

## Where Did the Coronavirus Come From? What We Already Know Is Troubling.

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• June 25, 2021

There were curious characteristics about the H1N1 influenza pandemic of 1977-78, which emerged from northeastern Asia and killed an estimated 700,000 people around the world. For one, it almost exclusively affected people in their mid-20s or younger. Scientists discovered another oddity that could explain the first: It was virtually identical to a strain that circulated in the 1950s. People born before that had immunity that protected them, and younger people didn't.

But how on earth had it remained so steady genetically, since viruses continually mutate? Scientists guessed that it had been frozen in a lab. It was often <u>found to be</u> sensitive to temperature, something expected for viruses used in vaccine research.

It was only in 2004 that a prominent virologist, Peter Palese, wrote that Chi-Ming Chu, a respected virologist and a former member of the Chinese Academy of Sciences, told him that "the introduction of this 1977 H1N1 virus" was indeed thought to be due to vaccine trials involving "the challenge of several thousand military recruits with live H1N1 virus."

For the first time, science itself seemed to have caused a pandemic while trying to prepare for it.

Now, for the second time in 50 years, there are questions about whether we are dealing with a pandemic caused by scientific research.

While the Chinese government's obstruction may keep us from knowing for sure whether the virus, SARS-CoV-2, came from the wild directly or through a lab in Wuhan or if genetic experimentation was involved, what we know already is troubling.

Years of research on the dangers of coronaviruses, and the broader history of lab accidents and errors around the world, provided scientists with plenty of reasons to proceed with caution as they investigated this class of pathogens. But troubling safety practices persisted.

Worse, researchers' success at uncovering new threats did not always translate into preparedness.

Even if the coronavirus jumped from animal to human without the involvement of research activities, the groundwork for a potential disaster had been laid for years, and learning its lessons is essential to preventing others.

Until the SARS outbreak, coronaviruses were considered fairly benign, causing only minor to moderate colds. Even five months after SARS emerged in southern China in November 2002, the Chinese government was covering up details about its threat, while the disease was spreading to other countries. By summer 2003, it had been contained, but not before infecting over 8,000 people and killing 774. Officials were able to suppress SARS because infected people spread it when visibly sick, making it easier to identify and isolate people. But it was a close call, and that roughly 10 percent case fatality rate raised alarms. Preventing the next coronavirus pandemic became a scientific priority.

By 2005, researchers — including Dr. Shi Zhengli, a virologist at the Wuhan Institute of Virology — <u>had identified</u> horseshoe bats as the likely primary host animal from which SARS had emerged. In the years that followed, scientists pursued bat coronaviruses in the field and studied them in the lab.

It is often assumed that SARS was spread to humans by palm civets, an adorable small mammal sometimes sold at wildlife markets, though by 2008, it <u>was suspected</u> that bat coronaviruses could directly infect human lung cells without needing an intermediary animal. By 2013, Dr. Shi's lab experiments showed this could happen.

Still, scientists sometimes worked with bats, bat samples and bat viruses under conditions that have since raised eyebrows.

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It is in the nature of viruses to continually mutate, with random accidents altering, adding or removing parts of its genome or bits of genetic code being exchanged with other viruses — recombination. This constant trial and error enables the emergence of features that can allow viruses to infect a new species.

In order to anticipate these jumps, humans have tried to steer this process. In what is sometimes called gain-of-function research, they genetically manipulate viruses to see how they can become more dangerous.

In <u>an article</u> in Nature Medicine in 2015, researchers from two of the major coronavirus laboratories in the world — Dr. Shi; Ralph Baric, a professor at the University of North Carolina at Chapel Hill; and others — wrote that they had bioengineered a coronavirus. The work was carried out in Dr. Baric's laboratory at U.N.C. They took a spike protein, the "key" that coronaviruses use to unlock and infect cells, from a horseshoe bat virus and combined it with a human SARS virus adapted for mice. They reported that this "chimeric" virus could

infect human cells, suggesting some bat viruses may be "capable of infecting humans without mutation or adaptation." This was the second time since Dr. Shi's 2013 experiments that a SARS-like bat coronavirus showed the ability in the lab to directly infect human airway cells.

This kind of genetic manipulation had already raised concerns, especially after laboratories in the Netherlands and the United States announced in 2011 that they had created strains of flu viruses using genetic material from the H5N1 influenza A virus, which is very deadly but generally can't yet spread among people. These new strains could spread by air among ferrets, which have humanlike lungs. The uproar had been immediate.

In defense of the 2015 coronavirus experiment by Dr. Shi and her colleagues, Peter Daszak, whose organization, EcoHealth Alliance, has worked closely with her and has been granted tens of millions of dollars in the last decade from the U.S. government, <u>said the findings</u> would allow scientists to focus on the greatest risk because it would "move this virus from a candidate emerging pathogen to a clear and present danger."

Others were more worried. "If the virus escaped, nobody could predict the trajectory," said Simon Wain-Hobson, a virologist at the Pasteur Institute in Paris.

Recent history provided plenty of reason for such concern.

Nearly every SARS case since the original epidemic has been due to lab leaks — six incidents in three countries, including twice in a single month from a lab in Beijing. In one instance, the mother of a lab worker died.

In 2007, foot-and-mouth disease, which can devastate livestock and caused a massive crisis in Britain in 2001, escaped from a drainage pipe leak at an English lab with the highest biosafety rating, BSL-4.

Even the last known person who died of smallpox was someone infected because of a lab incident in Britain in 1978.

In its first published survey of the reporting systems in American labs working with dangerous pathogens, the Centers for Disease Control and Prevention in 2012 reported 11 laboratory-acquired infections across six years, often in BSL-3 labs — the category of safety reserved for pathogens like tuberculosis. In each instance, the exposure was not realized or reported until lab workers became infected.

In January 2014, the C.D.C. <u>contaminated</u> a benign flu virus sample with deadly A(H5N1) but didn't discover the danger until months later. And in June 2014, it mistakenly sent improperly deactivated anthrax bacteria to labs, potentially exposing at <u>least 62 C.D.C. employees</u> who worked with the samples without protective gear. One month later, vials of live smallpox virus were found in a storage room at the National Institutes of Health.

In October 2014, after that string of high-profile incidents, the United States paused its funding of new gain-of-function research, with few exceptions. The moratorium was lifted in 2017.

Far more serious questions about scientific safety would soon arise.

On Dec. 30, 2019, a public email list run by the International Society for Infectious Diseases warned that an "unexplained pneumonia" had appeared in Wuhan, China, and reports connected the first cases to the city's Huanan seafood market. On Jan. 10, 2020, a Chinese scientist posted the genome of the virus — soon to be named SARS-CoV-2 — on an open internet depository, confirming that it was a coronavirus. The Chinese government denied that the virus was spreading among humans until Jan. 19, 2020; three days later, it announced a complete lockdown of Wuhan, a city of 11 million people.

About a week after the lockdown, Chinese scientists <u>published</u> a paper in The Lancet medical journal that identified bats as the likely source of the virus. The authors noted that the outbreak happened during local bat hibernation season and "no bats were sold or found at the Huanan seafood market," so they reasoned that it may have been transmitted by an intermediary animal.

Outbreaks can occur far from their source. The 2002 SARS outbreak started in Guangdong, about a thousand kilometers from the caves in Yunnan with the horseshoe bats from which SARS <u>is believed</u> to have emerged. Masked palm civets, farmed and traded across China, often in cramped, unsanitary conditions making them prone to outbreaks, were cited as the vehicle that SARS probably used to travel from Yunnan to Guangdong. Since SARS-CoV-2 was first detected at a market where live wild animals may have been sold, the wildlife trade was immediately suspected.

Social media users in China were <u>among the first</u> to be more skeptical. Did the spread of a disease from bats just happen to start in Wuhan, home to the Wuhan Institute of Virology, one of the few top bat coronavirus research facilities in the world? And what about the Wuhan Centers for Disease Control and Prevention, which also carries out bat research, a few hundred yards from the seafood market?

On Feb. 19, 2020, 27 prominent scientists <u>published</u> an open letter in The Lancet. They decried "conspiracy theories suggesting that Covid-19 does not have a natural origin."

As we consider its origin, the question is not so much whether SARS-CoV-2 could have gotten out of a lab — accidents happen — but whether it could have gotten in and how it would have been handled there.

Shortly after Wuhan was locked down in January 2020, it became apparent that SARS-CoV-2 was related to a virus that scientists had been aware of for years.

On Feb. 3, 2020, Dr. Shi and co-authors <u>announced</u> in Nature that they had found a virus in their database, RaTG13, whose genome sequence was 96.2 percent identical to SARS-CoV-2 and was previously detected in horseshoe bats of Yunnan.

Suspicious internet sleuths <u>combed through</u> genomic databases and found that RaTG13 was an exact match for a bat coronavirus called 4991 retrieved from a cave <u>implicated</u> in an unexplained outbreak of pneumonia in 2012 among miners who collected bat guano from a mine in Yunnan. Three of the six miners <u>died</u>.

In May 2020, a former science teacher from India, with the Twitter pseudonym TheSeeker268, found a 2013 master's thesis, as well as a 2016 Ph.D. thesis, supervised by George Fu Gao, the current director of the Chinese Center for Disease Control and Prevention. The master's thesis <a href="https://hypothesized">hypothesized</a> that the miners' illness was caused by direct transmission of a SARS-like coronavirus from a horseshoe bat. The Ph.D. thesis was more cautious but still called the outbreak "notable." It also revealed that a team from the Wuhan Institute of Virology had collected bat samples from the cave. The dissertation noted that all four of the miners who were tested for SARS antibodies had them in their blood a few weeks after they became ill.

None of those crucial facts — the name change or the link to the previous fatal outbreak possibly from a SARS-like coronavirus — were mentioned in the original paper about RaTG13. In an interview published in March 2020, Dr. Shi <u>said</u> fungus was the pathogen that had sickened the miners, not a coronavirus.

The questions persisted.

Last July, Dr. Shi <u>confirmed</u> that RaTG13 was indeed 4991 renamed. In November 2020, her paper in Nature was finally updated, additionally <u>acknowledging</u> what sleuths had also uncovered: Her team genetically sequenced RaTG13 in 2018. (The possible bat coronavirus link to the miner deaths was still not acknowledged.)

The less than forthcoming disclosure — a virus with two names, the connection to a deadly outbreak, shifting diseases and inconsistent stories — <u>fueled suspicions</u>.

Some <u>speculated</u> whether RaTG13 had been subjected to gain-of-function-type manipulation to create SARS-CoV-2. But RaTG13 is more like a distant cousin of SARS-CoV-2, meaning it is unlikely to have produced SARS-CoV-2 as an offspring, either through recent evolution in the wild or manipulation in the lab.

Even if RaTG13 had no role in the Covid-19 outbreak, questions were raised about why Dr. Shi and others seemed so unforthcoming about it. Then more questions were raised.

For example, the same group of internet sleuths that linked RaTG13 to the mine also uncovered that a genomic database maintained by the Wuhan Institute of Virology, with information about thousands of bat samples and at least 500 recently discovered bat coronaviruses, went offline in September 2019. The official explanation — that it was taken offline because it had been subjected to hacking — doesn't explain why it was never securely shared some other way with responsible independent researchers.

Such gaps made it harder to rule out worrying scenarios. If there had been a lab accident involving SARS-CoV-2 or a virus like it that had been collected in the wild or experimented on in the lab, the database might have been taken down so there would be less evidence that might help others connect the dots. Officials might have investigated possible lab cases and prematurely believed it was in the clear. However, cases can be asymptomatic, and they might have missed the one that started a transmission chain and allowed the virus to circulate quietly until a superspreader event in December.

The secrecy and the cover-ups have led to some frantic theories — for example, that the virus leaked from a bioweapons lab, which makes little sense, since, for one thing, bioweapons

usually involve more lethal pathogens with a known cure or vaccine, to protect those who employ them.

But much more mundane threats lurked.

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Dr. Shi's scientific work was dependent on collecting and analyzing hundreds of bat samples. And it was her work that showed the dangers associated with this endeavor. The 2013 paper by Dr. Shi, Dr. Daszak and others demonstrated that a live bat coronavirus from a Yunnan sample could bind to human lung cell receptors, showing that "intermediate hosts may not be necessary for direct human infection." That controversial 2015 experiment co-authored by a group of researchers that included Dr. Baric and Dr. Shi was carried out after they had found another bat coronavirus they suspected could infect humans, but it was difficult to cultivate. They then created that chimeric one using its spike. They showed that it, too, could infect human airway cells directly.

In October 2015, Dr. Shi's lab sampled <u>over 200 people</u> living within a few miles of two Yunnan bat caves and found that six tested positive for bat coronavirus antibodies, indicating past infection. All six reported having seen bats and only 20 people in total had reported seeing bats flying close to their homes, suggesting exposure created a great risk of infection.

The research practices, however, may not have always incorporated these lessons.

While a 2017 Chinese article <u>noted the caution</u> of the Wuhan Institute of Virology's workers and showed them hooded and some wearing N95 masks, later that year a Chinese state-TV story about Dr. Shi's studies <u>showed researchers</u> handling bats or bat feces with their bare hands or with exposed arms. A person on her team likened a bat bite to "being jabbed with a needle."

In a 2018 blog post that was later removed, Dr. Shi said that the job was "not as dangerous" as everyone thought. "The chance of directly infecting humans is very small," she wrote. "In most cases only ordinary protection will be taken," unless a bat was known to carry a virus that might infect humans. She repeated something similar in a 2018 TED Talk-style video, according to The Washington Post, noting that "simpler protection" — illustrated with slides of unmasked or surgically masked colleagues with bare hands — was appropriate because it was believed that bat pathogens usually required an intermediate host.

Dr. Shi <u>said</u> that all the research at the institute is done in strict accordance with biosafety standards and the lab is tested annually by a third-party institution.

The Wuhan C.D.C. also reportedly conducts research on bat-borne viruses.

One of its staff members, Tian Junhua, has developed a reputation for adventurous scientific discovery. A 2013 paper notes his team caught 155 bats in Hubei Province. The Washington Post reported that in a video released on Dec. 10, 2019, he boasted about "having visited dozens of bat caves and studied 300 types of virus vectors." Previously, he also talked about having made mistakes in the field, like forgetting personal protective equipment and being splashed with bat urine or accidentally getting bat blood on his skin, according to The Post.

And yet the <u>World Health Organization reported</u> that the agency denied ever storing or working with bat viruses in the lab before the pandemic.

This March the W.H.O. reported that the Wuhan C.D.C. lab "moved on 2nd December 2019 to a new location near the Huanan market." The W.H.O. report said there were "no disruptions or incidents" during the move. Given the Chinese government's lack of candor, that raises suspicions that lab samples, if not bats themselves, were being hauled around near the market at the time of the outbreak.

Many of these research practices weren't deviations from international norms. A bat field researcher in the United States told me she now always wears a respirator in bat caves but that wasn't standard practice before.

It isn't a wild idea to suggest that field research risks setting off an outbreak. Dr. Linfa Wang, a Chinese-Australian virologist based in Singapore who frequently works with Dr. Shi and pioneered the hypothesis that bats were behind the 2003 SARS epidemic, told Nature there is a small chance that this pandemic was seeded by a researcher inadvertently getting infected by an unknown virus while collecting bat samples in a cave.

Bats could create further risks if housed in laboratories, like the risk posed by the sale of wildlife in urban markets.

On Dec. 10, Peter Daszak, who organized The Lancet letter denouncing the questioning of Covid-19's natural origins and was announced as a member of the W.H.O. origins investigation committee last fall, <u>insisted it was</u> a conspiracy theory to suggest that there were live bats in labs he had collaborated with for 15 years. "That's not how this science works," <u>he wrote</u> in a tweet he later deleted. "We collect bat samples, send them to the lab. We RELEASE bats where we catch them!"

But evidence to the contrary has accumulated. An assistant researcher told a reporter that Dr. Shi took on the role of feeding the bats when students were away. Another news report in 2018 said a team led by one of her doctoral trainees "collected a full rack of swabs and bagged a dozen live bats for further testing back at the lab." The Chinese Academy of Sciences website has listed the Wuhan institute as having at least a dozen cages for bats, and in 2018 the institute applied for a patent for a bat cage. Dr. Shi has talked about monitoring antibodies in bats over time — which would not be done in a cave. Recently, another video surfaced that reportedly showed live bats in the institute.

Just a few weeks ago, Dr. Daszak changed his claims. "I wouldn't be surprised if," he said, "like many other virology labs, they were trying to set up a bat colony."

Meanwhile, no intermediary animal has yet been found, despite testing thousands of animals around Wuhan. Last month a former commissioner of the Food and Drug Administration, Scott Gottlieb, <u>said</u> this failure added to the evidence of a lab leak, although Dr. Daszak suggested that investigators look further, at wildlife farms in southern China.

But if bat-to-human transmission is how the spillover happened, no intermediary animal is necessary, since it could have been any interaction with a bat — by a villager or a field researcher.

Despite widespread assertions that bat viruses need an intermediary animal to spread to humans, research is not even settled on whether the palm civet spread SARS to humans from bats. We do know that palm civets amplified the outbreak once SARS arrived in the Guangdong market and that back-and-forth transmission between humans and civets was possible. However, the only widespread infected civet populations that researchers found were those at urban markets and sometimes at farms — where people are — and not in the wild. We know we can infect animals. Last year Denmark had to kill 17 million minks after they caught SARS-CoV-2 from people. It's possible that humans were the initial intermediary animal for civets and that the cute little creatures were framed.

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Other sources of risk were the lab activities themselves.

There has been a lot of speculation that SARS-CoV-2 was the result of genetic engineering. This hypothesis cannot be ruled out based on genomic analysis alone, and suspicion has grown because of the opaque response by Chinese authorities.

They have refused to share direct records from the lab. Dr. Shi echoed this stance in May when a group of scientists, including her co-author Dr. Baric, pushed for broader transparency. "It's definitely not acceptable," she <u>emailed a reporter</u> in response to the group's request to see her lab's records.

Meanwhile, throughout December 2019, Wuhan doctors suspected that a SARS-like virus was on the loose, and the local government <u>arrested whistle-blowers</u>, including at least one health care worker. The cover-up by Communist Party officials continued until the prominent SARS scientist Zhong Nanshan <u>traveled to</u> Wuhan on Jan. 18 and raised the alarm.

That said, circumstantial evidence casts some doubt on the claim that SARS-CoV-2 was bioengineered.

For instance, aspects of the virus that have made some suspect it was bioengineered could also be evidence that the virus evolved naturally. A lot of attention has been drawn to an unusual feature on its spike protein called a furin cleavage site, with which the virus can better infect a human cell. It's one of several odd features of SARS-CoV-2 that are weird enough that even virologists who greatly doubt lab involvement told me they were shocked to see it. In fact, even beyond the furin cleavage site, SARS-CoV-2 was a virus that scientists had never seen before. Evolution can be a random accumulation of weird, novel features. For the research on viruses that scientists like Dr. Shi do for high-level scientific publications, such a combination would be incongruous. Their work usually involves examining or changing one element of a virus at a time to find out what each element does and can be made to do. If your computer conked out, for instance, you wouldn't see what's wrong by simultaneously changing the power source, the cable and the electrical outlet. You'd test each one individually. Having a variety of unusual elements leads to hard-to-assess results, not a paper in Nature.

But even if we put aside directed engineering, regular lab work at the Wuhan labs has raised concerns.

In 2016 the Wuhan institute reported experimenting on a live bat coronavirus that could infect human cells in a BSL-2 lab — a biosafety level that has been compared with that of a dentist's office. Protective gear other than gloves and lab coats is usually optional at this level, and there's often no airflow control sealing ventilation between the work area and the rest of the building. Michael Lin, an associate professor of neurobiology and bioengineering at Stanford, told me it was "an actual scandal, recorded in print," that a SARS-like virus capable of replicating in human cells was worked on under such low safety conditions.

Just trying to culture bat viruses in the lab can create risks that the scientists may not even be aware of. While trying and failing to cultivate one strain, they might inadvertently culture another one they don't even know about. It's even possible, Dr. Lin told me, that viruses can coexist in a single sample and quietly recombine, giving rise to something novel but undetected. Under BSL-2 conditions or even sloppy BSL-3 conditions, researchers could get exposed to a pathogen they didn't know existed.

Several scientists who signed The Lancet letter denouncing the consideration of anything but natural origins have since said they are more open to lab involvement. One, Bernard Roizman, an emeritus virologist at the University of Chicago with four honorary professorships from Chinese universities, said he was leaning toward believing there was a lab accident.

"I'm convinced that what happened is that the virus was brought to a lab, they started to work with it," he told <u>The Wall Street Journal</u>, "and some sloppy individual brought it out." He added, "They can't admit they did something so stupid."

Charles Calisher of Colorado State University, another signatory, recently told ABC News that "there is too much coincidence" to ignore the lab-leak theory and he now believes "it is more likely that it came out of that lab."

Peter Palese, the virologist who wrote about the 1977 flu pandemic, said that "a lot of disturbing information has surfaced since The Lancet letter I signed" and that he wants an investigation to come up with answers.

Other scientists have also said they have changed their minds.

Ian Lipkin, the director of the Center for Infection and Immunity at Columbia University and a co-author of an influential article in Nature Medicine that argued in favor of a natural origin in March 2020, is also now more skeptical. "People should not be looking at bat viruses in BSL-2 labs," he told the science reporter Donald G. McNeil Jr. last month. "My view has changed."

Medical records of lab workers could help clarify such questions. Last July, Dr. Shi said "a possibility did not exist" that anyone associated with the institute may have gotten infected "while collecting, sampling or handling bats." She added that it had recently tested all institute staff members and students for antibodies showing past infection by SARS-CoV-2 or SARS-related viruses and had found "zero infection" and insisted that she could rule out this possibility for all labs in Wuhan.

It's hard to see how a careful scientist could dismiss even the slightest possibility for all labs, including those not her own. "Zero infection" would mean not a single case among the

hundreds of people at the institute, even though a study found that 4.4 percent of the Wuhan population had been infected.

Later, the W.H.O. team asked for more information about the earliest Covid-19 cases in Wuhan, including anonymized but detailed patient data — something that should be standard in any outbreak origin investigation — and were denied access.

All this leaves a lot of possibilities open and a lot of confusion.

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Since most pandemics have been due to zoonotic events, emerging from animals, is there reason to doubt lab involvement? Maybe if you look at all of human history. A better period of comparison is the time since the advent of molecular biology, when it became more likely for scientists to cause outbreaks. The 1977 pandemic was tied to research activities, while the other two pandemics that have occurred since then, AIDS and the H1N1 swine flu of 2009, were not.

Plus, once a rare event, like a pandemic, has happened, one has to consider all the potential paths to it. It's like investigating a plane crash. Flying is usually very safe, but when a crash does happen, we don't just say mechanical errors and pilot mistakes don't usually lead to catastrophes and that terrorism is rare. Rather, we investigate all possible paths, including unusual ones, so we can figure out how to prevent similar events.

Perhaps the biggest question has been what to read into the location of the outbreak, a thousand miles from the closest known viral relatives yet close to a leading research institution.

Sometimes the curiosity around the location has been waved away with the explanation that labs are set up where viruses are. However, the Wuhan Institute of Virology has been where it is since 1956, doing research on agricultural and environmental microbiology under a different name. It was upgraded and began to focus on coronavirus research only after SARS. Wuhan is a metropolis with a larger population than New York City's, not some rural outpost near bat caves. Dr. Shi said the December 2019 outbreak surprised her because she "never expected this kind of thing to happen in Wuhan, in central China." When her lab needed a population with a lower likelihood of bat coronavirus exposure, they used Wuhan residents, noting that "inhabitants have a much lower likelihood of contact with bats due to its urban setting."

Still, location itself is not proof, either. Plausible scenarios implicating research activities don't rule out other options.

This week, Jesse Bloom, an associate professor at the Fred Hutchinson Cancer Research Center, told me that when he recovered and <u>analyzed</u> a set of partial early Wuhan genetic sequences that had been <u>removed from a genomic archive</u>, it supported "substantial existing evidence that SARS-CoV-2 was circulating in Wuhan prior to the seafood market outbreak." Both the early reports from Chinese scientists and the more recent W.H.O. investigation this winter found many of the early cases had no connection to the seafood market, including the earliest acknowledged case so far, on Dec. 8, 2019. So the seafood market may not have been the original location of the outbreak.

It's also plausible that an outbreak could have started someplace else and was detected in Wuhan simply because it was a big city. Testing blood banks from across China, especially in areas near wildlife farms and bat caves, would help, but with limited exceptions, the Chinese government has not carried out such research — or allowed the sharing of the results if it has.

With so much evidence withheld, it's hard to say anything about Covid-19's origins with certainty, and even a genuine investigation would face challenges. Some outbreaks have never been traced to their origin.

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But even if we are denied answers, we can still learn lessons.

Perhaps the biggest one is that we were due for a bat coronavirus outbreak, one way or another, and the research showing bat coronaviruses' ability to jump to humans was a warning not heeded.

Scientists and government officials need to weigh the benefits and dangers of how we work with bats and viruses, in the field and the lab, especially since other public health investments may do much more to prevent a pandemic. It might be more effective to institute rigorous surveillance where threatening pathogens are known to thrive, and better prepare our institutions to react quickly and transparently to the first sign of an outbreak. Research can be weighted toward response rather than prediction; these overlap but aren't identical. Finding a dangerous virus in a cave or a petri dish might be useful, but it's a bit like poking a bear we are trying to avoid.

Field research on bats should have been done more carefully. Bat viruses should not be studied in BSL-2 labs, and research in BSL-3 labs should be done only under the strictest caution. Bats should be treated as a serious threat in labs. Human interactions with bats should occur under strict regulation and surveillance.

Alison Young, an investigative reporter who has long covered lab incidents, wrote that from 2015 to 2019, there were more than 450 reported accidents with pathogens that the federal government regulates because of their danger. Comparable rates of incidents were found in British labs — and research suggests lab accidents are not even always reported.

Some scientists have proposed imposing stricter controls and a stronger risk-benefit analysis for research on pathogens that could inadvertently spark pandemics. Some research may still be worth it, and there have been proposals to move such labs outside densely populated cities.

Cooperation with China on these issues is vital, including on lab safety and outbreak surveillance. Some argue that criticizing China's response to the pandemic and the scientific practices that might have led to it will imperil that cooperation. It's hard to see how angry opeds could make Chinese officials more intransigent than they already are.

People are understandably wary that these claims might demonize scientists from other countries, especially given the anti-Asian racism that has abounded. But why would perpetuating this state of events be to their benefit?

After a lab accident with anthrax bacteria in the Soviet Union in 1979 that killed dozens, leading Western scientists accepted the <u>Soviet government's excuses</u>, which all turned out to be lies. That doesn't help lead to better safety standards, including those that would benefit scientists in authoritarian countries.

But a better path forward is one of true global cooperation based on mutual benefit and reciprocity. Despite the current dissembling, we should assume that the Chinese government also doesn't want to go through this again — especially given that SARS, too, started there.

This means putting the public interest before personal ambitions and acknowledging that despite the wonders of its power, biomedical research also holds dangers.

To do this, government officials and scientists need to look at the big picture: Seek comity and truth instead of just avoiding embarrassment. Develop a framework that goes beyond blaming China, since the issues raised are truly global. And realize that the next big thing can simply mean taking great care with a lot of small details.