

## An Analysis of the Facts and Circumstances of the Worobey Science Perspective Paper Suggests it Makes No Contribution to the Investigation of the Origin of SARS-CoV-2

By Steven Quay, MD, PhD<sup>1</sup>

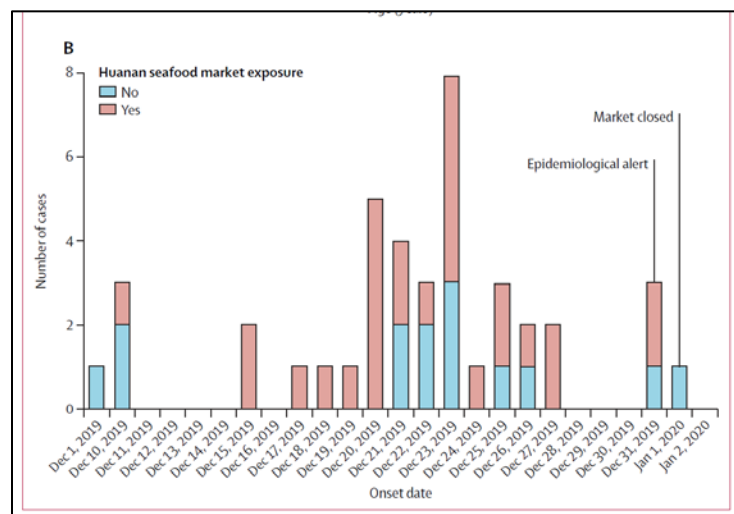
### Background:

- On January 24, 2020, a paper was published<sup>2</sup> in *The Lancet* with the first description of the hospitalized, clinical course of COVID-19. This paper was authored by 29 Chinese physicians from 16 prestigious hospitals and medical schools in China. This paper has never been amended or corrected. Here is the title and authors.

### Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China

Chaolin Huang\*, Yeming Wang\*, Xingwang Li\*, Lili Ren\*, Jianping Zhao\*, Yi Hu\*, Li Zhang, Guohui Fan, Jiuyang Xu, Xiaoying Gu, Zhenshun Cheng, Ting Yu, Jiaan Xia, Yuan Wei, Wenjuan Wu, Xuelei Xie, Wen Yin, Hui Li, Min Liu, Yan Xiao, Hong Gao, Li Guo, Jungang Xie, Guangfa Wang, Rongmeng Jiang, Zhancheng Gao, Qi Jin, Jianwei Wang†, Bin Cao†

- Data Collection for above paper:** “Two researchers also independently reviewed the data collection forms to double check the data collected. To ascertain the epidemiological and symptom data, which were not available from electronic medical records, the researchers also **directly communicated with patients or their families to ascertain epidemiological and symptom data.**” [emphasis added.]
- For those claiming SARS-CoV-2 was present in an intermediate animal host and that it spilled over at a live animal market, an ‘inconvenient truth’ from this paper was that three of the first four patients with COVID had NO association with the Huanan Market. See this figure from the paper:



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<sup>2</sup> [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(20\)30183-5.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)30183-5.pdf)

- Again, this data has never been challenged or retracted. It has been ignored, however.

## The Worobey Paper

### Timing of the First Patient

- Michael Worobey, evolutionary biologist from University of Arizona, published a short, peer reviewed “Perspective” in Science<sup>3</sup> claiming he knows the COVID-19 pandemic began at the Huanan Seafood market in Wuhan, China. This is based on his assertion that the first patient identified with COVID, an accountant with no connection to the market, was not really the first patient. He now claims the first patient was a vendor in the market.
- Worobey limits his analysis to the early cases as reported in the WHO report, which was published 14 months after the above, contemporaneous report. By the time of the WHO report there had been extensive obfuscation of early patients, etc.
- His only reference to the Huang paper noted above is to say: “Forty-one of the first known patients formed the basis of an influential study that reported that 66%—i.e., not all early cases—had a link to Huanan Market.”
- **Critically, Worobey fails to note in the Huang et al. paper that three of the first four patients had no connection to the market. Apparently, the reviewers of Worobey’s paper also missed this critical omission.**
- Worobey’s work does not appear to have involved any firsthand interviews in China but instead a review of a collection of videos and such found on the internet. It is unclear if he has made any attempt to document the veracity of any of his source documents.
- This has generated a media frenzy with titles proclaiming we now know COVID began in a market and not the Wuhan Institute of Virology, a leading coronavirus research center.
- This is not credible. Worobey’s own prior work indicates the epidemic began at least a month earlier and therefore patients from the market can be just as likely a super spreader event.
- In April 2021 this same Michael Worobey wrote a lengthy, peer reviewed paper<sup>4</sup> stating:
  - “Our results define the period between mid-October and mid-November 2019 as the plausible interval when the first case of SARS-CoV-2 emerged in Hubei province, China.”
  - “Consequently, the index case in Hubei likely contracted SARS-CoV-2 on or around 4 November 2019 (95% upper HPD: 15 October; 99% upper HPD: 7 October).”
  - “It is highly probable that SARS-CoV-2 was circulating in Hubei province at low levels in November 2019 and possibly as early as October 2019, but not earlier.”

<sup>3</sup> <https://www.science.org/doi/10.1126/science.abm4454>

<sup>4</sup> <https://www.science.org/doi/10.1126/science.abf8003>

- **Thus, his latest paper contradicts his own earlier paper! Maybe that is why the earlier paper had four other authors but this one he published alone.**
- Additional contrary evidence:
  - May 2020: "At first, we assumed the seafood market might have the virus, but now the market is more like a victim. The novel coronavirus had existed long before," **Gao Fu, director of the center and member of the National Committee of the 13th Chinese People's Political Consultative Conference,** said on Monday. Gao said he had gone to Wuhan to collect samples for COVID-19 researchers in early January, but no viruses were detected in the animal samples. Viruses were only found in environmental samples, including sewage.<sup>5</sup> Gao has not retracted or modified this statement.
  - First case reported by the Chinese authorities was a Hubei resident on November 17, 2019.<sup>6</sup>
  - The largest early study (from the Chinese PLA General Hospital, Beijing, China) of the first or root case of SARS-CoV-2 calculated it was on September 28, 2019.<sup>7</sup> This paper has not been modified or retracted.

### **Market Location of Early Patients and Environmental Specimens**

- The following map<sup>8</sup> shows the locations of the areas in which “Domesticated Wildlife Products” were sold (hashed boxes), where vendors who acquired COVID-19, and the positive and negative environmental specimens.
- These data have not been challenged.
- Wildlife stall locations: 10 wildlife stalls are identified. Seven in the most western section of the market and three east of Xinhua Road. All seven in the west and 2 of 3 in the east were tested.
- One of the stalls in the western section had a positive environmental specimen for SARS-CoV-2.
- No human cases are associated with the wildlife stalls.

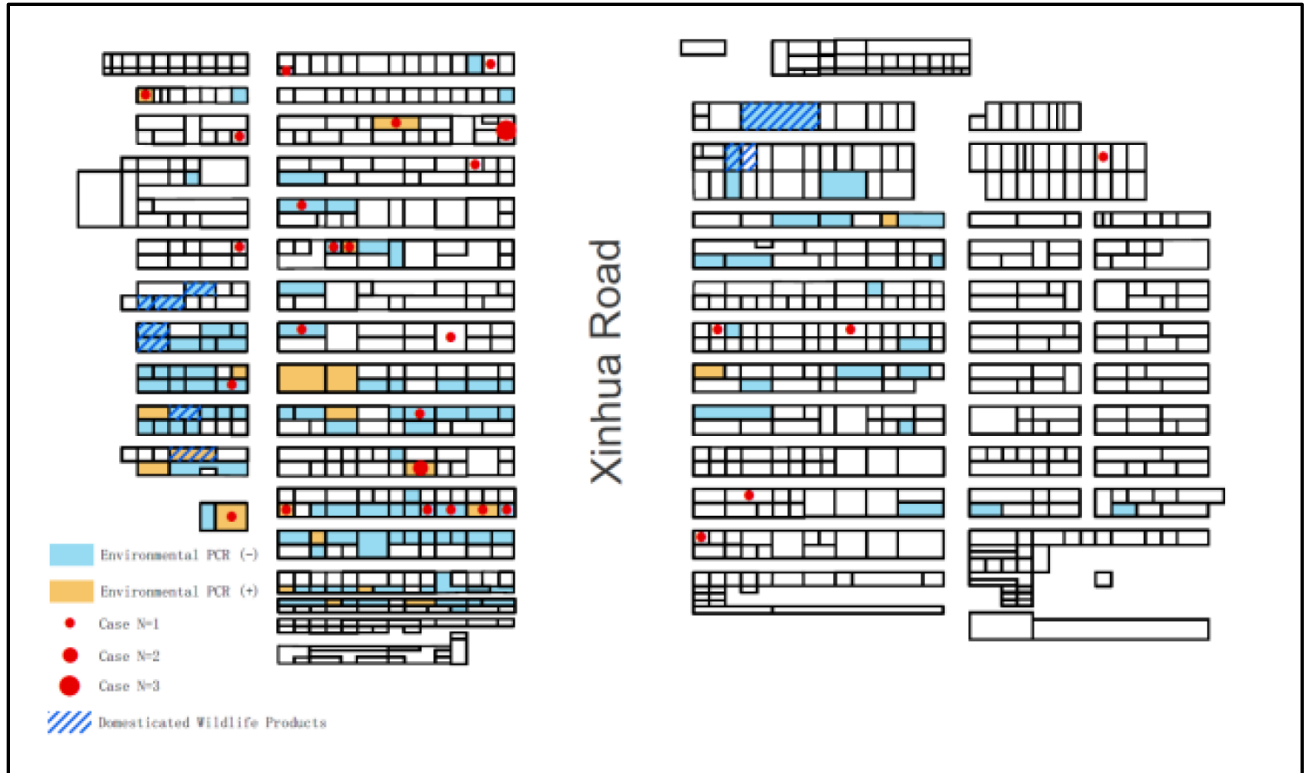
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<sup>5</sup> <https://www.globaltimes.cn/content/1189506.shtml>

<sup>6</sup> <https://www.scmp.com/news/china/society/article/3074991/coronavirus-chinas-first-confirmed-covid-19-case-traced-back>

<sup>7</sup> <https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7455167/>

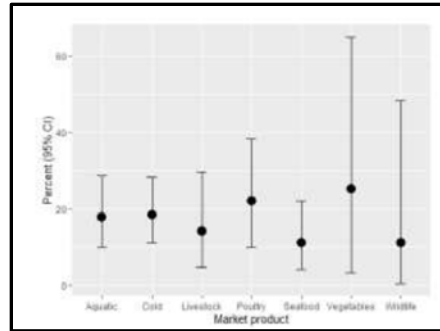
<sup>8</sup> Page 98 WHO Joint Report: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/origins-of-the-virus>



- Looking simply to see if there is a relationship between the presence of environmental SARS-CoV-2 and a human infection the table below was generated. The relationship is strong with a p-value of  $1.36 \times 10^{-5}$ . Infected humans and environmental specimens occur together, as expected.

Environment	Yes	13	9
	No	104	8
		No	Yes
		Human CoV-2	

- Below is a graph showing the relationship between environmental specimens positive for SARS-CoV-2 and the products sold in the stalls. Vegetable stalls had the highest sample percentage while seafood and wildlife were the lowest. However, the error bars indicate there is no statistical difference based on products sold.
- Certainly, the wildlife section does not have what might have been expected, an excess of positive environmental specimens.**



**No animal specimen from the Huanan Market nor any upstream supply chain sources ever tested positive for SARS-CoV-2**

The location and number of animal samples tested with respect to the Huanan Market is shown in Table 3 below. The variety of animals is also shown in Table 4 below.

Collection sites	Sample number	RT-PCR positive number
Huanan market	327	0
Warehouses related to the Huanan market	32	0
Cats, rats and other vectors and their droppings	92	0
Wuhan and other surrounding markets	6	0
<b>Total</b>	<b>457</b>	<b>0</b>

Species	Sample number	Animal number	RT-PCR positive number	Remarks
Rabbit/Hares	104	52	0	
Stray cat	80 <sup>a</sup>	27	0	Including faeces
Snake	80	40	0	
Hedgehog	67	16	0	
Muntjac	18	6	0	
Dog	17	7	0	Including one stray dog
Badger	16	6	0	
Bamboo rat	15	6	0	
Mouse	12	10	0	Captured around the market
Pig	6 <sup>b</sup>	NA <sup>c</sup>	0	
Chicken	5	5	0	
Chinese giant salamander	5	3	0	
Crocodile	4	2	0	
Wild boar	4	2	0	
Soft-shelled turtle	3	2	0	
Weasel	2	1	0	Captured around the market
Fish	2	2	0	
Sheep	1	1	0	
Others	16	NA <sup>c</sup>	0	
<b>Total</b>	<b>457</b>	<b>188</b>	<b>0</b>	

### The Raccoon Dog theme as Intermediate Host

- There seems to be a theme from the spillover proponents to claim raccoon dogs as the likely intermediate host.
  - They were apparently found in the Huanan market before December 2019 although at the time of the market closure the end of December 2019 they were said to not be present in the market.
  - Only one study exists<sup>9</sup> of infection of raccoon dogs with SARS-CoV-2 and it showed modest spread (only 2 of 3 animals could be infected via the airborne route). Unfortunately, this study used the D614G variant of SARS-CoV-2 which is at least three times more transmittable than the original, wildtype variant.
  - There are no studies of the original D614 virus, which is metastable and poorly transmissible.

### The patients from the market had only Lineage B virus variants and not the ancestral Lineage A variant: a series of less and less probable work arounds are proposed

- A challenge to the market origin is the undisputed finding that none of the human or environmental specimens had what has been agreed to as the original Lineage of the SARS-CoV-2. In the original paper<sup>10</sup> describing Lineage A and B by Rambaut, Holmes et al. they wrote:
  - “Fortunately, because of the early sampling and genome sequencing of COVID-19 cases in China, especially in Hubei province, it appears that the ‘root sequence’ of SARS-CoV-2 is known. **Many of the genomes from the earliest sampled cases are genetically identical and hence also probably identical to the most recent common ancestor of all sampled viruses. This occurrence is different to previous viruses and epidemics** and provides some advantages for the development of a rational and scalable classification scheme. Specifically, setting the ‘reference sequence’ to be the root sequence forms a natural starting point since direct comparisons in the number and position of mutations can be made with respect to the root sequence.” [Emphasis added.]
  - “We propose that major lineage labels begin with a letter. At the root of the phylogeny of SARS-CoV-2 are two lineages that we simply denote as lineages A and B. The earliest lineage A viruses, such as Wuhan/WH04/2020 (EPI\_ISL\_406801), sampled on 5 January 2020, share two nucleotides (positions 8,782 in ORF1ab and 28,144 in ORF8) with the closest known bat viruses (RaTG13 and RmYN02). Different nucleotides are present at those sites in viruses assigned to lineage B, of which Wuhan-Hu-1 (GenBank accession no. MN908947) sampled on 26 December 2019 is an early representative. Hence,

<sup>9</sup> <https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7706974/>

<sup>10</sup> <https://www.nature.com/articles/s41564-020-0770-5>

although viruses from lineage B happen to have been sequenced and published first<sup>8,9,10</sup>, it is likely (based on current data) that the most recent common ancestor (MRCA) of the SARS-CoV-2 phylogeny shares the same genome sequence as the early lineage A sequences (for example, Wuhan/WH04/2020).”

- When the above assignments were made it was not understood that there was a Lineage-based epidemiology finding. No early Lineage A patient had an association with the Huanan market and no Lineage B patient did NOT have such a relationship.
- This data supported a first human infection of Lineage A, a human-to-human transmission of Lineage A and then the two mutations to become Lineage B occurred, and then entry of a Lineage B patient to the market and a super spreader even began.
- Worobey makes the following arguments on the Lineage topic:
  - “The recent discovery that there may be no true lineage A or B intermediates in humans also raises the possibility of separate spillovers of both lineages.”
    - Accepting this hypothesis requires rejecting 13 sequenced genomes with intermediate sequences that all have the same sequencing error in the same spot in the genome.
    - Rejecting these 13 intermediates between A and B lineages is based on the false assumption that all variant production in human-to-human transmission can only be a single SNV. Analysis of three family clusters shows a substantial number of single transmissions in which there are two or more mutations.<sup>11</sup>

### **What happened a few days ago?**

NYT writes:

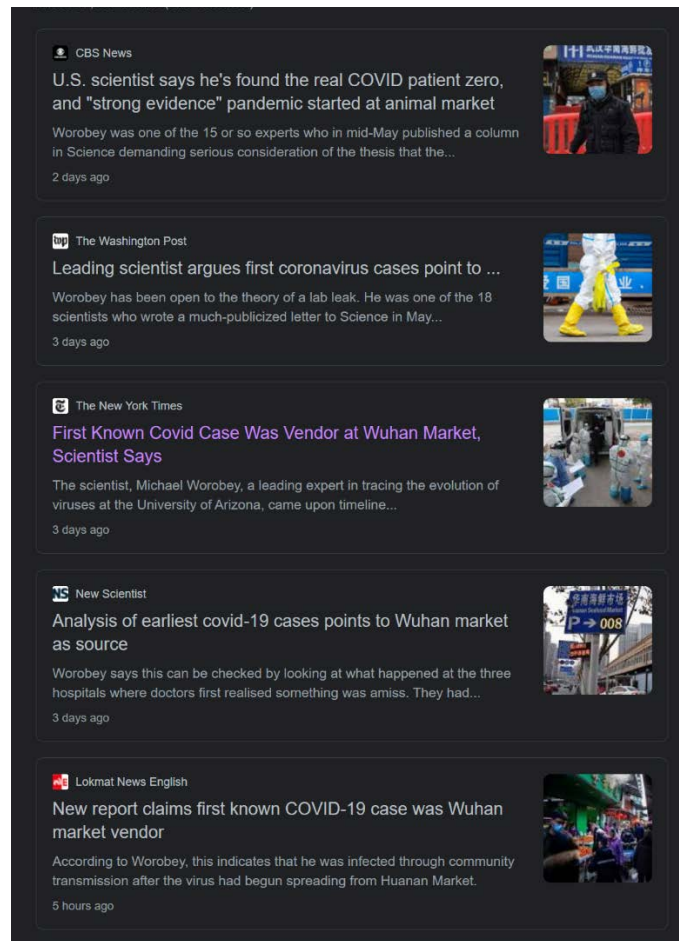
“A scientist who has pored over public accounts of early Covid-19 cases in China reported on Thursday that an influential World Health Organization inquiry had most likely gotten the early chronology of the pandemic wrong. The new analysis suggests that the first known patient sickened with the coronavirus was a vendor in a large Wuhan animal market, not an accountant who lived many miles from it.”

Worobey’s new paper:

The press went wild with this. For the first time, the NYT put this on the front page:

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<sup>11</sup> SC Quay, unpublished data.



## Conclusion:

- If it was believed that the pandemic began in December 2019 than the epidemiology of patients from December 2019 would be helpful in identifying the origin of the infection. If the December cases are appearing weeks or months after the Index Case, then the December epidemiology is less valuable.
- Nonetheless, the earliest data on the relationship to the Huanan market, which has never been refuted, documents three of the first four cases had no relationship to the market.
- Abundant evidence exists that the first patient with COVID-19 was in Wuhan, China and was infected sometime between the end of September 2019 and late November 2019. This includes Worobey's own prior work.
- We do not know who that first patient is, where they lived, their market association, etc.
- By early December the 'spaciotemporal' signal from the unknown 'Index Patient' was lost through repeated human-to-human transmission. Therefore, classifying or reclassifying one of the three early patients with no exposure to the market to a later infection date does not change the probative value of those early cases, which is minimal.
- The uncritical media response to this paper suggests a desire to close the debate on the origin of SARS-CoV-2 and to undermine the extensive evidence which is most consistent with a non-spillover event as the origin.