

# EDITOR'S MESSAGE

## COVID-19: A look back, one year into the 2020 pandemic

Dan Vidovic

---

It has now been approximately one year since the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the causative agent of coronavirus disease 2019 (COVID-19). In the past year, scientists and healthcare workers have repeatedly needed to shift their practices as an endless supply of research continued to reshape their understanding. This past year has shown us the importance of global collaboration and unity. In the next few paragraphs, I'll briefly touch on some of the major points of the COVID-19 pandemic and provide brief updates on some of the initial evidence

It is believed that patient zero can be traced back to a 55-year old man from Hubei, China who contracted COVID-19 in Nov 17, 2019, over a month before cases appeared in nearby Wuhan at the end of December 2019<sup>1</sup>. More recent evidence, however, shows this may not be the case. Serological blood testing of Italian patients enrolled in a lung cancer screening trial for SARS-CoV-2 antibodies revealed that up to 14% of trial participants had either IgG or IgM antibodies against the virus as early as September 2019, over two months before the hypothesized patient zero contracted the virus in Wuhan<sup>2</sup>. Given that an antibody immune response takes weeks to develop, it is possible the virus was present as early as the summer of 2019; this new information could reshape the history of the pandemic.

While initially thought to have had its zoonotic origins in a wet market in Wuhan, tissue samples of market animals reveal an absence of virus<sup>3</sup>, making it unclear exactly where or when the virus made the jump from animals to humans. Pre-existing coronaviruses nearly identical to SARS-CoV-2, which are able to infect human cells in vitro, have been circulating in bats for years<sup>4,5</sup>. Furthermore, novel coronaviruses similar to SARS-CoV-2 have been found in pangolins as well<sup>6,7</sup>. Currently, it is thought that bats serve as the initial source of a myriad of coronaviruses, including high-risk strains capable of possibly infecting humans and those which are spread to pangolins. Pangolins are therefore likely the reservoir host, which mediate virus mutation and zoonotic transmission to humans. Indeed, pangolins were sold at wet markets throughout Chinese cities, including at the Wuhan market thought to be the initial origin of SARS-CoV-2. Again, with the potential of a new timeline for the virus' inception, it may be possible that the Wuhan wet market simply mediated a superspreader event, rather than being the

initial birthplace of SARS-CoV-2. Only further time and epidemiological study will reveal the exact origins of SARS-CoV-2.

Early on in the pandemic, in the absence of any substantial evidence, hydroxychloroquine (often in combination with the antibiotic azithromycin) was claimed to be an effective treatment for COVID-19<sup>8,9</sup>; a claim that was prematurely and grossly overstated by both media and politicians alike. We now know that this combination treatment is mostly useless, and in fact causes marked QTc prolongation and liver toxicity compared to placebo-controls<sup>10</sup>. Remdesivir, an antiviral drug originally developed and unsuccessfully used by Gilead Sciences in 2009 to treat hepatitis C, RSV, Ebolavirus, and Marburg virus, was also in the spotlight early in the pandemic, as it had previously demonstrated anti-viral effects against SARS-CoV-2 in vitro<sup>11</sup>. Ongoing uncertainty in the evidence collected by numerous trials (some of which showed benefit, and others which did not) over the last 9 months have ultimately lead the World Health Organization (WHO) to recommend against the use of remdesivir for COVID-19<sup>12</sup>. To date, the only WHO-recommended treatment for severe to critical disease is systemic corticosteroids such as dexamethasone<sup>12</sup>. Since the late acute respiratory distress syndrome-like manifestations of COVID-19 are mostly due to cytokine storm rather than viral replication<sup>13</sup>, these evidence-based recommendations seem appropriate.

In the last year, it has become abundantly clear that there is little prospect in identifying "magic bullet" medical treatments to significantly improve COVID-19 patient outcomes. For that reason, many biopharmaceutical companies immediately began assembling vaccine platforms to assess for the possibility of a vaccine against COVID-19. Moderna, the first company to produce a vaccine candidate, began platform assembly in January 2020, just over a month after China had announced the emergence of the novel respiratory virus. This fast turn-around-time is in part due to the simplicity of their platform. The vaccine is a messenger RNA (mRNA), a simple molecule that provides instructions to the host's cells to create SARS-CoV-2 spike protein. The spike protein is then recognized as antigen to the immune system, which produces a potent immune response. The most recent results of Moderna's phase III trials, just released in mid-November, reveal a very promising 94.5% efficacy with no serious adverse

events in trial participants<sup>14</sup> (these results have not been peer-reviewed by a journal, but are pending review and approval by the FDA and other regulators). A very similar platform also using an mRNA encoding a modified spike protein developed by BioNTech (and manufactured by Pfizer) had preliminary phase III findings revealing a 95% efficacy<sup>15</sup>. Both of these vaccines are the first mRNA-based platforms to be trialed in the world; the long-term efficacy and safety of these platforms has yet to be determined. However, their ability to be rapidly mobilized and adapted to different pathogens (requiring just an mRNA sequence of a potential antigen) may change the course of vaccinology indefinitely. The Pfizer and Moderna vaccines are both currently expected to be granted emergency use approval in multiple countries in coming days or weeks. Over 50 other vaccine candidates are still undergoing phase I-III trials<sup>16</sup>.

The speed at which this pandemic has propelled global scientific unity and advancement has likely never been seen in the history of humankind. As of writing this editorial, there have been over 76,000 publications indexed on MEDLINE under the search term “COVID”. This is significantly more research published this year on COVID than HIV, hepatitis C, influenza, and Ebola combined. The collective efforts of hundreds of thousands of scientists, healthcare workers, and members of the public has been paramount in putting up a fight against this pathogen. Immense sacrifices have been made, and many loved ones lost. In a sense, this pandemic has matured us as a human race. For the past year, many of us have lived a new normal: unable to socialize, see loved ones, missing important life milestones, losing jobs, and mourning for life to go back to the way it was. Many have realized what we take for granted in everyday life, and how difficult it can be to cope in the absence of our normal routine. It has been a long, isolated, and difficult year, but we’re now just beginning to see the light at the end of the tunnel. Barring any major challenges with vaccine uptake, we should see a slow return to normal over the next year. And hopefully, in one to two years’ time, this journey we’ve all unwillingly taken will just be part of our collective history.

*Dan Vidovic*  
*Editor-in-Chief*

## References

1. Bryner, J. 1st known case of coronavirus traced back to November in China. *livescience.com* <https://www.livescience.com/first-case-coronavirus-found.html>.
2. Apolone, G. et al. Unexpected detection of SARS-CoV-2 antibodies in the prepandemic period in Italy. *Tumori J.* 0300891620974755 (2020) doi:10.1177/0300891620974755.
3. Letzter, R. The coronavirus didn't really start at that Wuhan 'wet market'. *livescience.com* <https://www.livescience.com/covid-19-did-not-start-at-wuhan-wet-market.html>.
4. Wrobel, A. G. et al. SARS-CoV-2 and bat RaTG13 spike glycoprotein structures inform on virus evolution and furin-cleavage effects. *Nat. Struct. Mol. Biol.* 27, 763–767 (2020).
5. Ge, X.-Y. et al. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature* 503, 535–538 (2013).
6. Lam, T. T.-Y. et al. Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins. *Nature* 583, 282–285 (2020).
7. Han, G.-Z. Pangolins Harbor SARS-CoV-2-Related Coronaviruses. *Trends Microbiol.* 28, 515–517 (2020).
8. Yao, X. et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.* 71, 732–739 (2020).
9. Gautret, P. et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int. J. Antimicrob. Agents* 56, 105949 (2020).
10. Cavalcanti, A. B. et al. Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19. *N. Engl. J. Med.* 383, 2041–2052 (2020).
11. Lo, M. K. et al. GS-5734 and its parent nucleoside analog inhibit Filo-, Pneumo-, and Paramyxoviruses. *Sci. Rep.* 7, 43395 (2017).
12. Rochwerg, B. et al. A living WHO guideline on drugs for covid-19. *BMJ* 370, m3379 (2020).
13. Tang, Y. et al. Cytokine Storm in COVID-19: The Current Evidence and Treatment Strategies. *Front. Immunol.* 11, (2020).
14. Grady, D. Early Data Show Moderna's Coronavirus Vaccine Is 94.5% Effective. *The New York Times* (2020).
15. Thomas, K. New Pfizer Results: Coronavirus Vaccine Is Safe and 95% Effective. *The New York Times* (2020).
16. Zimmer, C., Corum, J. & Wee, S.-L. Coronavirus Vaccine Tracker. *The New York Times* (2020).