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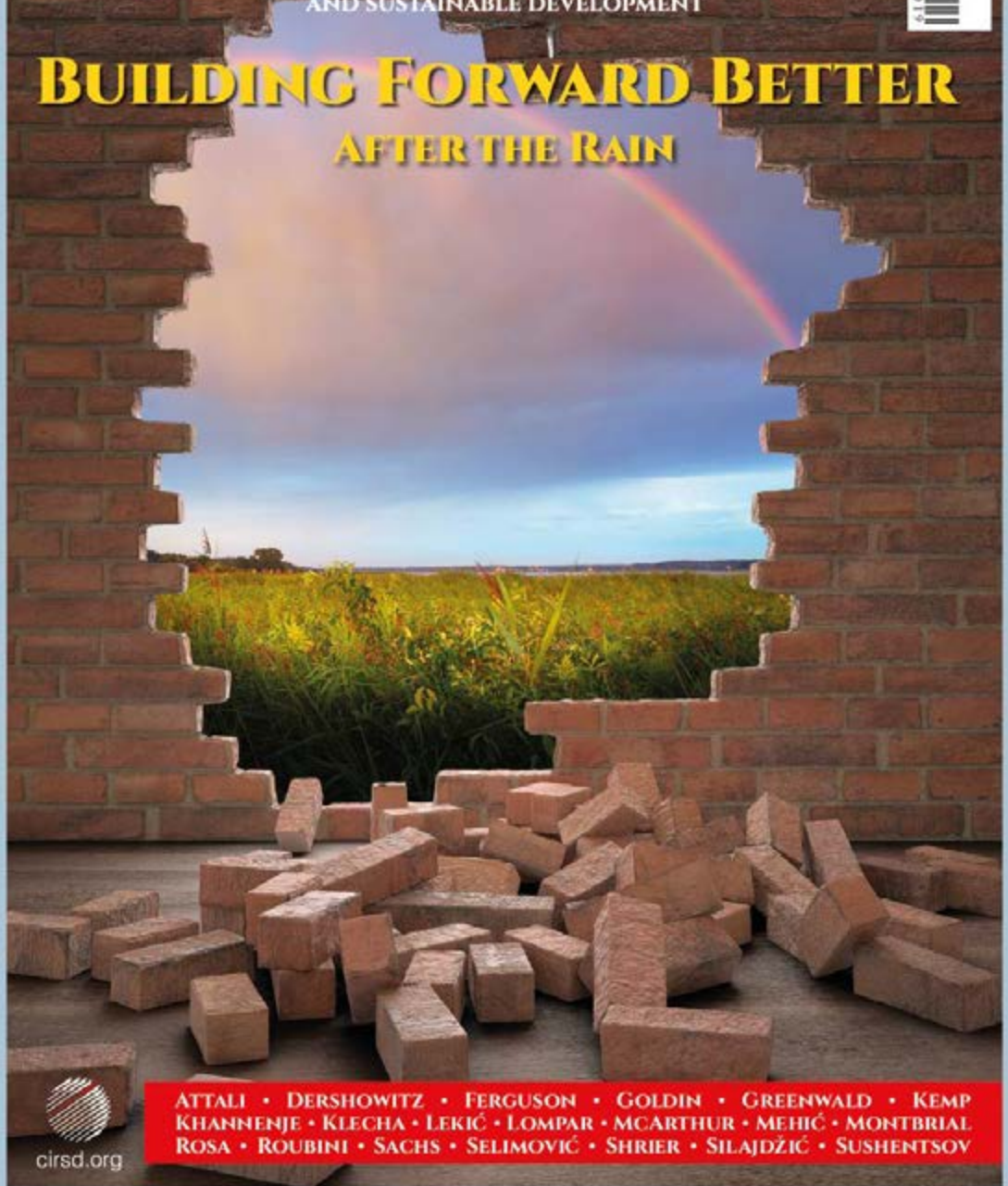

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THE ORIGINS OF COVID-19 AND THE URGENT CASE FOR U.S.-SINO COOPERATION

Jeffrey D. Sachs

AS of mid-2021 the world reached nearly 4 million confirmed deaths from COVID-19. By any standard, the global response to the pandemic has been awful. From the very start, there was a dire shortfall of global cooperation. If there is one lesson from the coronavirus pandemic, it is that our very survival depends on cooperation among the major world powers. When they fight over COVID-19, or climate change, or cybersecurity, or other crucial challenges, the entire world loses.

Throughout the pandemic, countries have acted on their own, often selfishly and shortsightedly. They have set their own COVID-19 strategies, scrambled for their own supplies (masks, ventilators, vaccines—you name it), decided on their own pandemic priorities, set their own rules for international travel, and generally failed to learn from each other about best practices—much less to come to each other's urgent assistance. While a global mechanism for vaccine distribution (known as COVAX) was established early in the pandemic, it failed in practice to deliver vaccines to the developing countries. The vaccine-producing countries used most of their vaccine production during the first half of 2021 for themselves, leaving the rest of the world waiting in line for half a year to receive immunizations.

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Photo: Guliver Image/Getty Images

Xi Jinping responding to criticism at Tinanmen during the CPC's centenary ceremony.

To make matters worse, throughout the period of the pandemic, the United States has engaged in heated criticism of China. Former President Donald Trump accused China of countless offenses and the new Biden Administration has continued Trump's harsh rhetoric vis-à-vis China. This has stymied cooperation on vital steps to end the pandemic, such as a global plan for sending vaccines to the developing nations in the second half of 2021.

One of the areas of greatest contention between the United States and China has involved the origin of the pandemic. Many American politicians—especially from the right wing—have accused China of causing the pandemic as the result of some kind of research-related incident that they believe started the pandemic. Yet these American criticisms are misplaced. If by some chance the virus did arise in the course of scientific research, it is likely that the research in question actually involved a joint program involving American and Chinese scientists working together. Rather than pointing fingers at each other, the United States and China should be cooperating with each other, not only to determine the origin of the pandemic, but in the steps urgently needed to end the pandemic and to recover from it.

POSSIBLE ORIGINS

There are two main hypotheses regarding the possible origin of SARS-CoV-2, the virus that causes COVID-19. The first hypothesis is that SARS-CoV-2 arose as a natural occurrence when the virus passed from an infected animal to a human in a natural setting, a farm, or a food market. The ultimate source of the virus is very likely to have been a horseshoe bat. A natural spillover might have involved the transmission of the virus directly from a bat to a human, or indirectly from a bat to an intermediate host (such as a wild animal or farm animal) and from there to a human.

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The second hypothesis is an infection related to research work that was underway on SARS-like viruses (that is, viruses related to the virus that caused the SARS epidemic in 2002-2004). SARS-like viruses have been under intensive study since the original SARS epidemic. The Wuhan Institute of Virology is one of the leading centers for the study of such viruses, and the possibility arises that the virus might have emerged in the course of research at the Wuhan Institute of Virology.

If we are to prevent future outbreaks, determining the source of the current one must be a high priority.

The two hypotheses also direct our attention to two different sets of concerns and policy measures, both of which require our attention. Diseases that emerge from the transmission of viruses from wildlife to humans (so-called natural zoonoses) call for precautionary measures in human interactions with animal reservoirs of potentially deadly pathogens—for example in land-clearing, farming, consumption of bushmeat, and rearing and trade of livestock. Natural zoonotic events have caused many deadly epidemic diseases in recent decades, including HIV/AIDS, Ebola, SARS, and MERS.

Emerging infectious diseases can also arise in the course of research on viruses and other pathogens. History records cases of scientists and laboratory workers being infected by pathogens they were studying. In the case of SARS-CoV-2, a research-related infection could have occurred in many ways. A researcher might have become infected while collecting samples of viruses and viral particles in natural habitats of horseshoe bats or other animals that may have harbored the virus. Or an infection may have occurred in a laboratory where scientists were working with previously collected virus-containing samples or virus isolates.

Another, related scenario involves infection of laboratory personnel with viruses collected from a natural source and subsequently genetically manipulated in the laboratory, including changes that might make a bat-origin virus more likely to infect humans.

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Both hypotheses—natural zoonosis and research-related infection—are viable at this stage of the investigation. Those who have claimed that a natural origin is the only viable hypothesis overlook the extensive research activity that was underway in the field and in laboratories on SARS-like viruses, including in Wuhan, China, where the first outbreak was identified, and in the United States. Those who claim that a research-related infection is the only viable hypothesis overlook the frequency of natural zoonotic transmissions of viruses, such as the SARS outbreak, and the many ways that a natural event could have occurred with SARS-CoV-2 somewhere in China and then been brought to Wuhan by an infected individual or an animal brought to market. Much confusion has resulted from conflating a research-origin hypothesis with a particular version of this hypothesis, in which the infection occurred following targeted manipulation of the virus to enhance its human adaptation.

Since the start of the pandemic, proponents of each hypothesis have made exaggerated, premature, and unjustified claims for their preferred hypothesis. Early in the epidemic, several scientists declared that there was overwhelming evidence that SARS-CoV-2 originated in wildlife and that alternative theories of a research-related release of the virus amounted to "conspiracy theories." Other early observers, followed by several American politicians including President Donald Trump, U.S. Secretary of State Mike Pompeo, and members of the U.S. Congress, claimed that there was enormous evidence of a laboratory release of the virus, pointing to the research activities underway in laboratories in Wuhan.

CURRENT STATE OF THE DEBATE

Some scientists noted early on that both hypotheses were plausible. The subsequent research to date into the origin of COVID-19 has so far proved to be inconclusive, not only keeping both major hypotheses alive, but also undermining strident claims by some representatives of the two main camps.

Originally, there was some hope that the SARS-CoV-2 genome itself would quickly reveal the origin of the virus, either by finding a nearly identical virus in nature (such as in a horseshoe bat or in an intermediate host such as a pangolin) or by proving definitively that the virus had undergone genetic manipulation in a laboratory setting.

Those hopes for a clear and quick resolution of the debate have so far not materialized. The SARS-CoV-2 genome is consistent with either a natural occurrence or a research-related occurrence. This is clearly the case if a researcher was infected while collecting virus samples in the field, because the virus would have arisen directly from nature, but the origin would still be research-related. To add to the complexity, the field researcher might have had a mild or asymptomatic case, so that even the researcher and his or her colleagues were unaware of the infection from the field, and that it was now being transmitted directly to other human beings.

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On the other hand, the SARS-CoV-2 genome displays no conclusive "genomic fingerprint" of artificial manipulation, such as a clear recombination of genetic material that would have been impossible in a natural setting.

For their part, proponents of the view that SARS-CoV-2 arose from a natural zoonotic event hoped that the animal harboring SARS-CoV-2 might be quickly identified—for example, on farms or in wet markets—or that the virus would be found directly in horseshoe bats. This hope, too, has so far failed to materialize, though of course it may still happen. Such discoveries often occur many years after an initial outbreak. Still, scientists are yet to identify a bat reservoir or intermediate mammalian host that may have served as the natural reservoir of the virus.

Nonetheless, there are some very important and concerning facts that have arisen during the first year and a half of the epidemic that bear heavily on the origin of the epidemic. The general public and the policy community have become increasingly aware of the intensive research on SARS-like viruses that was underway in the United States, China, and elsewhere—both in collecting viral samples from the field and in studying their infectivity and pathogenicity (ability to cause disease) in the laboratory.

We have learned that much of this work can be classified as "gain of function" (GoF) research. This generic term involves modifying viruses to acquire new biological functions, and particular attention has been focused on so-called GoF Research of Concern (GOFROC)—a category that includes research that may enhance the human transmissibility and/or pathogenicity of potential pandemic pathogens. Experiments at the Wuhan Institute of Virology involving the modification of bat-origin coronaviruses to express proteins that are likely to enhance entry into human cells are viewed by many scientists as falling squarely into the category of GOFROC.

Rather than pointing fingers at each other, the United States and China should be cooperating with each other, not only to determine the origin of the pandemic, but in the steps urgently needed to end the pandemic and to recover from it.

Many biosafety experts have long argued that such work—used to reveal target hosts more quickly, improve prediction of outbreaks, and develop vaccines and therapeutic drugs—requires much greater oversight, control, and scrutiny, including a transparent account to the public of the research activities. In the United States, the latest National Institutes of Health (NIH) guidelines—dated January 9th, 2017 and entitled *Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P2CO)*—include the proviso that, "to the maximum extent possible, agencies' enhanced PPP [potential pandemic pathogen] review mechanisms should provide transparency to the public regarding funded projects involving the creation, transfer, or use of enhanced PPPs."

We have also learned that the NIH funded American and Chinese scientists to work collaboratively on collecting samples of SARS-like viruses in the field, and bringing them back to the Wuhan Institute of Virology for advanced genetic analysis. Within the research work that took place there, studies have included the creation of chimeric genetic recombinants of SARS-like viruses to study their capacity to infect human cells and to cause disease. We have also learned that some of the viral clone work done at the Wuhan Institute of Virology took place in Biosafety Level 2 (BSL2) facilities, which many scientists consider to offer inadequate protection against a laboratory release of viruses, even if the NIH seems to approve such work in BSL2 facilities.

THE NEED FOR U.S.-CHINA COOPERATION

Neither American nor Chinese authorities have yet been sufficiently forthcoming to date to enable researchers to advance our understanding of the origin of SARS-CoV-2. In mid-May 2021, the NIH declared that it did

not support GoF research that could have led to the COVID-19 pandemic, saying that it had never "approved any grant that would have supported 'gain-of-function' research on coronaviruses that would have increased their transmissibility or lethality for humans."

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Unfortunately, the NIH has not yet revealed the actual research that it *has* financed and supported. It is in fact common knowledge in the American scientific community that the NIH has indeed supported genetic recombinant research on SARS-like viruses that many scientists describe as GOFROC. The peer-reviewed scientific literature reports the results of such NIH-supported recombinant genetic research on SARS-like viruses. But the process for reviewing the biosafety of possible GOFROC studies is opaque, revealing to the public neither the names nor qualifications of the individuals involved in the review process, nor the substance of the discussions, nor even the investigators or projects being reviewed.

More specifically, it is clear that the NIH co-funded research at the Wuhan Institute of Virology that deserves scrutiny under the hypothesis of a laboratory-related release of the virus. This research has involved the collection in natural settings of potentially dangerous SARS-like viruses and then infection experiments on these viruses, such as a November 2017 peer-reviewed article that appeared in the journal *PLOS Pathogens* entitled "Discovery of A Rich Gene Pool of Bat SARS-related Coronaviruses Provides New Insights into the Origin of SARS Coronavirus."

A recent NIH grant to co-fund work at the Wuhan Institute of Virology describes "Aim 1" and "Aim 3" of the research project as follows (excerpted from the Abstract):

"Aim 1. Characterize the diversity and distribution of high spillover-risk SARSr-CoVs in bats in southern China. We will use phylogeographic and viral discovery curve analyses to target additional bat sample collection and molecular CoV screening to fill in gaps in our previous sampling and fully characterize natural SARSr-CoV diversity in southern China. We will sequence receptor binding domains (spike proteins) to identify viruses with the highest potential for spillover which we will include in our experimental investigations (Aim 3)."

"Aim 3. In vitro and in vivo characterization of SARSr-CoV spillover risk, coupled with spatial and phylogenetic analyses to identify the regions and viruses of public health concern. We will use S protein sequence data, infectious clone technology, in vitro and in vivo infection experiments and analysis of receptor binding to test the hypothesis that % divergence thresholds in S protein sequences predict spillover potential."

(Aim 2 involves surveillance of high-risk populations that have contact with bats.)

The question about origins is not about one government or another; it is even less a geopolitical issue or a matter of blaming China and exonerating the United States.

It is also clear that NIH-supported Chinese and American scientists have much more to share about the nature of this work. This includes records of trips to horseshoe bats' natural habitats and other settings to collect specimens of SARS-like viruses; safety precautions taken or not taken during such visits; and the repository of viral samples, live viruses, genomic sequences, and other relevant genetic information. It also includes the laboratory records of experiments on SARS-like viruses, including the record of chimeric viruses produced, tested, and cultured in the laboratory; the safety precautions taken or not taken during such research; other laboratory-related data; and a full accounting of potential infections among Wuhan Institute of Virology workers.

Top researchers on Wuhan Institute of Virology projects have stated categorically that they were not dealing with viruses that are close to SARS-CoV-2. All laboratory notebooks and other relevant information should be opened by the Chinese and American scientists working on this project for detailed scrutiny by independent experts.

RIGOROUS INVESTIGATION, NOT FINGER-POINTING

The question about origins is not about one government or another; it is even less a geopolitical issue or a matter of blaming China and exonerating the United States. If there was indeed a laboratory-related release of SARS-Cov-2, it may well have occurred in a project funded by the United States government, using methods developed and championed by American scientists, and as part of an American-led and American-financed program to collect and analyze potentially dangerous viruses, including in China.

To learn as much as possible regarding the origin of SARS-CoV-2, an international and independent investigation to examine the alternative hypotheses is urgently needed, and the American and Chinese governments should cooperate fully and transparently with such

an inquiry. In the meantime, scientists, politicians, pundits, and those weighing in on social media should acknowledge the uncertainties that currently prevail.

They should also acknowledge that the tragedy of the pandemic has already shed light on how to prevent future outbreaks and pandemics. Because natural zoonotic events are inevitable, we must establish much better global surveillance and warning systems, and of course early response systems when outbreaks occur. We need credible communications channels to prevent rapid global transmission of newly emergent zoonotic diseases, and to create institutional mechanisms that enable the speediest search for potential treatments, diagnostic tests, vaccines, and other tools and best practices to contain an outbreak. In short, we must be better prepared to share relevant scientific and technological know-how in a more honest, transparent, and credible manner than has been true during the current pandemic.

China's economic and technological rise has created a dangerous psychological reaction in American politics, according to which China is viewed as an unrelenting threat to the United States rather than as a potential partner in global problem-solving.

But there is also a risk of future research-related outbreaks of pandemic diseases. Governments need to upgrade the transparency, oversight, and biosafety of any projects that actively seek dangerous pathogens in nature and return them to laboratories, recognizing the multiple risks involved. Similarly, the tools of genomic manipulation have advanced so rapidly that the potential to create new deadly pathogens in the laboratory and accidentally or even deliberately release them is a very serious concern. The world currently lacks adequate international and national safeguards and transparency on such dangerous work, and the risks are compounded by the secretive bioweapons research programs several governments sponsor that help to fund this work.

The Lancet COVID-19 Commission, which I chair, will carefully scrutinize these issues in advance of its final report in mid-2022, with the overriding aim of recommending policies to prevent and contain future disease outbreaks. The Commission's technical work will be conducted by independent experts who were not themselves involved directly in the U.S.-China research under scrutiny. The scientists who were involved should explain fully the nature of their work. In the meantime, the Commission will tap experts in biosafety to help assess the relevant hypotheses on the origins of SARS-CoV-2 and to recommend ways and means to prevent and contain future outbreaks, whether resulting from naturally occurring zoonotic events or research-related activities.

Overriding Need for Great Power Cooperation

China's economic and technological rise has created a dangerous psychological reaction in American politics, according to which China is viewed as an unrelenting threat to the United States rather than as a potential partner in global problem-solving. The result is rising acrimony between Beijing and Washington. Yet the acrimony is a dead-end, leading to an inability of the two countries to work together even on challenges of direct and urgent shared concern, such as ending the pandemic.

There are two practical hopes for restoring economic relations and diplomacy between the United States and China. The first is for American and Chinese leaders to recognize their overwhelming mutual interest in cooperating. The second is for the rest of the world to insist on such cooperation.

Either way, the benefits of greater cooperation would be very far reaching, not only speeding the end of the pandemic, but also arriving at shared solutions to climate change and global economic recovery and much else coming over the horizon in the time ahead.