create SARS-Cov-2, the pandemic virus? At around the same time, a group of miners who had been working at the mine had fallen ill with lung infections. Could RaTG13 have been responsible for this?

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This thread of reasoning was strung by a new type of disease detective whose skills lay not in the traditional disciplines of virology or epidemiology, but rather in the ability to scour the internet for information. Their findings were not disseminated through peer-reviewed scientific journals (the traditional method of spreading science) but on the Internet through social media networks such as X or Twitter as it was then known.

Social media sites, blogs, and websites were the only routes through which this hypothesis could reach the public, as there was little that could pass for scientific evidence to back it. But it gained traction because it seemed plausible. So much of what happens in China is opaque to the outside world; the idea that laboratories in China were doing secret work on viruses, perhaps to create bio-weapons, was not hard to believe.

Perhaps one of the earliest such threads on X was posted by Luigi Warren, the head of a California-based biotechnology company. He wrote on 11 May 2020 that Shi Zhengli, the head of the coronavirus research team at the Wuhan Institute of Virology, had covered up the link between the virus sample she had collected in Yunnan and SARS-Cov-2: "For unknown reasons Shi Zhengli has obfuscated the connection between SARS-2's nearest known relative and her own research." He suggested the virus sample she had collected in Yunnan "might have undergone some calisthenics" in her lab before it escaped and caused the pandemic.





As it travelled across social media, this hypothesis gathered new adherents and new embellishments. A young man living in Bhubaneswar who goes by the Twitter handle @TheSeeker268 came across Luigi Warren's post and decided to dig for more details on the miners. "The first time I heard about the sick miners, I had a flash of insight," he said in an interview to the *Times of India*. "Everyone's typing queries on Google. Let me explore the Chinese academic publications and see if there are any skeletons in the closet." Eventually he came across two theses, one a masters and the other doctoral, by Chinese students that mentioned the sick miners. These became further evidence for those who believed that the miners had been infected by a SARS-like virus that Shi had collected and then worked on.

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Around the same time, a husband and wife team of biologists living in Pune, Monali Rahalkar and Rahul Bahulikar, were struck by the work done in the University of North Carolina in a laboratory run by Ralph Baric on creating chimeric viruses and that Shi's laboratory had collaborated with them. "We knew that Baric's laboratory was working on building chimeric viruses and hence it was possible to make genetically engineered viruses, particularly SARS-like coronaviruses. We knew that Shi's lab had collected a bat coronavirus, RaTG13, that was 96.2% similar to SARS-Cov-2," they said in an interview.

While this idea of Chinese scientists collecting bat viruses in remote mountain caves, working on them in labs under poor bio-security, and then either accidentally or deliberately letting a virus loose on the world seemed plausible, it was scientifically improbable that RaTG13, the virus that was the focus of attention early on had been transformed to SARS-Cov-2.

Though RaTG13, the bat virus in the Wuhan Institute collection that was closest to SARS-Cov-2, was 96.1% similar in its genome to SARS-Cov-2, the two viruses were still a long distance apart in terms of evolution. While they had shared a very distant common ancestor, RaTG13 was not the virus from which SARS-Cov-2 descended. It was at best a distant cousin.

Virologists agree that given this evolutionary distance it would be impossible to transform RaTG13 into SARS Cov-2, particularly since SARS-Cov-2 itself did not exist. Researchers would have needed to experiment with a virus without really knowing what the end destination would be.

Current technology allows virologists to tinker with viruses with small additions and deletions to a known virus genome. But transforming RaTG13 into SARS-Cov-2 would involve far more than tinkering. It would involve creating a completely new virus for

which no blueprint existed, a process that would involve juggling with an almost infinite number of permutations and combinations of nucleotides, the building blocks of RNA and DNA.

As Wang Linfa, a virologist and professor at the Duke-NUS school of medicine in Singapore, put it in to me an interview in July 2024, "Anyone with a good lab and enough funding can engineer a virus with mutations. You can change a bit here and a bit there." However, transforming RaTG13 into SARS Cov-2 would be more than changing a few features of a virus. It would be the equivalent of creating a virus from scratch, given the 1,000 nucleotide difference between them. It would involve playing with four possible combinations of nucleotides in 1,000 different positions by trial and error until you got a combination that worked biologically.

"There would be four to the power 1,000 possible combinations," he pointed out. "You can't even model the number of combinations on a computer; your computer would burn out. If you cannot model the virus on a computer, can you imagine putting it together in a wet lab?"

Wang added, "We can modify a known virus, but *de novo* synthesis of a virus (or creating a virus from scratch) is impossible because nature selects; evolution is a highly sophisticated process. Amongst those thousands of residues you get two or three wrong, the virus won't replicate; or will not transmit."

The RaTG13 to SARS-Cov-2 theory is scientific nonsense, but that does not rule out the possibility that the Wuhan Institute had secretly collected an early version of SARS-Cov-2 and was growing it in the laboratory. If biosafety was poor, it was possible that one or more people in the lab had become infected and then passed the virus on to the broader population.

Samples that revealed coronaviruses were either partially or fully sequenced. Sequencing is expensive, and only viruses that are thought to be of interest are fully sequenced.

Over the course of nearly two decades of bat virus hunting, Shi, the chief coronavirus researcher at the Wuhan Institute, is estimated to have collected around 20,000 faecal, saliva, and blood samples from bats, which are stored in freezers at her lab. But the viruses that exist in these samples are hardly ever grown in the laboratory. It takes patience and a great deal of luck to be able to recover and grow a viable virus from the often damaged and jumbled fragments of viral genetic material in the samples.

Instead, these samples were searched using RtPCr to see whether they contained coronaviruses. Samples that revealed coronaviruses were either partially or fully sequenced. Sequencing is expensive, and only viruses that are thought to be of interest were fully sequenced.

The focus of Shi's research from the early 2000s to the pandemic was to find bat coronaviruses that were genetically close to SARS, particularly those that used ACE2 receptors, the same receptors that SARS and SARS-Cov-2 use to lock onto human cells. These viruses were thought to be potentially capable of evolving into viruses that could infect humans and were fully sequenced and catalogued in databases.

While sequencing has become easier with newer technologies, actually growing a virus out of a blob of faecal matter or a saliva sample is not easy. Out of the several thousand samples they had, Shi's lab succeeded in growing three live viruses, including the first bat coronavirus that had been successfully extracted from a sample and grown in a laboratory. Growing each of these three different bat coronaviruses was a scientific achievement, and the results were published in leading international scientific publications such as *Nature*, the *Journal of Virology* and *PLOS Pathogens*.

The three bat viruses that were had been grown or were growing in the laboratory and could conceivably have leaked were less than 80% genetically similar to SARS-Cov-2 and could not have even evolved into SARS-Cov-2, let alone cause a pandemic.

This leaves the possibility that Shi had collected a close progenitor of SARS-Cov-2 and had managed to grow it secretly in the laboratory, from where it leaked and infected laboratory workers. Laboratory leaks are known to happen. The SARS virus, for example, leaked from laboratories in Singapore, Taiwan and Beijing, infecting small numbers of laboratory researchers in 2003 and 2004.

Was there any reason for Shi to discover a bat virus with receptors that could infect humans and culture it in a laboratory without publishing it in a major scientific journal?

These incidents occur across the world, including in countries with the most advanced bio-security systems. To name a few other recent examples of viruses escaping from laboratories, a lab worker at a polio vaccine facility in the Netherlands was infected with polio in 2022. A laboratory worker was infected with Ebola in Hungary in 2018. A researcher was infected with Zika in the United States in 2016.

In all these cases, a known virus escaped from a laboratory and its spread was contained. If SARS-Cov-2 was being secretly cultivated and spread outside the laboratory into the wider world before it could be contained, it would be unusual.

Was there any reason for Shi to discover a bat virus with receptors that could infect humans and secretly culture it in a laboratory without publishing it in a major scientific journal and getting the acclaim that went with that?

Wang of Duke-NUS Medical School in Singapore, who has worked with Shi and mentored her for some decades, pointed out that the Wuhan Institute had been trying for 20 years to culture viruses from wild samples, and each time they did so, they rushed to publish in leading global journals. "If SARS-Cov-2 was from an animal virus that Shi Zhengli's laboratory was able to culture, I would assure you [...] they would write a paper overnight and submit it [...] that's what we scientists do. Any bat coronavirus using ACE-2 is a major scientific paper [...] I always say before any lab leak, you would see a publication about the virus in *Nature*."

Even a report by the US intelligence community concluded that SARS-Cov-2 was not a bio-weapon and had not been genetically engineered, indicating that it was not part of any secret research project.

It has been argued that Shi was running a secret military project to create a bio-weapon and that SARS-Cov-2 was a virus that leaked from this project. This would indeed have been reason for secrecy. But there is no evidence of this. Even a report by the US intelligence community concluded that SARS-Cov-2 was not a bio-weapon and had not been genetically engineered, indicating that it was not part of any secret research project.

Besides being home to the Wuhan Institute of Virology, Wuhan is central China's biggest city, which is also home to a thriving trade in farmed and wild animals that are prized in Chinese traditional medicine and cuisine. The explanation favoured by most virologists and epidemiologists is that like SARS in 2002, SARS-2 spread from wildlife sold in the markets of Wuhan, in particular one market, the Huanan Seafood Market.

Despite its name, the seafood market sold more than seafood. Its crowded stalls had a variety of live animals, including palm civets and racoon dogs, animals that can be infected with bat coronaviruses. In 2002, SARS passed to human beings in Guangdong province in southern China through markets where palm civets were being sold.

The explanation favoured by most virologists and epidemiologists is that like SARS in 2002, SARS-2 emerged from wildlife sold in the markets of Wuhan, in particular one market, the Huanan Seafood Market.

One way to definitely establish that animals at the market were the source would have been to test the animals. But the Wuhan authorities shut the market down on 1 January 2020 and destroyed all the live animals and seafood that was being sold there. As K.Y Yuen – a professor at Hong Kong University who was part of a fact finding team that went to the market on 18 January – put it, it was as if a crime scene had been cleaned up. "We found it cleaned and emptied. Whatever animals had been there had been slaughtered or taken away," he told me in an interview in August 2024.

Why the Wuhan authorities did this is not clear. One reason could be they thought that since most cases seemed to be linked to the market, the outbreak would die if everything in the market was destroyed and the place cleaned up. It was, however, still possible to take environmental samples from the stalls after it was shut down and 33 of the 543 samples tested had traces of the new virus, indicating that it was definitely present in the market until 1 January 2020, the day it was shut down.

Huanan market is roughly 17 kilometres away from the Wuhan Institute of Virology, on the other bank of the Yangtze River, which flows through the city. The first people to fall ill in the months of December and early January either lived in the vicinity of the market or worked there. When they fell ill, they all went to hospitals around the market.

Had the virus leaked from the Institute, it is logical to think that the first people to be infected would be the community living in the vicinity. The first hospitals they would have gone to would have been hospitals in the same area. Yet doctors in these hospitals did not

report any unusual cases of pneumonia turning up for treatment in December. In contrast, it was doctors in hospitals around the market who sounded the first alarm about patients with unusual pneumonia that did not respond to normal treatment.

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As Eddie Holmes, a professor of virology at the University of Sydney put it in an interview to *This Week in Virology*, a podcast hosted by Vincent Racaniello, a professor of Columbia University, "The earliest cases we have date back to December 2019. If you plot those cases on a map of Wuhan, they cluster very strongly around the market." He pointed out that "these were not just market workers, but also people who had no connection to the market, indicating that the outbreak was radiating outward from the market to the community."



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Though the animals sold at the market were destroyed, and Wuhan officials denied that there were any of the mammalian species that could have been infected with SARS-Cov-2, other evidence has emerged to indicate that animals susceptible to SARS were being sold at the market. A team of Chinese and western researchers who were studying the animals at the market reported that racoon dogs, bamboo rats, badgers, and civets were on sale, cramped into tiny insanitary cages that would also allow disease to spread rapidly from one infected animal to another.

China has firmly shut the door on any further studies on the origins of SARS-Cov-2, and given how polarised the debate has become, this is unlikely to change.

In a remarkable piece of scientific investigation, a team of researchers led by Michael Worobey of the University of Arizona linked the positive environmental samples that Chinese investigators had collected from the market, reconstructed floor plans of the market with photographic evidence of mammals sold at the market, and compiled business registries with details of which vendors were at which stall at the market. It zeroed in on an area in the southwest corner of the market where live mammals were known to have been sold before Covid-19 struck, and where positive environmental samples were found in drains and sewer pipes. "These findings suggest that infected animals were present at the Huanan market at the beginning of the Covid-19 pandemic," the team wrote.

Worobey and his team then looked at the first 155 cases of Covid-19 that had been reported in December and using geospatial mapping techniques found that they were clustered around the Huanan market in a way that was extremely unlikely to have happened randomly.

The presence of animals such as civets that were known to be susceptible to SARS-like coronavirus in the market, the clustering of coronavirus positive samples in that part of the market where these animals were likely to have been sold, and that the earliest human cases clustered close to Huanan market all indicate that the market played a major role in either originating the epidemic or in amplifying it.

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As we saw earlier, had the virus leaked from Wuhan Institute of Virology one would expect the first cases to be clustered around there. Rather than a market, the infection was likely to have spread between people in a variety of more likely settings – supermarkets, malls, cinemas or sporting arenas. People in Wuhan tend to do their shopping in supermarkets and smaller stores, not in crowded, often insanitary, live animal markets. If so many early cases clustered around Huanan market, it would indicate this was because there was a source of infection in the market.

This begs the question of how these animals got infected by a bat origin coronavirus. Understanding the route of transmission from bat to an intermediary host or hosts would require extensive sampling of both farmed as well as wild animals that are traded both legally

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as well as illegally and tracking down the supply chains of animals to the market. This is unlikely to happen.

China has firmly shut the door on any further studies on the origins of SARS-Cov-2, and given how polarised the debate has become, this is unlikely to change. Beijing's position now is that the virus came to the country from elsewhere, perhaps even from Europe or the United States and therefore there is nothing to be gained by searching for its origins in China. Two alternative theories that China is propagating is that the overseas participants at the World Military Games that were held in Wuhan at the end of October 2019 might have brought the infection with them, or that frozen food from overseas might have contained the virus. Both these theories are as speculative as the laboratory leak theory.

If there is a lesson to be learnt from the origins of Covid-19, it is that our relationship with the animal world needs to change drastically to reduce the risk of the next pandemic.

Even in the case of SARS in the early 2000s, it took several years to trace its closest relative to bats in Yunnan. The route that virus took to travel thousands of kilometres to infect civets in the markets of Guangdong province is still unknown. We will probably never know where and which animals were first infected by an early ancestor of SARS-Cov-2.

All we know is that the evidence available at present indicates that animals in a particular section of Huanan market were infected with the virus and in all likelihood passed it on to humans working and visiting the market, who then took it to the rest of the city, from where it spread to the rest of the world. And if there is a lesson to be learnt from the origins of Covid-19, it is that our relationship with the animal world needs to change drastically to reduce the risk of the next pandemic.

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