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Searching for SARS-CoV-2 origins: confidence versus evidence



In our July, 2022, Editorial—entitled *Searching for SARS-CoV-2 origins: the saga continues*—we wrote: “To discover the source of an outbreak we must work forward without preconceptions, following wherever the evidence leads”. Last month, several news outlets reported that two US agencies investigating the origins of SARS-CoV-2, the Energy Department and Federal Bureau of Investigation (FBI), had information suggesting that the COVID-19 pandemic had resulted from a laboratory leak. With current genome editing technology it is easy to manipulate a virus in a laboratory, but it is much easier to manipulate public opinion with political language.

Given the extent of the COVID-19 pandemic it is understandable that updates in SARS-CoV-2-origins research will be of wide public interest. In 2021, the US Energy Department did not favour any hypothesis on the origins of SARS-CoV-2 but, in March, 2023, this stance changed and the government agency updated their position to favouring with “low confidence” that the virus originated from a laboratory in China. The FBI agrees with the laboratory hypothesis with “moderate confidence”. This language—ie, the unclear, unquantified, and unsubstantiated scale of confidence—is ambiguous and unhelpful. The headline-grabbing proclamations have not been supported by any newly published data and the reports on which they are based remain classified, ironic given the disapproval the USA has expressed over the lack of transparency from China.

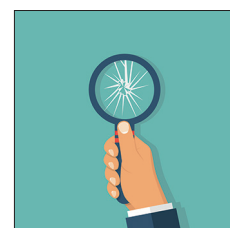
Peer-reviewed evidence available to the public points to the hypothesis that SARS-CoV-2 emerged as a result of spillover into humans from a natural origin. A geospatial analysis reports that 155 early COVID-19 cases from Hubei Province, China, in December, 2019, significantly clustered around a food market in Wuhan, China. Many genomic studies report that SARS-CoV-2 has nucleotide differences that could only have arisen through natural selection and such differences are evenly spread throughout the genome. Phylogenetic studies map these nucleotide changes and suggest that they have not diverged from the bat coronavirus RaTG13 that was being researched at the Wuhan Institute of Virology, suggesting it is unlikely that SARS-CoV-2 emerged as a result of this research and instead they shared a common ancestor. Taken together, these findings support the

hypothesis that SARS-CoV-2 was the result of enzootic circulation before spillover into people.

It might never be established exactly when and how SARS-CoV-2 entered the human population, particularly if samples from the market animals remain unanalysed. But, if incontrovertible evidence did emerge in favour of either hypothesis, what would change in terms of protecting future human health? Suggestions that knowing the precise origin of SARS-CoV-2 would help prevent the next pandemic are dubious given the difficulty in predicting which unknown pathogen will emerge as the next threat. Another suggestion that knowing the origin will provide some healing to the people who were affected by the COVID-19 pandemic has more weight, but will ultimately not reverse the loss that many people experienced. An evidence base that supported the laboratory hypothesis might result in stricter regulations for research of biorisks, and an evidence base that supported the natural hypothesis might result in stricter surveillance of the human–animal interface. Both these public health measures should already be in place and are now being revisited following the COVID-19 pandemic.

The hypotheses debate is reminiscent of the discussions on the origins of HIV. In the late 1980s and '90s a now-debunked hypothesis that a batch of the oral polio vaccine introduced HIV similarly captured media attention but was eventually refuted following publication of many robust genomic and phylogenetic studies. There is a key difference between searching for the origins of HIV versus SARS-CoV-2. When HIV/AIDS emerged, HIV affected a subsection of the population and public activism was needed to put AIDS on political agendas. Such advocacy is not needed for COVID-19, which is so ingrained in politics and the media that government intelligence reports are being written and partially communicated to the public. However, one lesson the HIV/AIDS epidemic offers is that establishing the origin of a pathogen requires many studies over a period of time; then, once a large evidence base is gathered and can be objectively interpreted, a consensus can eventually be reached. It is difficult for such a consensus to be reached for SARS-CoV-2 if empty rhetoric that does not present informative data continues to be relayed to the public. ■ *The Lancet Microbe*

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