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COVID-19: Viral origins, vaccine fears and risk perceptions

On 30 March 2021, the Joint WHO-China mission investigating the origins of the SARS-CoV-2 virus released their much awaited report.[1] For some, it was an anti-climax as the source still remains unknown, and others were concerned that the assessment was not extensive enough. The WHO's Director General, Dr Tedros Ghebrejesus, remarked that further data and studies was still needed and that "all hypotheses remain on the table".[2]

So what have we learned? Firstly, the likeliest explanation is that the virus spilled over from its animal reservoir (*Rhilophilus* bats) to humans, possibly through an intermediate animal host that has not been identified. This would be in keeping with the zoonotic origins of SARS-CoV-2's other coronavirus cousins (the four human coronaviruses, MERSCoV2 and SARS-CoV). This highlights the need for enhanced biosecurity measures globally if we are to track and prevent the spread of new zoonotic pathogens to human populations.[3] This will require greater international collaboration, sharing of intelligence, as well as epidemiological, zoonotic and genomic surveillance.[4] It also highlights the ongoing risks at the human-wildlife interface such as in farmed wild animals, live animal markets and wet markets where the potential for transmission is increased.[5] We also learned that certain settings can act as amplification sites, as was the case with the Wuhan wet market, that was initially thought to be the source but now looks likely to have been where there was an amplification effect and superspreading.[6]

Unsurprisingly, the inability of the scientific mission to find a conclusive source has helped to maintain the conspiracy theory that the virus origins were from a laboratory rather than nature. This illustrates a perennial problem: scientists formulate theories and arrive at measured conclusions based on the strength of the evidence to hand. Where there is insufficient or inadequate evidence, their conclusions have to be more nuanced and caveated, and they express the uncertainties in keeping with scientific practice. However, for the public and media, the demand is for simple certainty, absolutes, that fit preferably in a headline or a social media tweet. Scientific uncertainty comes across as ambiguity and causes confusion.[7]

On a related note, is the ongoing saga regarding the safety of the Oxford-AstraZeneca COVID Vaccine. Its roll out in Europe has been dogged by initially hesitance by some countries to deploy it on the grounds of insufficient safety or efficacy evidence. Most recently are the concerns of the association with a very rare condition, Cerebral Venous Sinus Thrombosis (CVST). Germany had observed 13 cases of CVST after 1.6 million immunisation doses[8] but the UK on the other hand has seen 50 cases of CVST from 20.6 million vaccine doses given (as of 5 April 2021).[9] One theory put forward is that this phenomenon is due to the vaccine triggering the development of an prothrombotic disorder caused by platelet-activating antibodies that clinically resembles heparin-induced thrombocytopenia.[10] This is plausible, but has yet to be scientifically confirmed. The reason for the marked discrepancies in adverse event rates between countries is not clear although one possibility may be that most of the UK doses were given to older population groups where the likelihood of this event may be rarer. Similar fears have emerged for the Johnson & Johnson vaccine in recent weeks.

However, association does not imply causation, nor are we certain at this juncture that it is a true signal. Even if this association turns out to be true, there is also a need to put the risks in context and communicate it effectively to the public and policymakers so that rationale conclusions are made. For example, the incidence of CVST after immunisation is roughly 8.1 per million doses in Germany and 1.2 per million in the UK. Pre-COVID, the reported incidence of CVST is 2-5 per million population.[11] The

background incidence and possible immunisation-related incidence are therefore of similar magnitude. On the other hand, CVST has been recognized as a complication of SARS-CoV-2 infection.[12] Moreover, the risk of death, assuming an infection fatality rate of 0.54%,[13] is of the order of 54,000 deaths per million persons infected. In other words, the balance of benefit to harm with immunisation is strongly in favour of immunisation, a conclusion reached by both the World Health Organisation[14] and European Medicines Agency[15]. The benefit of immunisations would be much greater in areas where there are high levels of infections. The risks therefore have to be placed in context.

Unfortunately, public risk perception is fallible and susceptible to scare stories. The public are likely to fear the rarer and more exotic adverse events, and therefore overestimate low-probability but high-consequence risks that grab media attention. There is also the phenomenon of ambiguity aversion, where communicating scientific uncertainty decreases public perceptions of vaccine effectiveness and therefore interest in vaccination, and leads to a loss of trust in health officials.[16]

At the present time when the virus continues to surge worldwide, with new epidemic waves from Poland to Brazil to India, there can be no room for vaccine hesitancy. The biggest risk for us all is the emergence of new viral variants that have acquired vaccine-escape that can undo the progress made so far in tackling the pandemic. There are already variants of concern that have emerged in South Africa (B.1.351 variant) and Brazil (P2 variant) that have shown reductions in vaccine efficacy, that is thus far thankfully limited.[17] Neither is there a full-proof border control system that can keep infection out of a country indefinitely that does not entail crippling social and economic costs to the country. Finally, we will also need to address the important issue of global vaccine equity. If we want to get out of the pandemic's stranglehold, we will need to get as many people vaccinated as we can everywhere and as soon as we can.

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