U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

HEARING CHARTER

Principles for Outbreak Investigation:
COVID-19 and Future Infectious Diseases

Wednesday, July 14, 2021
12:00 p.m. EDT
Zoom

PURPOSE

The purpose of this hearing is to discuss the principles for investigating infectious disease outbreaks in the context of public interest in the origins of COVID-19. The hearing will consider how infectious diseases normally emerge; how understanding disease origins helps protect public health; methods for tracing outbreaks to a discrete origin; the scientific datasets and access that investigators need; and the principles for transparency, scientific integrity, objectivity, and public communication that accompany an ideal outbreak investigation.

WITNESSES

- **Dr. David Relman,** Thomas C. and Joan M. Merigan Professor, Stanford University School of Medicine, and Senior Fellow, Center for International Security and Cooperation, Stanford University
- **Dr. Stanley Perlman,** Professor of Microbiology and Immunology, University of Iowa
- **Dr. Connie Price,** Chief Medical Officer, Denver Health, and Professor of Medicine, Division of Infectious Diseases, University of Colorado School of Medicine
- **Dr. Suzan Murray**, Program Director, Smithsonian Global Health Program, Smithsonian National Zoo & Conservation Biology Institute.

OVERARCHING QUESTIONS

- What are the scientific questions used to determine the origins of a virus?
- What are the data sets, interviews, samples, and visual inspections that inform an outbreak investigation?
- What are the principles for transparency and data access in the investigation of an outbreak, particularly one with international consequences? What should they be?
- How do our international health treaties and global governance structures provide for information/data sharing around infectious disease outbreaks? Where do they fall short?

BACKGROUND

World Health Organization Report on Origins

In July 2020, the WHO sent an initial team of two experts to China to investigate the origins of SARS-CoV-2. However, this inquiry did not include any visit to the city of Wuhan.[1] On November 5, 2020, the World Health Organization (WHO) announced the Terms of Reference for a more fulsome Global Study of Origins of SARS-CoV-2. The charge established through negotiations between the WHO and China was:

(i) explore how the circulation of SARS-CoV-2 might have started; and
(ii) (ii) gather evidence from the cluster of cases identified in December 2019 for potential links and clues as to its origin.[2]

A team of 17 Chinese and 17 international subject matter experts were selected through a joint negotiation between WHO and China. The team established working groups on epidemiology, animals and the environment, and molecular epidemiology and bioinformatics. It convened in Wuhan and conducted its investigation from January 14 through February 10, 2021.[3] Data reviewed included national surveillance data, pharmacy records of medication purchases, and mortality and pneumonia-specific mortality rates.

On March 30, 2021, the World Health Organization (WHO) released its Global Study of Origins of SARS-CoV-2. It considered four possible Pathways of Emergence:

- Direct zoonotic transmission
- Introduction through intermediate host followed by zoonotic transmission
- Introduction through the cold/food chain
- Introduction through a laboratory accident

The WHO team found that the most likely origin of SARS-CoV-2 is a natural origin through an intermediate host. The closest related viruses in assessed wildlife were found in bats, but the evolutionary characteristics suggest that the virus may have evolved in an intermediate host before jumping to humans. The animals and environment group were not able to identify an intermediate species or detect SARS-CoV-2 in samples of bats and other wildlife across China. The WHO team opined that SARS-CoV-2 “preceded the initial detection of cases [in early December 2019] by several weeks."

The cold/food chain hypothesis, while assigned a “very low” probability by the WHO Study, was controversial in the broader research community for even being considered. A theory about viral transmission through imported frozen food was first reported in Chinese media outlets last summer and gained traction after China’s CDC released a statement October 2020.[4] Critics of the WHO process allege that the theory’s inclusion is a sign that the Chinese government had

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[1] https://www.ft.com/content/f9dea077-66fb-4734-9d1d-076dc93568e1
[2] https://www.who.int/publications/m/item/who-convened-global-study-of-the-origins-of-sars-cov-2
[3] https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part
[4] https://www.cnet.com/news/a-frozen-food-fallacy-the-coronavirus-origin-story-that-doesnt-stack-up/

undue influence over the report and may be a strategy to distract from China's handling of early coronavirus cases and shift the blame for the pandemic. Critics also note that the WHO report called the laboratory incident theory the "least likely," but failed to review all data and records from the Wuhan Institute of Virology (WIV).

Overall, according to subject matter experts[5] and the U.S. government,[6] the WHO report provided some new information on the origins of SARS-CoV-2, but did not provide sufficient evidence to justify the report's conclusions on the four considered hypotheses. Scientists and world leaders continue to call for additional data-driven inquiry, led by experts.[7]

Timeline of the SARS-CoV-2 Debate

At the start of the pandemic, SARS-CoV-2 was widely assumed to have a zoonotic origin due to its similarity to the SARS and MERS viruses. At the time, this assumption was relatively noncontroversial in the public discourse. On February 3, 2020, the White House Office of Science and Technology Policy requested the National Academies to "examine information and identify data requirements that would help determine the origins of 2019-nCoV, specifically from an evolutionary/structural biology standpoint.[8] This request was posed as part of an effort to "better understand animal/human and environmental transmission aspects of coronaviruses." There was no suggestion in the request of anything but zoonotic origin.

Alternate theories regarding a lab leak did arise in January and February of 2020, but those theories were advanced primarily by non-experts. On March 7, 2020, *The Lancet* published a statement from prominent public health scientists condemning "conspiracy theories suggesting that COVID-19 does not have a natural origin,"[9] which helped cement the appearance of a scientific consensus around natural origin. On April 30, 2020, the Office of the Director for National Intelligence issued a press release that both concurred with "the wide scientific consensus that the COVID-19 virus was not manmade or genetically modified" and acknowledged that the intelligence community was still investigating the possibility of an accidental release from a laboratory.[10] Researchers from Lawrence Livermore National Lab issued a classified report in May of 2020 that found that a lab leak was possible.[11]

When the WHO Study was published on March 30, 2021, the WHO's own Director General issued a concurrent statement saying that the lab leak hypothesis should remain under

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[5] https://science.sciencemag.org/content/372/6543/694.1
[6] http://downloads.vanityfair.com/lab-leak-theory/USG_Analysis_of_COVID-19_Origins%20Report_April_5_2021.pdf?_ga=2.180968805.399198319.1625757827-1804681798.1623079155
[7] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01419-7/fulltext
[8] https://www.nationalacademies.org/documents/link/LD006CF17B5004C7B41F63CD7E0A0F4EDF738C451F32/fileview/D20D1390AB906330493E8A40B27E965A6761F4117EA2/OSTP%20Coronavirus%20Request%20to%20NASEM_02.06.2020.pdf
[9] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30418-9/fulltext
[10] https://www.dni.gov/index.php/newsroom/press-releases/item/2112-intelligence-community-statement-on-origins-of-covid-19
[11] https://www.cnn.com/2021/06/07/politics/covid-lab-leak-theory-classified-report/index.html

consideration.[12] That same day, 14 governments, including the U.S., issued a joint statement calling for greater transparency in the next phase of the investigation.[13]

On May 13, 2021, a second letter signed by 18 renowned scientists was published in *Science* magazine, calling for an origins investigation that seriously considered "both natural and laboratory spillovers."[14] The high profile of the authors and the publication empowered a more frank discussion in the scientific community about the need for further inquiry. On May 26, 2021, President Biden tasked the Intelligence Community "to collect and analyze information that could bring us closer to a definitive conclusion" on the origins of COVID-19 and report back in 90 days.[15] On June 15, 2020, the Presidents of the National Academies of Sciences, Engineering and Medicine (NASEM) jointly called for further investigation of the origins of COVID to be conducted with a non-partisan lens and with scientific integrity.[16] On July 5, 2021, the authors of the March 2020 letter that discounted the lab leak hypothesis published a new letter in *The Lancet*. It affirmed their continued belief that COVID-19 was zoonotic in origin, but acknowledged that more information was required regardless of whether COVID-19 arose from nature or "might somehow have reached the community via an alternative route."[17]

State of the Science

The origin of COVID-19 is still uncertain. To conclusively verify a zoonotic origin for COVID-19 would require finding the animal which serves as a natural reservoir for the virus and, if applicable, identify the animal intermediary(s) through which the virus passed from the original animal to humans. In the case of the 2003 SARS virus, this effort took 15 years.[18]

A known bat coronavirus called RaTG13 was found to have 96% similarity to the genomic sequence of SARS-CoV-2.[19] Given the plethora of un-sequenced coronaviruses in the wild, the discovery of RaTG13 indicates that a predecessor of SARS-CoV-2 could still be found. Researchers continue to survey animal populations to search for an intermediate host or a coronavirus that shares the distinctive features of SARS-CoV-2.[20,21]

No direct evidence of a lab leak is known to the public at this time. The WIV's lead coronavirus researcher has denied having samples of SARS-CoV-2 or a predecessor virus in the laboratory prior to the pandemic.[22] Some proponents of the lab leak theory point to certain distinctive

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[12] https://www.who.int/news/item/30-03-2021-who-calls-for-further-studies-data-on-origin-of-sars-cov-2-virus-reiterates-that-all-hypotheses-remain-open

[13] https://www.state.gov/joint-statement-on-the-who-convened-covid-19-origins-study/

[14] https://science.sciencemag.org/content/372/6543/694.1

[15] https://www.whitehouse.gov/briefing-room/statements-releases/2021/05/26/statement-by-president-joe-biden-on-the-investigation-into-the-origins-of-covid-19/. Ninety days will expire on August 24, 2021.

[16] https://www.nationalacademies.org/news/2021/06/let-scientific-evidence-determine-origin-of-sars-cov-2-urge-presidents-of-the-national-academies

[17] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01419-7/fulltext

[18] https://www.nature.com/articles/d41586-017-07766-9

[19] https://www.nature.com/articles/s41586-020-2012-7

[20] https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25976

[21] https://www.sciencedirect.com/science/article/pii/S096098222030662X

[22] https://www.nytimes.com/2021/06/14/world/asia/china-covid-wuhan-lab-leak.html

features in the genomic sequence of SARS-CoV-2.[23] Expert virologists differ in their interpretation of the genomic sequence, with some suspecting laboratory intervention and others believing the distinctive features are not anomalous or unexpected. Non-circumstantial evidence would be needed to affirm a lab leak theory.

Researchers continue to weigh the available evidence and identify what new data needs to be collected to resolve COVID-19's origins.[24] There seems to be a general consensus among experts that a zoonotic origin remains the most likely scenario, and further study of animal coronaviruses is needed to both understand this pandemic and to prepare for the next one. However, few scientific experts who have addressed the subject publicly in 2021 have argued that a lab leak origin can be ruled out entirely. Many have suggested that it may never be possible to conclusively rule it out.

Investigations of Previous Epidemics

While the world is anxious to know as much as possible about the virus that has killed over four million people across the globe, it is important to contextualize the search for an answer. Ebola, which first emerged in 1976 and most significantly spread between 2014-2016, still evades our full understanding. It is widely understood to be a zoonotic disease, but after years of investigation, researchers have still not found the natural reservoir.[25] Investigations into SARS and MERS, both coronaviruses, can provide perspective on how outbreak investigations have been conducted in recent memory.

SARS first emerged in November 2002, detected as an atypical case of pneumonia in southern China. Over the next two years, 8,096 probable cases were detected, killing 774 people worldwide. By May 2003, a WHO consensus document discussed what was known at the time about whether SARS could be considered a zoonotic infection, and concluded that no evidence existed that wild animal species that tested positive for the virus were the source of human infection.[26] About a year after the initial infections were detected, researchers determined that the likely intermediate host of the SARS virus was the civet, sold in live animal markets in Guangdong Province, China.[27] While it was suspected early on that bats were the original source of the virus –their immune systems carry and tolerate a very high number of viruses[28] – it wasn't until 2017 that researchers identified the strains of coronavirus that likely mixed and transferred to humans. The strains were identified in samples taken from a cave 1,000 kilometers from the original outbreak.[29]

The Middle East Respiratory Syndrome (MERS) outbreak was first identified in 2012. An international team of experts was assembled and sent to Saudi Arabia to investigate the

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[23] https://www.wsj.com/articles/the-science-suggests-a-wuhan-lab-leak-11622995184

[24] https://zenodo.org/record/5075888#.YOY3-xMzaDX

[25] https://www.gov.uk/government/publications/ebola-origins-reservoirs-transmission-and-guidelines/ebola-overview-history-origins-and-transmission#natural-reservoir

[26] https://www.who.int/csr/sars/en/WHOconsensus.pdf

[27] https://science.sciencemag.org/content/302/5643/276

[28] https://www.washingtonpost.com/science/why-do-bats-have-so-many-viruses/2020/07/10/0327f584-b65e-11ea-a8da-693df3d7674a_story.html

[29] https://www.nature.com/articles/d41586-017-07766-9

outbreak's spread in Saudi hospitals. In cooperation with the Saudi Ministry of Health, researchers from the U.S., Canada, and the United Kingdom reviewed medical records, determined exposure pathways, estimated incubation periods, and sequenced the viral RNA.[30] Their findings were published in the New England Journal of Medicine in August 2013. The ability of the team to review the medical records and collect additional samples, with the cooperation of the Saudi Arabian government, was crucial in understanding how to stop the spread of a disease with a 35 percent mortality rate.[31] The importance of international collaboration and scientific transparency in the MERS investigation was noted in a 2015 National Academies workshop summary.[32]

The global scale and rate of infection SARS-CoV-2 is orders of magnitude greater than any infectious disease we have seen in recent history. However, prior investigations of smaller outbreaks help illustrate the importance of patience, scientific transparency, objectivity, and international collaboration.

China's Record on Transparency

China's record on information sharing during COVID-19 has been poor. In accordance with the International Health Regulations, China did notify the WHO of the initial outbreak on December 31, 2021. By January 11, the genomic sequence of SARS-CoV-2 had been made available, but only because it was leaked by a Chinese scientist to an Australian scientist and published online.[33,34] China agreed to participate in the WHO investigative team, but maintained veto power in the selection of experts, limited the WHO team to brief Q&A sessions, and withheld access to some of the raw data from the WIV, Huanan Market, and area hospitals with early cases. Researchers with experience working with Chinese scientists told Committee staff that they believe the information China has shared with the WHO team is as good as the international community is likely to get. One researcher suggested that a wet market origin of COVID-19 could be more consequential to China than an accidental lab leak because of the cultural significance of wet markets.

It is apparent that the Chinese government has withheld key data sets and interviews from investigators, that other important data sets were never collected, and that other evidence was destroyed, whether incidentally or intentionally. Significant details on the WIV's operations have been withheld from the WHO and other investigators. Some proponents of the lab leak theory have conflated obfuscation by China with direct evidence, but the mere "withholding of information" would not itself be a particularly applicable to the process of determining origins according to the best practices for outbreak investigations established in the CDC Field Epidemiology Manual.[35] The absence of data is not data. However, the CDC Manual does note that data inadequacy – irrespective of *why* it is inadequate – can lead to inconclusive results.

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[30] https://www.nejm.org/doi/full/10.1056/nejmoa1306742

[31] https://www.who.int/news-room/fact-sheets/detail/middle-east-respiratory-syndrome-coronavirus-(mers-cov)

[32] https://www.nap.edu/read/18975/chapter/9

[33] https://www.who.int/news/item/29-06-2020-covidtimeline

[34] https://virological.org/t/novel-2019-coronavirus-genome/319

[35] https://www.cdc.gov/eis/field-epi-manual/index.html

International Data Sharing Obligations

The WHO's International Health Regulations (IHR) of 2005 are the primary global governance framework that require data sharing at the beginning of a potential international health emergency. The language of this mandate is broad:

> *Following a notification, a State Party shall continue to communicate to WHO timely, accurate and sufficiently detailed public health information available to it on the notified event, where possible including case definitions, laboratory results, source and type of the risk, number of cases and deaths, conditions affecting the spread of the disease and the health measures employed; and report, when necessary, the difficulties faced and support needed in responding to the potential public health emergency of international concern.*[36]

WHO's Review Committee on Functioning of IHR (2005) during the COVID-19 Response has called for new technology to allow for the automatic sharing of real-time emergency information and the sharing of genomic sequencing.[37] In addition, researchers have called for new protocols standardizing the type and format of data around international health events, as well as whom they can contact in order to gain access.[38]

The cooperation of the nation where an infectious disease outbreak is first identified is indispensable to conducting any complete outbreak investigation. The United States and the World Health Organization will not resolve the details of the origins of COVID-19 without the partnership of the scientific community in China.[39]

Laboratory Biosafety

Regardless of what conclusions the scientific community may reach regarding the origins of COVID-19, the question has inspired a conversation about laboratory biosafety. The WHO defines four biosafety levels (BSLs) for laboratories according to the risk posed by organisms being handled and the types of experiments performed.[40] Based on these stratified levels of risk, WHO specifies the equipment, procedures, and design features of the lab required to conduct experiments safely. The CDC's Biosafety in Microbiological and Biomedical Laboratories (BMBL), known as the "Bible" of lab safety in the United States, articulates more detailed requirements for each BSL within its borders:[41]

- BSL-1 (lowest): Basic safety procedures and no special design features are needed.
- BSL-2: Moderate-risk agents require equipment that can decontaminate lab waste.

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[36] International health regulations (who.int)

[37] Report of the Review Committee on the Functioning of the International Health Regulations (2005) during the COVID-19 response (who.int)

[38] Wanted: rules for pandemic data access that everyone can trust (nature.com)

[39] https://slate.com/news-and-politics/2021/04/blinken-blasts-china-failure-transparency-covid.html

[40] https://www.who.int/publications/i/item/9789240011311

[41] https://www.cdc.gov/labs/BMBL.html

- BSL-3: Infectious agents with some risk of airborne transmission require biosafety cabinets, controlled air flow, and filtered ventilation system.
- BSL-4 (highest): Deadly and infectious agents with high risk of aerosol transmission require maximum containment and full-body, air-supplied suits.

The U.S. has eleven BSL-4 facilities. Each are regularly inspected with oversight from the CDC and other federal agencies as appropriate. Globally, 23 countries maintain 59 BSL-4 facilities, with further proliferation of BSL-4 facilities expected. Countries must report the existence of the BSL-4 facilities under the Biological Weapons Convention, and organizations such as International Experts Group of Biosafety and Biosecurity Regulators (IEGBBR) enable limited international coordination around best practices with BSL-4 labs. However, there is no international authority with oversight of the maintenance of BSL-4 facilities and safe practice of research involving deadly agents. As a result, laboratory biosafety practices are neither consistent nor transparent from country to country.

The March 2021 WHO Study suggested that "although rare, laboratory accidents do happen."[42] But a review conducted by the Government Accountability Office (GAO) in 2014 found that laboratory accidents are not particularly rare.[43] Broad concerns over the public health risk posed by improper laboratory handling of infectious agents are not necessarily unfounded. The last documented death from smallpox was the result of a 1978 laboratory accident in the United Kingdom.[44] The last documented outbreak of SARS before it was contained in 2004 was deemed a result of biosecurity failures at a virology laboratory in Beijing.[45] While the lab-leak theory is not supported by any direct evidence known to the public at this time, the lack of consistency and transparency around BSL-3 and BSL-4 facilities abroad has enabled global speculation that the WIV could be culpable.

Infectious Disease Outbreak Monitoring Infrastructure

In addition to analytical teams that can be dispatched to investigate after an infectious disease outbreak is recorded, standing public health surveillance systems provide information on the onset, location, and severity of outbreaks. Traditionally, surveillance systems relied primarily on syndromic surveillance, in which local health facilities track standardized lists of symptoms among their patients and provide information on potential outbreaks to public health officials.[46] However, the COVID-19 pandemic demonstrated that many patients can be infected prior to detection of an outbreak via syndromic surveillance. More proactive surveillance system would allow detection of pre-pandemic viruses before they become highly harmful to humans.

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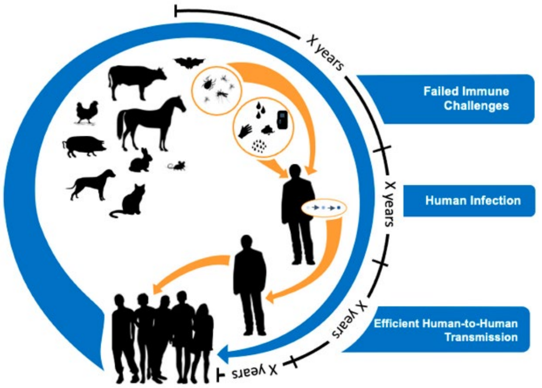
[42] https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part Page 119
[43] https://www.gao.gov/assets/gao-14-785t.pdf
[44] https://www.bbc.com/news/uk-england-birmingham-45101091
[45] https://www.sciencemag.org/news/2004/07/sars-crisis-topples-china-lab-chief
[46] https://www.cdc.gov/nssp/overview.html



Viral evolutionary theory indicates that animal viruses can become dangerous human viruses over time. It is rare for animal viruses to have the ability to successfully infect an individual human, much less have the ability for human-to-human transmission. The process of an animal virus becoming a human virus usually requires not just one but several "intermediate hosts" to enable a variant with the ability to infect a human. Moreover, the final host that allows a variant to become fully adapted to humans may be human themselves. This process of selecting for highly transmissible variants among human hosts is playing out in real time with the spread of the delta COVID-19 variant (B.1.617.2), which the CDC now estimates accounts for over 51% of cases in the U.S.[47]

Under evolutionary processes, it requires many years for an animal virus variant to have the ability to successfully infect humans, much less for it to be able to efficiently transmit among humans and to become more harmful.[48] With good surveillance in place, this lengthy process gives virologists time to detect viruses before they become dangerous to humans. For example, assays collected of Liberians in 1982 identified Ebola antibodies in over 5% of people sampled, decades prior to the West Africa Ebola outbreak in 2014. [49]

Epidemiologists have recommended integrated biological and behavioral surveillance among healthy communities to help identify potential zoonotic disease spillover at known hotspots. Assuming natural origins, this strategy may have helped detect COVID-19 virus in its earlier stages. Southern China is home to the bats known to carry SARS-like coronaviruses, such as the one that caused the 2003 SARS pandemic and the one most closely associated with SARS-CoV-2.[50] Long-term, regular surveillance at hotspots for emerging disease is the backbone of a pandemic threats warning system.

PREDICT, a project of the U.S. Agency for International Development (USAID) Emerging Pandemic Threats Program founded in 2009, works as an early pandemic prediction system.[51] Other relevant efforts include the Global Virome Project, STOP Spillover, and DEEP VZN.[48] During this century, the frequency of outbreaks are expected to increase, driven by trends of globalization, urbanization, and climate change. A more complete pandemic threats warning system could help control future infectious disease outbreaks.

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[47] https://www.npr.org/sections/coronavirus-live-updates/2021/07/06/1013582342/delta-is-now-the-dominant-coronavirus-variant-in-the-u-s

[48] https://www.mdpi.com/1999-4915/13/4/637

[49] https://theconversation.com/the-next-pandemic-is-already-happening-targeted-disease-surveillance-can-help-prevent-it-160429

[50]https://www.nature.com/articles/s41586-020-2012-7

[51] https://www.usaid.gov/sites/default/files/documents/1864/predict-global-flyer-508.pdf