MUDDY WATERS

THE ORIGINS OF COVID-19

The end of the beginning...

By The Muddy Waters Group

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Muddy Waters Group Investigation Executive Summary

Introduction

SARS-CoV-2, the virus that causes COVID-19, has caused the deaths of over 1,113,000 Americans. COVID-19 continues to cause serious illness in the U.S. and around the world. Variants of the virus can cause repeated infection in those previously infected as well as vaccinated. Three years after its emergence in Wuhan, exactly how SARS-CoV-2 first emerged as a respiratory pathogen capable of sustained human-to-human transmission remains the subject of active debate.[1] Experts have put forward two dominant theories on the origins of the virus.[2] The first theory is that SARS-CoV-2 is the result of a natural zoonotic spillover.[3] The second theory is that the virus infected humans as the result of a research-related incident.[4]

The information contained in this Source Reference Document reflects 18 months of extensive research and accompanying analyses of these two plausible hypotheses. This document was the product of a multi-disciplinary effort by medical, scientific, legal, political and general policy analysts to catalog open source (unclassified) information relevant to the respective theories. Both hypotheses are plausible. The natural zoonotic spillover hypothesis is weakened by the absence of key epidemiological and genetic data from the Huanan Seafood Market. However, data required to support a natural zoonotic source is dependent on information provided by China, and that is incomplete or contradictory. The preponderance of circumstantial evidence supports an unintentional research-related incident.

1. Epidemiology Favors Late October-Early November Emergence

China's official position is that the COVID-19 outbreak began no earlier than December 8, 2019. Several data sources, however, challenge this assertion. Epidemiological and genetic models indicate that the likely earliest incidence of SARS-CoV-2 human infections occurred mid-October to early, mid-November 2019.[5] Multiple official, technical and media outlet reports similarly suggest a late October to mid-November emergence of the virus.

Epidemiological data supplied by China to the WHO during the China-WHO 2021 joint investigation showed an increase in adult Influenza-Like-Illness (ILI) accompanied by negative laboratory influenza tests during week 46 (November 11 to 17) 2019 from a single adult sentinel Wuhan hospital.[6] This atypical finding, described as an epidemiological outlier, was noted by the WHO Scientific Advisory Group for the Origins of Novel Pathogens (SAGO) in June 2022 as an "unexplained increase in ILI in adults from Wuhan."[7]

In October 2020, epidemiologists published an analysis using China National Health Commission data showing a significant increase in ILI incidence in November 2019. The increase in reported ILI cases occurred at least one month earlier than the clinical reports of pneumonia of unknown cause by China's conventional hospital and outpatient surveillance system.[8] The number of November ILI cases was statistically significantly higher than reported in the previous 5 years (2014–2018). These same researchers recorded the peak of reported COVID-19 illnesses during Week 6 of 2020.[9] The interval from the ILI outlier noted at week 46 to the peak COVID-19 incidence is approximately 13 weeks. The researchers suggested that the November ILI spike were unrecognized initial COVID-19 cases.[10]

Using similar data, U.S. researchers analyzed WHO global influenza surveillance data early in the COVID-19 pandemic. Their study identified similar epidemiological outliers in influenza-negative ILI incidence that served as an early indicator of COVID-19 community transmission.[11] Influenza-negative ILI surveillance data from 16 of 28 countries over a four-year period (2015-2019) identified increases in influenza-negative ILI that occurred on average 13.3 weeks before the occurrence of peak COVID-19 incidence. China was not one of the 28 countries analyzed in their study.

The 13-week interval reflects the average time from the introduction of SARS-CoV-2 to the maximum incidence of recognized cases. COVID-19's clinical characteristics of asymptomatic and low acuity illness for the infected majority and severe disease occurring in a minority with pre-existing conditions may contribute to this apparent latency. In lieu of widespread diagnostic testing, the recognition of its spread would be dependent on the accrual of severe cases over time. The prevalence of the disease circulating in a community would not be recognized until the number of severe cases exceeded existing baselines or hospital capacities.

The ILI increase associated with influenza-negative laboratory tests in Wuhan during Week 46 of 2019 is approximately 13 weeks before the peak incidence of COVID-19 cases in late January-early February 2020 (Weeks 5 and 6 of 2020). Thus, this may represent the initial emergence of SARS-CoV-2 in Wuhan. Validation of this association requires additional data from China and further analysis.

Eyewitness accounts, media reports, epidemiological modeling and additional academic studies further support October 28 to November 10 as the window of emergence. Diplomats stationed at the U.S. Consulate General in Wuhan have attested to observations of what they believed at the time to be the early onset of a 'bad flu' season. The Deputy Consular Chief recalled: "By mid-October 2019, the dedicated team at the U.S. Consulate General in Wuhan knew that the city had been struck by what was thought to be an unusually vicious flu season. The disease worsened in November."[12] These observations were reported to the U.S. Embassy in Beijing during this period.

A January 2021 U.S. Department of State factsheet stated the following: "The U.S. government has reason to believe that several researchers inside the WIV became sick in autumn 2019, before the first identified case of the outbreak, with symptoms consistent with both COVID-19 and common seasonal illnesses."[13] A June 2020 published Harvard University study found an unusual increase in Wuhan hospital traffic during the same period.[14] Satellite imagery showed a significant increase in vehicles parked at major Wuhan hospitals – an indicator previously established as a proxy for hospital occupancy rates – in this period compared to October and November of 2018.[15] Search queries made on the Chinese search engine *Baidu* for terms like "cough" also increased substantially in October and November, 2019.[16]

In August 2021, a veteran *Washington Post* policy columnist reported that at least one of the WIV researchers became ill in early November, 2019 and exhibited symptoms highly specific to COVID-19, including the loss of smell and ground-glass opacities in his lungs.[17] The Office of the Director of National Intelligence's (ODNI) Updated Assessment on COVID-19 Origins cautioned that "information indicating that several WIV researchers reported symptoms consistent with COVID-19 in the Fall of 2019 is not

diagnostic of the pandemic's origins. "Even if confirmed, hospital admission alone would not be diagnostic of COVID-19 infection."[18]

Several media reports provided further suggestive evidence. An Australian journalist interviewed a frontline Wuhan doctor who conveyed that he and his colleagues saw a growing number of patients exhibiting fever and respiratory difficulties in early November, 2019.[19] The physicians realized that a coronavirus, likely SARS, was the causative agent by early December.[20] Further, a Wuhan University biostatistics professor gave an interview in which he discussed his work to compile a nationwide database of COVID-19 cases.[21] According to the epidemiologist, several suspected cases predated the earliest official cases in December, 2019. "There were two patient cases in November, with onset on November 14 and November 21, 2019, and five or six cases before December 8, 2019."[22] Two other media outlets published information from leaked hospital data from pneumonia patients in Wuhan with suspected COVID-19. These reports identified two separate suspected case-clusters in early October and November 2019.[23,24]

Unpublished People's Republic of China (PRC) Government data identified the first COVID-19 case in mid-November. A veteran *South China Morning Post* reporter reviewed an official China CDC document that showed a 55-year-old from Hubei province contracted the virus on November 17, 2019. It is the supposed earliest publicly confirmed case of COVID-19.[25] On November 25, 2019, a 25-year-old Welsh teacher in Wuhan fell ill with flu-like symptoms. The teacher developed pneumonia on December 6, 2019 and was hospitalized.[26] On January 16, 2020, the hospital informed the teacher by letter that he had been infected by the novel coronavirus.[27] The timing of the initial COVID-19 cases is not by itself revealing of the origins of the virus.

2. Precedent of Zoonotic Spillovers & Likelihood of an Animal Origin

In a vacuum, the natural zoonotic spillover hypothesis is a plausible explanation for how the COVID-19 pandemic started. Applied to the facts here, however, there are a number of gaps and anomalies in the SARS-CoV-2 outbreak. The early COVID-19 pandemic is different compared to the emergence of infectious diseases via past natural zoonotic spillovers, most notably the 2003-2004 SARS-CoV outbreak.

Recent natural zoonotic spillovers of respiratory viruses with pandemic potential have left behind evidence of where and how they occurred.[28] Though the number of such occurrences is relatively few, early or failed animal-to-human transmissions, or "dead-end" spillovers, typically leave behind serological evidence. This evidence is in the form of antibodies in humans and animals that were exposed and infected but did not effectively transmit the virus to others.[29] Failed transmissions also typically leave behind genetic evidence.[30] Samples retrieved from infected humans during the 2003-2004 SARS outbreak contained genetic mutations that reflected its circulation and adaptation in palm civets, the intermediate species, for example.[31]

It would be expected that environmental samples collected from wet markets that were positive for SARS-CoV-2 would likely show evidence of animal genetic adaptation. A study authored by the former Director of China's CDC George Fu Gao, analyzed 1,380 samples collected from the environment (923) and animals (457) within the Huanan Seafood Market in early 2020. His study identified 73 SARS-CoV-2 positive environmental samples. Three live viruses were successfully isolated from these environmental

samples. None of the samples taken from the 18 animal species found in the market were positive for SARS-CoV-2. The three live viruses from environmental isolates were sequenced. These viruses shared 99.980% to 99.993% similarity with human isolates recovered from Wuhan (HCoV/Wuhan/IVDC-HB-01) and showed no evidence of animal adaptation.[32]

Two sets of evidence that have been used to support a spillover origin are discussed later in this report: the location in the market where positive environment detections of SARS-CoV-2 were obtained; and the existence of two lineages of SARS-CoV-2 among the earliest known cases.

Like the 2003 SARS outbreak, H7N9 influenza, first reported in China in March 2013, started with multiple independent viral introductions into humans across multiple disparate locations. The total number of human H7N9 infections numbered less than 500.[33] The natural zoonotic spillovers of 2003 SARS and 2013 H7N9 influenza occurred in multiple locations over several months, while the SARS-CoV-2 outbreak originated in one location, Wuhan, over a few weeks.

A number of epidemiologists, virologists and, at first, the Chinese government have asserted that the COVID-19 pandemic originated from a natural zoonotic spillover occurring at the Huanan Seafood Market in mid- to late December 2019. They declared that this was the origin of the pandemic.[34] China Government officials have subsequently asserted that SARS-CoV-2 was imported on the surface of frozen seafood, by infected people or animals or originated from a U.S. military laboratory. Support for these alternative theories is limited to government-controlled publications in China and are not credible.[35] The limited epidemiological data provided by PRC officials continues to hamstring efforts to better understand the early trajectory of the virus. PRC officials continue to suppress and manipulate COVID-19 data.

As recently as January 2023, *Reuters* reported that "China's COVID-19 data is not giving an accurate picture of the situation there and underrepresents the number of hospitalizations and deaths from the disease, a senior official at the World Health Organization said…."[36] As stated in the WHO's June 2022, Scientific Advisory Group for the Origins of Novel Pathogens report: "To date, neither the virus progenitors nor the natural/intermediate hosts have been identified."[37]

The absence of key epidemiological and genetic data of the initial outbreak raises questions about the likelihood of the Huanan Seafood Market serving as the location of SARS-CoV-2 emergence. Data supports the presence of potential susceptible animals such as palm civets and raccoon dogs at the Huanan Seafood Market. There have been no documented positive SARS-CoV-2 animal samples from any Wuhan wet market. Nor have vendors of these animals tested positive. Further, the suspected natural hosts, bats or pangolins, were not sold at the Huanan market. The initial response efforts by local authorities to immediately close the market, remove all live animals and sanitize the facility could have impacted the likelihood of recovering viable environmental samples.[38] The genetic sequencing of environmental samples recovered from the Huanan market, however, shows them identical to recovered human clinical samples.[39]

To date, China has not acknowledged the infection or positive serological sample(s) of any susceptible animal prior to the recognized outbreak. Genetic analysis of published SARS-CoV-2 sequences from the early outbreak does not show evidence of genetic adaptation reflecting passage through a

susceptible animal species such as a palm civet, raccoon dog or mink.[40,41] To this end, no intermediate host has been identified.[42]

Despite these facts, three data points do present themselves to support the zoonotic origin theory. First, approximately 33 percent of the earliest known human COVID-19 cases (with symptom onset dates in mid- to late-December 2019) were associated with the Huanan Seafood Market in Wuhan.[43] Second, several animal species susceptible to SARS-CoV-2 were sold live and in poor animal welfare conditions at the market.[44] Finally, the identification of genetic sequences of raccoon dogs in samples taken from the market in early 2020 confirm that this susceptible intermediate host was at the market at the time of the outbreak. As noted, "there is no data…associating SARS-CoV-2 with the presence of any of these animals."[45] These data themselves, however, do not explain the origin of the COVID-19 pandemic.

3. Plausibility of a Research-related Incident & Laboratory-acquired infections

There are a substantial number and diverse ways research-related incidents can occur.[46] Incidents that result in infections are classified as laboratory-acquired infections. According to published research, the cause of **over 80% of laboratory-acquired infections (LAI) are never conclusively determined**.[47] Only 18% of the infections were due to identified accidents caused by carelessness or human error.[48] Factors that contribute to the risk of such incidents are several-fold. Younger workers, those with less technical training and men experience more accidents than older workers, those with more training or women.[49] The recognition and isolation of a new infectious agent can result in a LAI caused by the new isolate but not be recognized, for example.[50]

The risk of exposures to infectious agents is a function of safety training, safe work practices, safety equipment and laboratory design. Infectious agent research includes exposures to higher concentrations of infectious agents than found in clinical diagnostic laboratories.[51] The common routes of exposure are ingestion, percutaneous inoculation (needle-sticks, cuts, animal scratches and bites) and inhalation.[52] Of these, inhalation represents the most insidious avenue of infection because aerosols and droplets are often invisible and difficult to detect.[53]

China's entry into highly pathogenic agent research did not formerly start until the 1980's, several decades after many developed countries began their efforts.[54] China lagged behind in biosafety concepts, relevant standards, practices for high-containment laboratories and research and development of biosafety equipment.[55] As a consequence, China could only domestically produce a portion of biosafety equipment needed and were dependent on foreign sources.

After the 2003 SARS outbreak, China prioritized constructing a national network of biosafety containment laboratories. It created an expert laboratory biosafety team. Laboratory biosafety laws, regulations, standards, and guidelines were drafted and published. Despite these achievements, China's progress in biosafety advanced slower than its aspirations for and efforts in research of highly pathogenic microorganisms. Its capacity for innovation remained weak.[56] The creation of independent intellectual property rights supporting research and development of domestic biosafety techniques and equipment fell short of western countries.[57] China still faced many laboratory biosafety challenges that was subject to both international and national concern.

While any laboratory is susceptible to LAI's, as early as 2015, some western scientists called into question whether the potential benefits to be gained from the WIV's coronavirus research involving the genetic manipulation and creation of chimeric viruses was worth the considerable risks to public health.[58] In 2017, other scientists warned of the potential dual-use applications of such research, and worried about "pathogens escaping" in light of China's history of laboratory leaks, particularly several LAI involving SARS.[59] These warnings coincided with the opening of the WIV's Biosafety Level (BSL) 4 laboratory in January 2017.[60] A January 2018 U.S. Department of State cable reported that "the new lab had a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory."[61] The cable further cautioned that the WIV's work with bat coronaviruses potentially posed a risk of a SARS-related pandemic.[62] The WIV's research focused principally on bat coronaviruses, but other Wuhan institutes (Wuhan and Huazhong Agricultural Universities) and agencies (Hubei and Wuhan Centers for Disease Control) conducted research on animal-related coronaviruses.

In March 2019, then CCDC Director George Gao warned about potential natural, accidental, and deliberate biological threats. He specifically identified laboratory risks:

> A potential major risk stems from stocks of concentrated infectious pathogens stored in laboratories and the absence of adequate biosecurity measures. Non-compliance of approved biocontainment and biosafety protocols could result in accidental or deliberate release of pathogens into the environment…[G]enetic modification of pathogens, which may expand host range as well as increase transmission and virulence, may result in new risks for epidemics…synthetic bat-origin SARS-like coronaviruses acquired an increased capability to infect human cells. Thus, modifying the genomes of animals (including humans), plants, and microbes (including pathogens) must be highly regulated.[63]

In May 2019, Yuan Zhiming, the General Secretary of the Communist Party of China (CCP) Committee of the Wuhan Branch of the Chinese Academy of Sciences (CAS), thus responsible for oversight of CAS activities in Wuhan, and Director of the WIV National Biosafety Laboratory (BSL-4); echoed Gao's concerns. Zhiming specifically expressed issues with China's biocontainment labs. He described uncertain funding for laboratory construction, operation, and maintenance. He highlighted neglected maintenance, insufficient operational funds, and a lack of specialized managers and engineers to operate BSL-3 labs.[64] Zhiming also urged authorities to "promptly revise the existing regulations, guidelines, norms, and standards of biosafety and biosecurity."[65]

On April 3, 2019, the WIV held its annual conference on laboratory security and safety.[66] The WIV's director delivered opening remarks stating that "the safety work of the institute is the precondition and guarantee for succeeding at all of the other work at the institute."[67] She continued with the theme of holding researchers accountable for safety incidents, demanding that, "all operations inside the laboratory must be carried out in strict adherence to professional standards and procedures with no tolerance for any kind of wishful thinking and that steps must be taken, to strengthen safety management for students."[68]

That same month, the WIV submitted 13 of 17 total patents submitted in 2019 for biosafety related improvements. The applications covered a range of remedial actions for physical containment (hermetically sealed doors), wastewater treatment, decontamination (autoclaves and chemical showers), and maintaining negative air pressure in the high-containment laboratories (exhaust air management). The number of patents, by itself, is not unusual. High-containment laboratories constantly seek to improve, through innovation, the biosafety posture of their facility. The nature of the issues and problems the WIV was remediating is revealing to their state of biosafety at that time.

One patent addressed the problem of maintaining airtight seals on gas-tight doors and cites the potential problem of existing door seals that developed slow leaks over time. Another patent addressed developing a manually operated auxiliary exhaust fan to maintain negative pressure and improve disinfection of biosecurity laboratories' HEPA filters.[69] Another described improving the design and operation of biosafety autoclave sterilizers. This patent described problems of being unable to achieve required sterilization temperatures, potential leaks around the autoclave doors and excessive condensation of autoclaved infectious materials.[70]

Despite these apparent biosafety challenges, the WIV's research continued apace to identify potential human pandemic-causing SARS-related coronaviruses and medical countermeasures to mitigate them. In pursuit of this task, researchers collected hundreds of SARS-related bat coronaviruses from across China and Southeast Asia. The risk of research-related incidents begins with field expeditions where researchers first collect bat samples. The WIV and other Wuhan institute (CCDC) researchers operated in a challenging setting with limited light and sometimes only with partial personal protective equipment and exposed skin. It also placed researchers at considerable risk for potential bites, scratches and needle-stick injuries while collecting field samples from bats.

As a result of field expeditions by 2019, the WIV had collected, at a minimum, approximately 20,000 bat and other animal virus samples from across China.[71] The WIV's formerly public database reportedly contained more than 2,000 entries consisting of sample and pathogen data, including full and partial viral genomic sequences, collected from bats and mice. The database also reportedly held an estimated 100 unpublished sequences of the beta-coronavirus subgenus to which SARS-CoV-2 belongs.[72] The existence of these undisclosed sequences raises the possibility that strains may exist that are closer progenitors to SARS-CoV-2.

After collection, samples were transported back to Wuhan. These isolates routinely underwent initial evaluation in BSL-2 settings where they were first evaluated, usually by graduate students, for the presence of SARS-related beta coronaviruses. If viruses were present, researchers then attempted to isolate and sequence the virus. [73] Full length viruses were then grown in a variety of cell cultures including human cells to assess the ability to infect different cell types. Viruses that could infect human cells would then be tested for pathogenicity in humanized mice or susceptible intermediate hosts such as palm civets in BSL-3 laboratories.[74] Finally, researchers evaluated the effectiveness of existing medical countermeasures against these newly discovered viruses.

If researchers failed to recover a full-length viral sequence, they would attempt to isolate the spike protein or the part of the spike that attached to the cell (the receptor binding domain) of the discovered viral

fragment. To evaluate the pandemic potential of non-viable coronavirus fragments, researchers spliced the sequence of the spike protein or its receptor binding domain onto already characterized viable SARS-related viruses creating chimeric viruses that could grow in cell culture.[75] Starting no later than 2017, WIV researchers created chimeric viruses that had potentially greater human affinity (transmissibility) and virulence.[76] The resulting chimeric SARS-related viruses would then be evaluated for its infectivity in human cells and pathogenicity in humanized mice.

In 2018, their research interests expanded with the intent to artificially insert genetic sequences for human furin cleavage sites to evaluate their pandemic causing potential in SARS-related coronaviruses. Furin cleavage sites (FCS) are found in other human pathogens such as avian influenza, HIV and Ebola viruses and are known to increase their infectivity.[77] In 2018, no SARS-related virus had been found with a complete FCS. Another Wuhan research institute demonstrated the precedent of inserting an FCS into an animal (pig) alpha coronavirus in 2015, for example.[78]

In March 2018, EcoHealth Alliance with the WIV as a collaborating institute submitted a grant proposal titled "Project DEFUSE: Defusing the Threat of Bat-borne Coronaviruses" to the Defense Advanced Research Projects Agency (DARPA).[79] Beside expanding the process of evaluating newly discovered spike proteins on chimeric SARS-related viruses, researchers proposed artificially inserting "human-specific" FCS to evaluate their effects on viral growth in human cells and pathogenicity in humanized mice.[80] These experiments could create chimeric SARS-related viruses with FCS that had not yet been found or perhaps did not exist in nature. DARPA did not approve or fund this proposal.

One of the notable genetic findings of SARS-CoV-2 is the presence of an FCS. It is the first SARS-related beta coronavirus found with one.[81] Its presence in SARS-CoV-2 has been the subject of active scientific and public debate since the beginning of the pandemic. It is assessed to be an essential characteristic resulting in the high human infectivity and pathogenesis of SARS-CoV-2.[82] "The presence of a furin cleavage [site]… is therefore highly unusual, leading to the smoking gun hypothesis of manipulation that has recently gained considerable attention as a possible origin of SARS-CoV-2."[83] The intent to insert an FCS highlights the additional risks experimenting with chimeric viruses with enhanced infectivity.

Widely accepted biosafety guidelines hold that initial evaluation of SARS-related bat coronaviruses should be conducted in at least BSL-3 laboratories because of the risk of creating infectious aerosols.[84] National Institute of Health guidelines specify, however, that research that create chimeric SARS-related coronaviruses that results in a virus that can infect human lung cell culture or humanized mice should be conducted in BSL-3 level conditions or above.[85] Experiments conducted at enhance BSL-3 conditions at a U.S. university in 2015, spliced a spike protein from a fragment of a SARS-related virus onto a viable (backbone) beta coronavirus that was then grown in culture. Performing this experiment at an enhanced BSL-3 level was justified because the resulting SARS-related chimeric virus could infect human airway cells and had the potential to "cause pathogenesis *in vivo* and escape current therapeutics."[86]

By contrast, the WIV's biosafety guidelines apparently allowed its researchers, including graduate students, to conduct initial evaluation of SARS-related bat coronaviruses in BSL-2 laboratories.[87] For example, a WIV graduate student conducted similar coronavirus research as the U.S. university, creating chimeric SARS-related viruses able to infect human cells.[88] The WIV graduate student described the

process of "rescuing" coronaviruses that were difficult to isolate, adapt and grow in a laboratory in a 2017 dissertation.[89] The student indicated that "[t]he proliferation and cell infection experiments of live [SARS-related] virus (including recombinant viruses) were performed in [WIV's] BSL-2…laboratory in compliance with [WIV] biosafety regulations."[90] In a written interview provided to *Science* and published July 31, 2020, Shi Zhengli confirmed that at least some of the WIV's coronavirus research were performed in BSL-2 conditions.[91] Only after the outbreak of COVID-19 did laboratory safety guidelines in China require coronavirus research to be conducted at minimum of BSL-3 conditions.[92]

At least until the COVID-19 pandemic, it is apparent that researchers at the WIV were working with SARS-related coronaviruses in inappropriate biosafety levels. One goal of this research was to identify and evaluate SARS-related viruses that were more capable of infecting human cells. In the two years leading up to the pandemic, publications by and interviews with WIV's researchers attest to increasingly sophisticated coronavirus experiments using humanized mice, bats, and palm civets to achieve this goal.[93,94]

4. Summation of Events Leading to the Pandemic

The full scope and scale of animal experiments conducted at the WIV in 2018 and 2019 are unclear. As of 2018, the WIV was infecting transgenic mice that expressed human ACE2 receptors, the receptors known to be utilized by SARS coronaviruses to gain entry into human cells and palm civets with chimeric SARS-related coronaviruses.[95] The limited published information on the results of these experiments indicate that SARS-related bat coronaviruses could infect and cause low pathogenicity in humanized mice and no pathogenicity in civets.[96] The full results of these experiments have never been published even though Shi Zhengli said they would be.[97] Consequently, the WIV as a sub-grantee of NIH grants, was terminated for failing to produce its laboratory notes and other records relating to these experiments.[98]

Nonetheless, it is clear that the convergence of sophisticated coronavirus research, government demands for scientific breakthroughs and biosafety problems at the WIV appears to have peaked in the late-summer or early-fall of 2019.[99] From June to August, 2019, WIV leadership published multiple reports expressing concerns about biosafety shortcomings due to limited availability of equipment and trained personnel.[100] Multiple PRC government medical and public health entities in Wuhan began procuring pathogen detection (polymerase chain reaction-PCR) instruments and conducting infectious disease outbreak exercises and drills.[101]

In mid-September of 2019, the WIV took their sample and sequence database offline and enhanced physical security of its campus. Wuhan officials conducted an emergency response drill on September 18, 2019 at its international airport that included identifying and responding to an arriving passenger infected with a novel coronavirus.[102] Also in September 2019, China's National People's Congress reviewed draft legislation to strengthen the management of laboratories involved in pathogen research and improve adherence to national standards and requirements for biosafety. It specified that:

> [L]ow-level pathogenic microorganism laboratories shall not engage in pathogenic microorganism experiments that should be conducted in high-level pathogenic microorganism laboratories…High-level pathogenic microorganism laboratories engaging in experimental activities of highly

> pathogenic or suspected highly pathogenic microorganisms shall be approved by the health or agriculture and rural authorities at or above the provincial level. For pathogenic microorganisms that have not been discovered [not found in nature] or have been eliminated…relevant experimental activities shall not be carried out without approval.[103]

During the week of November 11 to 17, 2019, two publications of interest were noted. A November 12, 2019 report first published in August 2019 was reposted by the WIV BSL-4 laboratory's Communist Party Branch. It explicitly referenced the challenges that the researchers had to overcome in establishing their laboratory: the "three no's." As they described it, "no equipment and technology standards, no design and construction teams, and no experience operating or maintaining" a high-containment laboratory.[104] In this same post, they described overcoming these challenges but unlike the August version it detailed the risk of potential laboratory leaks and infections and possible past biosafety incidents involving "high pathogen microorganisms."[105] The post also described that "every time this has happened" the BSL-4 Party members would respond.[106]

A few days later, a second article was published on November 15, 2019 in a Wuhan daily newspaper. Entitled "Explore the Institute of Model Animals of Wuhan University, which ***used*** to be one of the battlefields against SARS" (emphasis added). The article detailed the historic role of the Institute in SARS–related vaccine research. It also stated that the animal BSL-3 laboratory had undergone renovations in 2015 and was "currently" awaiting "final process of re-approval."[107] This inaccurate, possibly deceptive story, contradicts 2018 published research in the journal *Virologica Sinica* describing a SARS-related vaccine challenge study in Rhesus monkeys performed at the University's Institute in 2017.[108]

On November 19, 2019, the WIV hosted a special senior leadership biosafety and security training session. The session was led by the senior CAS biosafety/biosecurity official who traveled from Beijing to relay "important oral and written instructions" (*pishi*) from senior PRC leadership to the WIV regarding the "complex and grave situation facing [bio]security work".[109] From the report, CCP leadership were made aware of "safety and security work" issues at the WIV.[110] At the same session, the Deputy Director of the WIV's Office of Safety and Security "pointed to the severe consequences that could result from hidden safety dangers, and stressed that the rectification of hidden safety risks must be thorough, and management standards must be maintained."[111] The November 19, 2019 senior leadership session was followed by a two and a half day remedial biosafety training course for WIV researchers and individuals from other Wuhan research institutes, including the Wuhan University.

November 19, 2019 is the same day that the WIV issued a short suspense, sole source procurement notice for an air incinerator to address some problem or failure of a biosafety autoclave at the WIV's original downtown campus. The need to install air incineration to the autoclave exhaust after serial HEPA filtration suggests some concern about the risk of an infectious aerosol escape. This procurement may be related to an April 2019 WIV patent describing changes in the design and operation of biosafety autoclaves at the WIV.[112] The changes appear to be at variance with standard biosafety autoclave procedures.

Two other WIV patents submitted on November 15, and December 11, 2019 address the potential for research-related accidental puncture wounds and a failure of HEPA filtration for specialized animal-

related biocontainment transportation equipment due to possible corrosion.[113,114] These patents raise the possibility of other potential biosafety issues occurring contemporaneously with the initial outbreak of SARS-CoV-2.

An additional WIV patent submitted a year later on November 13, 2020, outlined the need to reformulate a liquid disinfectant used in high containment laboratories. As described, long-term use of the disinfectant caused "corrosion of metal components such as stainless steel, thereby reducing the protection of … facilities and equipment…shorten its service life and cause economic losses, but also lead to the escape of highly pathogenic microorganisms into the external environment of the laboratory, resulting in loss of life and property and serious social problems."[115] Whether this particular WIV patent reflects remedial actions to address corrosion problems identified in the December 2019 patent is not known.

November 2019 also appears to be the timeframe that PLA researchers began development of at least two SARS-CoV-2 vaccines. People's Liberation Army (PLA) Professor Zhou Yusen, Director of the 5th Institute at the Academy of Military Medical Sciences (AMMS), worked with the WIV, and possibly at the WIV, episodically, for several years prior to the pandemic.[116] Zhou or AMMS researchers may have been working at the WIV no later than the Fall of 2019 conducting research for a paper that he coauthored with two WIV researchers, Shi Zhengli and Chen Jing, on a known adverse effect of SARS-related vaccines and antibody treatments.[117] There is reason to believe Zhou was engaged in SARS-related coronavirus animal vaccine research with WIV researchers beginning no later than the Summer or early Fall of 2019. Zhou submitted one of the first COVID-19 vaccine patents on February 24, 2020.[118]

The patent includes mouse-derived serological data from vaccine-related experiments which experts, consulted with during this investigation, assess could not have been completed unless Zhou's team began work on vaccine development before the known outbreak of the COVID-19 pandemic in late-December 2019. The research required both access to the sequence of and the live SARS-CoV-2 virus. Several experts assessed that Zhou likely would have had to start this vaccine development research no later than November 2019 to achieve the February patent submission date. Zhou later published transgenic mouse infection and vaccine challenge studies in mice, including humanized mice and non-human primates.[119,120,121] The location(s) where Zhou's animal vaccine challenge studies were performed was not disclosed.[122,123] There is reason to believe that these vaccine experiments were performed at the original WIV's downtown Wuhan campus and possibly at the Wuhan University Institute of Animal Models located approximately a mile from the WIV.

PLA AMMS Major General Wei Chen led a second, separate, effort to develop another candidate COVID-19 vaccine. Chen collaborated with the China state-owned biopharmaceutical company SinoPharm. Chen's vaccine experiments with humanized mice, ferrets and non-human primates occurred at the Harbin veterinary research facility BSL-4 laboratory in northern China.[124] Human clinical trials began in mid-March 2020. Chen submitted a patent for her vaccine March 18, 2020.[125] Based on this timeline, experts believe Chen would have had to begin her vaccine efforts no later than early December 2019. Chen's vaccine candidate was also dependent on the availability of SARS-CoV-2's genetic sequence that would not be published until January 11, 2020. However, unlike Zhou, there is no evidence that Chen's vaccine efforts were associated geographically or temporally with the initial COVID-19 outbreak in Wuhan.

During the same time period as experts suggest Zhou began vaccine development against a SARS-related coronavirus in late fall 2019, likely at the WIV, Wuhan experienced an increased incidence of influenza-like-illness (ILI).[126] The U.S. State Department and other media reporting indicated cases of COVID-19 may have occurred as of mid- to late October or early to mid-November 2019.[127,128] As noted earlier, an ILI spike coincided with negative influenza reporting for week 46 of 2019 (November 11 to 17). This epidemiological outlier comports with published analysis suggesting it may be an early indicator of COVID-19 community transmission.[129] This increased ILI incidence occurs approximately 13 weeks before the recorded surge of COVID-19 cases in Wuhan in early February 2020. Validation of this finding, however, is precluded by the lack of access to the underlying source data provided to the WHO from China.

Despite evidence supporting the plausibility of both hypotheses, critical gaps in data and information remain particularly substantiating a zoonotic outbreak. Further investigation and examination are required to address outstanding questions pertaining to both possibilities. The confluence of potential ILI incidence in Wuhan in early to mid-November coincides with anecdotal reports of early cases of COVID-19. It also comports with several accepted epidemiological and molecular models estimating COVID-19 initial emergence in Wuhan. It also coincides with remedial and response-related actions taken by WIV and PRC governmental officials.

The preponderance of information supports the plausibility of an unintentional research-related incident that likely resulted from failures of biosafety containment during SARS-CoV-2 vaccine-related research. The identified underlying biosafety issues increased the likelihood that such containment failures were not immediately recognized. The possibility of unrecognized biocontainment breaches combined with SARS-CoV-2's clinical characteristics of asymptomatic and mild clinical illness in the majority of infections, likely confounded early recognition and containment of the initial outbreak. Such initial unrecognized infections could serve as the nidus of the outbreak of COVID-19 in Wuhan and is a plausible proximate cause of the pandemic.

a. Table 1. Pros & Cons of Zoonotic Origin Hypothesis

PROS	CONS
Historical Precedent; SARS & MERS	No animal intermediate host identified:
Bat coronavirus like RaTG-13 & Banal series with >96% similarity to SARS-CoV-2 found in nature	No animal or human serological (antibody) evidence of infection in either human or animals associated with the live animal supply chain of the Huanan animal market prior to the recognized outbreak
Presence of susceptible (palm civets, raccoon dogs & mink) live animal markets in Wuhan	Timing: December market associated cases unlikely first cases of COVID-19
Wet Market animals maintained in poor conditions	Geography: Location of outbreak (Wuhan) considered negligible risk for natural bat coronavirus emergence
Positive environmental samples from the market from the western section that traded wildlife/animal products implicating the presence of racoon dogs in proximity of environmental samples positive for SARS-CoV-2	Lack of genetic adaptation to animal species (higher initial affinity for human tropism & transmission SARS-CoV-2 > SARS)
Mutations post human spillover increased viral fitness in humans	Lack of multiple emergence/introduction events found in previous zoonotic related outbreaks.
	Lack of documented infection in wet market animals or animal vendors or handlers
	Presence of Furin Cleavage Site
	High degree of human homology of environmental samples from the Huanan Seafood Market center around bathrooms
	China's competence investigating previous zoonotic outbreaks. (e.g., 2016 & 2019 Swine Acute Diarrheal Syndrome)

b. Table 2. Pro & Cons of Research-related Origin Hypothesis

PROS	CONS
Biosafety issues at the WIV & other laboratories	Lack of published/known precursor or backbone virus like SARS-CoV-2 at the WIV
Required remedial biosafety training & possible corrective actions (air incinerator etc.)	Zoonotic Historical Precedent; SARS & MERS
Documented WIV Coronavirus recombinant research	Bat coronavirus like RaTG-13 & Banal series found in nature
Conducted in BSL-2 settings	Presence of susceptible (palm civets, raccoon dogs & mink) live animal markets in Wuhan
Geography: Location of outbreak in Wuhan (Wuchang District)	Wet Market susceptible animals maintained in poor conditions
Presence of Furin Cleavage Site	
High degree of genetic homology of initial strains	
Animal cases secondary to human exposure (mink, cats, hamsters etc.)	
Flawed high-containment (BSL-3 & 4)laboratory design with possible documented biocontainment failures/vulnerabilities	
Reports of WIV researchers becoming ill with symptoms and clinical findings (loss of small and ground-glass opacities on chest x-rays)	

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