Supplementary Information

Implications of haplotype switching for the origin and global spread of COVID-19

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We address here issues that have emerged through the pandemic, some consistent with our explanations offered and others apparently in contradiction.

A.COVID-19 in Barcelona Sewer System March 2019?

This claim was made in a paper on a pre-print server and has been widely reported in both the popular press and social media (Chavarria-Miró et al 2020). There is no discussion anywhere on PCR precautions for COVID-19 genome contamination given that Spain has been saturated with viral genomes for many months. One positive 2019 date suggests contamination. Also, there was no mention of the technical precautions against contamination and sensitivities they have taken. In such a heavily contaminated environment PCR is notorious for finding contaminants. The issue is not discussed. The authors say "Technical details are included in the Appendix" yet those relating to controls, contamination etc. could not be found. The key text is: "This possibility prompted us to analyse some archival WWTP samples from January 2018 to December 2019 (Figure 2). All samples came out to be negative for the presence of SARS-CoV-2 genomes with the exception of March 12, 2019, in which both IP2 and IP4 target assays were positive. This striking finding indicates circulation of the virus in Barcelona long before the report of any COVID-19 case worldwide." This is a classic PCR contaminant pattern, a false positive in a heavily contaminated environment - a false positive outlier with another explanation. Our assessment is replicated by others who have read the paper, see comments at the site <u>https://www.medrxiv.org/content/10.1101/2020.06.13.20129627v1</u>

B. COVID-19 Outbreaks in Ships at Sea

A key task we have with outbreaks in ships at sea lies in separating infections brought to the ship by passengers or supplies prior to departure *versus* unexpected and hitherto unexplained, outbreaks at sea. That is the challenge, and we included in the main text only the strong data and observations (*Al Kuwait, Echizen Maru*). However there is in addition an overall pattern that needs to be addressed, as many other types of ships became engaged with COVID-19 outbreaks while at sea. All these observations are, we believe, consistent with, and best explained by, the in-fall of COVID-19 dust clouds from the tropospheric jet streams. We document the numerous other reports of this type that appeared in the media from February 2020, particularly the *Princess* cruise ships. These ships would be expected to have a high proportion of elderly retirees and thus many who may have co-morbidities and thus would be quite vulnerable to common cold and flu-type respiratory diseases. As indicated some of these outbreaks may be accounted for by already infected travellers boarding the ships and infecting others by P-to-P spreads and fomite contamination (e.g. luggage from contaminated airplanes and airports). Some outbreaks such as the *Al Kuwait* animal transportation ship (empty and approaching Fremantle, Western Australia at time of outbreak) are not so easy to understand by conventional P-to-P infectious disease theory.

• *MV Greg Mortimer*- In the case of the outbreak on the *MV Greg Mortimer* a small cruise ship to Antartica (Ing et al 2020) there is a suggestion of a possible at-sea viral dust exposure in the South Atlantic at a time we have previously argued that viral dust clouds were known to be spreading into the Southern Hemisphere over South America, particularly Brazil (Wickramasinghe et al 2020b). However, the alternative view that

the coronavirus was introduced, either on their person or luggage, by passengers who travelled to Argentina by airplanes from already infected zones cannot be excluded. This introduction of virus would have had to occur despite pre-screening of passengers which took place- thus " all 128 passengers and 95 crew were screened for COVID-19 symptoms, and body temperatures were taken before boarding. No passengers or crew that had transited through China, Macau, Hong Kong, Taiwan, Japan, South Korea or Iran in the previous 3 weeks were permitted to board, given that these countries were where COVID-19 infection was most prevalent at the time. Multiple hand hygiene stations were positioned throughout the ship and especially in the dining area."

Almost all passengers on board were infected, and the great majority had mild infections. All the relevant data are highly detailed as the medical practitioners among the passengers actively organised the sampling, surveillance and testing of passengers, in real time. "Of the 217 passengers and crew on board, 128 tested positive for COVID-19. Of the COVID- 19 -positive patients, 19% (24) were symptomatic; 6.2% (8) required medical evacuation; 3.1% (4) were intubated and ventilated; and the mortality was 0.8% (1). The majority of COVID-19-positive patients were asymptomatic (81%, 104 patients). We conclude that the prevalence of COVID-19 on affected cruise ships is likely to be significantly underestimated, and strategies are needed to assess and monitor all passengers to prevent community transmission after disembarkation." This description can also apply to the infection experience on the *Diamond Princess* (Ioannidis 2020).

Events on the *MV Greg Mortimer* unfolded thus – "The first recorded fever on board the ship was a febrile passenger on day 8. Isolation protocols were immediately commenced, with all passengers confined to cabins and surgical masks issued to all. Full personal protective equipment was used for any contact with any febrile patients, and N95 masks were worn for any contact with passengers in their cabins. The crew still performed duties, including meal services to the cabin doors three times a day, but rooms were not serviced. Expedition staff helped with crew duties at meal service. ...Further fevers were detected in three crew on day 10, two passengers and one crew on day 11, and three passengers on day 12". ..." As Argentina had closed its borders, and permission to disembark at Stanley, Falkland Islands, was refused, the ship sailed to Montevideo, Uruguay, arriving the evening of day 13...The majority of febrile patients had improved with symptomatic treatment and were afebrile on arriving at Montevideo."...." Of the 217 passengers and crew on board, 128 tested positive for COVID-19 (59%). These included all passengers who tested negative" by an antibody test... and " there were 10 instances where two passengers sharing a cabin recorded positive and negative results".

While 128 (59%) of the population tested positive, "fever and mild symptoms were present in only 16 of 128 COVID-19- positive patients (12.5%), with another 8 medically evacuated (6.2%) and 4 requiring intubation and ventilation (3.1%). There has was one death (0.8%)... with a total of 24 COVID-19-positive patients who were symptomatic (19%), with the majority being asymptomatic (104 patients or 81%)."

This is a valuable study and is consistent with the observations by Herbert Rebhan on the *Al Kuwait* sheep ship.

 Outbreak on "American Triumph" an Alaskan factory fishing vessel
As this paper was being finalised another report of outbreaks of COVID-19 among many crew from a fishing boat was reported. viz. "Alaska fishing boat has 85 crew members infected with virus"
The Associated Press via The Charlotte Observer, July 20 https://www.charlotteobserver.com/news/article244351137.html

• *Aircraft Carriers* - Both US ships in North West Pacific (*USS Theodore Roosevelt* and *USS Ronald Reagan*) and the French aircraft carrier *Charles de Gaulle* (operating we assume in the North Atlantic) reported many thousands of cases, but details of these at-sea outbreaks are hard to examine and verify properly as the information release has been limited.

In late March the two U.S. aircraft carriers were in the western Pacific and both reported cases of the new coronavirus among their crews. After eight sailors on the U.S. aircraft carrier *Theodore Roosevelt* tested positive for COVID- 19 the ship went to Guam, where the rest of the crew would be tested (Stashwick 2020, Evans 2020). The *Theodore Roosevelt* was out of action for 10 weeks, docked in Guam while the crew was tested. More than 1150 of its 4800 crew tested positive and one sailor died.

The French aircraft carrier *Charles de Gaulle* arrived at its base in the bay of Toulon, southern France, Sunday April 12, 2020. The French Defence Ministry said in a statement that around 40 sailors initially showed symptoms compatible with COVID-19. However the coronavirus was shown to have infected more than 1,000 sailors aboard the *Charles de Gaulle*. (Schaeffer and Ganley 2020).

Apart from these basic details little else was shared with the US or French public.

• *Princess cruise ships*- In the case of the *Diamond Princess* operating in the South China Sea/Sea of Japan in February the timing and location of the outbreaks at sea are certainly consistent with a fragment of the Wuhan viral dust cloud drifting into the South China Sea. The report of the level of COVID-19 antibody positive subjects on the ship suggests widespread exposure on the ship, by P-to-P or fomites or both (Ioannides 2020).

The sudden outbreak on the *Grand Princess* off California mid to late February (Snowden 2020) involved exclusively the Wuhan L haplotype, both non-mutated, and lightly mutated with some P-to-P spreads (Steele and Lindley 2020). The news reports suggest many infected persons were crew The timing is consistent with a presumptive viral dust cloud affecting the USA West Coast at this time, much like the 1968 H3N2 influenza virus, also originating in China, which affected the USA from the West to East coasts in such a similar directional manner in 1968 (Wickramasinghe et al 2020a).

NOTE: The study discussed in the main text on airborne transmission that was published in PNAS by Zhang, Li et al has been challenged in a Letter transmitted to the PNAS editorial board

(https://metrics.stanford.edu/sites/g/files/sbiybj13936/f/files/pnas_loe_061820_v3.pdf)

C. Hyper and Non-Random Recombination Mechanisms in Coronavirus Adaptation?

Supplied by EJS : Can these odds be reduced by a special type of hypermutation-recombination mechanism deployed by coronaviruses? That is to say, a non-random complex mechanism involving a recombination process via multiple variant strain infections of the same cell – a type of replicase -linked strand jumping (copy choice) known to happen in part in experimental selection situations (Masters 2006) or as for influenza virus the recently described process of host-virus hybrid gene formation involving cleaved and 5'-m7Gcapped host transcripts to prime viral mRNA synthesis (Ho et al 2020). To put simply: recombination of preexisting variant SNV sequence templates which are all stitched together in a single host cell to arrive at a perfect COVID-19 sequence match – a form of natural genetic engineering? Each new sequence then would be a mosaic of blocks of sequence copied from other variant templates, a mosaic pattern much like the PCR recombinant pattern that can be generated by Taq or Pfu polymerases PCR runs from multiple different templates in vitro (Zylstra et al 1998). What are the odds given current known data on the sequence similarity of the closest bat strain RaTG13 which is 96.2% similar to, or 1140 SNV differences from, SARS-CoV-2? These considerations are reminiscent of the earlier discussions (1960s through 1980s) over targeted recombinational 'gene conversion' mechanisms of somatic hypermutation (SHM) in rearranged antibody variable genes (reviewed in Steele 1991). SHM is now known to be achieved by a combination of both locustargeted APOBEC and ADAR deaminase mutagenesis and an error-prone reverse transcription process involving the Y family DNA repair polymerase, DNA Polymerase – eta (η) (Lindley and Steele 2013, Steele

2016, Franklin, Steele and Lindley 2020). Given that a reverse transcription step is not known to be involved at any stage of the coronavirus replication cycle – unlike HIV or Hepatitis B Virus - COVID-19 recombination would be driven by replicase 'strand jumping' coupled to deaminase hypermutagenesis. The SNV differences between the closest match strains to COVID-19 are formidable and it has to remain doubtful that such a mechanistic process in the cytosolic membraneous webs harbouring the "replication and transcription factories" actually can be assembled for the availability of variant templates in close proximity. In the case of HIV a strong case can be put that even this retrovirus may have co-opted the B lymphocyte somatic hypermutation mechanism to its own adaptive variation strategy (Steele and Dawkins 2016) but hypermutation is not a feature of COVID-19 in the human passages examined (Steele and Lindley 2020). Finally, however, COVID-19 recombination variation patterns were not an easily recognizable feature over the first three months of human disease episodes and passage at explosive epicentres as assessed in Steele and Lindley (2020).

D. Recent Epidemics in USA June -July 2020

Apparent "2nd Wave" epidemics with rising numbers of cases showed up in a number of southern and western states of the USA. This appears to be part of a general pattern - the first wave being followed by large epidemics in the north-eastern regions states New York, New Jersey, Maryland, Washington DC in March-April 2020. So the infective explosions occurred in a patchy manner across different regions. Some examples are shown, from Google Searches viz " <Type in State> covid-19 cases by county". These patterns suggest the descent of viral-laden dust clouds of varying size and viral load are now striking (as July 18 2020) the southern and western states in the USA, to varying degrees.





Daily change



Each day shows new cases reported since the previous day · Updated less than 5 hours ago · Source: Wikipedia · About this data





Each day shows new cases reported since the previous day · Updated less than 5 hours ago · Source: Wikipedia · About this data



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