The SARS-CoV-2 pandemic: Personal reflexions one year on

Andrew Bamji*

FRCP, Retired Consultant Rheumatologist, Rye, East Sussex, England

As an interested and medically qualified observer the author has tracked the progress of the coronavirus pandemic for over a year. It is far from over but already there are questions about the handling of the problem from clinical, scientific and political perspectives. In this personal reflexion he examines some of the issues that have arisen. These include over-reliance on modeling, failure to appreciate nosocomial transmission and failure to introduce appropriate and timely treatments due to misunderstanding of the cause of severe illness and risk factors for its development. Questions remain over the accuracy of testing and the attribution of death to the virus. Major concerns are the failure of the UK government and its advisers to heed advice from external sources while relying on the wrong experts, and the inappropriate presentation of statistics. The one major success story is the rapid development and administration of vaccines as a result of good science and bypassing bureaucracy.

1. INTRODUCTION

The coronavirus pandemic is far from over, but after one year of its presence its management, both in the UK and elsewhere, has raised numerous questions. These range through the political and philosophical to the clinical and ethical. The basis of science itself has been called into question. Statistics have been used and abused. There has been delay, misinformation and suppression of views. Decisions have been taken on the advice of those who know not that they know not. Expert views have been sought from the wrong experts; facts have overturned many hypotheses but the failure to heed alternative experts who have based their views on facts and experience has been shameful. It has happened before; Galileo struggled to overturn the considered views of established "science" and a reading of pandemic history shows that many of the mistakes and faults in this pandemic have historical precedents [1].

In this article I shall not consider the first question: where did the coronavirus come from? Whether it came from a bat, pangolin or laboratory release is a political matter that will probably never be resolved. It is here, so we must deal with it whatever. My perspective is UK-centric for simplicity. I shall discuss prevention of spread; vaccination; consequences of severe disease and its management; and information and the rôle of the media and the world wide web. I have a personal perspective as an interested but informed observer of events. In my professional career my bread and butter as a rheumatologist was the management of immunologically mediated diseases. I am long retired from the National Health Service but have read extensively about this pandemic and others. I have reached my own conclusions about management and its failings, which have changed over time; I have kept a diary of events underpinned by facts and statistics [2]. This is more like Daniel Defoe's *Journal of the Plague Year*—which is fictionalized—than Samuel Pepys' diary, where the plague is frequently mentioned but only in passing [3,4]. I have concluded that with the exception of the development of vaccines—something which was only possible through the science of genomics—there have been many errors which have fueled debate, argument and pain.

SARS-CoV-2 is a coronavirus variant. Other coronaviruses have been identified as human pathogens in the past and the current one seems prone to mutation. It has been remarkable in both its high infectivity and its ability to cause severe respiratory and systemic illness which, once developed, has a high mortality. It probably arrived in the UK from the EU and not directly from China, in all probability being introduced separately and in different parts of the country from Italy, Spain and France. Once here it spread rapidly; hospital beds filled up and intensive care facilities came under huge pressure. Although at first it was thought to produce an influenza-like illness, it became clear that it was worse than that.

2. THE GOVERNMENT'S RESPONSE

The Government called upon its scientists to advise. As a result, a "lockdown" was introduced; protective equipment was arranged, albeit slowly, and emergency intensive

* E-mail address: bamji@btinternet.com

Journal of Biological Physics and Chemistry **21** (2021) 12–17
Received 19 February 2021; *accepted* 1 March 2021

doi: 10.4024/02BA21A.jbpc.21.01

care facilities were constructed with a speed only seen previously in wartime. But several mistakes were made: protective equipment was initially inadequate; hospital beds were cleared of elderly patients who were returned to care homes to make room for the expected influx, but it was not realized that hospital-acquired SARS-CoV-2 was widespread, hence these discharged patients carried the virus into the care homes. The risk of developing severe disease was much higher in the elderly, hence patients bounced back into hospital, while mortality in the homes was very high. Even worse was the growing realization that nosocomial transmission was common, and estimates of the possible proportion of patients who acquired the virus in hospital have been as high as 60%, which is a severe indictment of hospital hygiene [5].

At least at the beginning the government made it clear that many of its measures were designed to stop the National Health Service from being overwhelmed and it succeeded in this aim—at the cost of sufferers from other illnesses being subjected to serious and life-threatening delays in treatment.

An answer to the question of whether lockdowns actually result in falls of incidence remains unclear. In theory a lockdown must reduce transmission; in practice there have been sufficient exceptions to lockdown (such as for emergency and essential workers) and insufficient compliance with rules and recommendations (such as the wearing of masks outside) to ensure that a lockdown is not a lockdown at all. Furthermore the tracking of incidence rates shows that changes in incidence are not exactly aligned with the dates of lockdowns. There is then an endless cycle of lockdown and release: as infection rates rise, it is suggested that draconian lockdown measures were delayed too long, and as they fall that they have been kept in place for too long. I cannot see a resolution of the dilemma. However, if vaccination reduces the risk of serious illness, and if serious illness can be effectively treated when it appears, then the impact of infection is mitigated to an extent that may allow it to be treated as no worse than a bad bout of influenza.

Trying to eliminate the virus entirely is an impossibility. It has been argued that if smallpox could be eradicated then the same should be true for SARS-CoV-2, forgetting that the smallpox virus did not mutate and that its transmission was never from asymptomatic carriers. We will have to live with SARS-CoV-2 just as we do with the coronaviruses that cause the common cold [6].

3. TESTING

Initially testing was confined to those with symptoms, but later extended once it was realized that asymptomatic infection might cause spread. However the testing programme was and is fraught with problems. The reverse transcription polymerase chain reaction (PCR) test detects viral fragments. It uses an amplification process expressed as a cycle threshold (Ct). If this is set too high then minute amounts of viral material may be detected that cannot possibly be infectious. There is consensus worldwide that a Ct of greater than 35 will lead to too many false positives; over 40 and many believe that the test produces junk results. The test was not designed for population screening; as a result, several countries have abandoned it. But in the UK some laboratories are running Cts of 40–45, according to a Freedom of Information response [7].

It is also irresponsible to refer to positive tests as representing "cases" of infection. But that is how they have been reported daily. Increasing numbers have caused alarm—but the relevant statistic is what *proportion* of the tests done are positive. If you find 10,000 positives on a sample size of 200,000 that's the same as finding 30,000 on a test population of 600,000. Examining the *percentage* of positive tests shows a much more accurate picture of the real prevalence of test positivity [8]. Neither does a positive test represent "Covid-19". It represents the finding of bits of the SARS-CoV-2 virus. They are not the same. I will discuss this later.

But while the PCR test may be oversensitive, the other quick test in use, the lateral flow test, may not be sensitive enough. It looks for a viral antigen, which has to be present in sufficient quantity to read positive. Thus early, low viral load infections may be missed. This may not matter; the degree of spread from virus carriers has yet to be determined. However, if management strategies are based on test results that are dubious then that is worrying.

4. WHOM TO TREAT?

Herein lies an ethical dilemma. If a health service is overwhelmed, how do you treat everybody equally? The simple answer is that you cannot. Much as with wartime battlefield management you have to set priorities. Triage in war (and there are three steps, hence the name) involves rapidly patching up those who have minor wounds, treating intensively those with more severe injury and abandoning altogether those whose case is beyond hope. During the coronavirus pandemic such a system was needed, leading to serious and highly charged debate about whose life was worth more or less. But in a constrained system—where there may be a lack of beds, but just as important a lack of staff because they themselves are ill or isolated because of contact with infected patients—such decisions must be made, uncomfortable though they are.

5. HOW TO TREAT?

Those with minor symptoms may need no specific treatment. However the development of severe symptoms may occur very rapidly. Thus it would be helpful to have predictors of deterioration available to every household.

Severe disease, Covid-19, is characterized by respiratory distress and failure, with other associated systemic effects. But in the early stages respiratory compromise may go unnoticed because, for reasons not fully understood, the falling blood oxygen saturation fails to trigger breathlessness, so patients seem to be OK—so-called "happy hypoxia". However there then follows a pattern of lung failure as the alveolar cells become increasingly damaged and are unable to facilitate oxygen transfer to the blood. There also develop cardiac and renal problems and problems with blood clotting. The worse these become, the more likely there will be a bad outcome.

Advice has been to isolate at home if there are symptoms (which include dry cough and loss of sense of smell) and call for help if and when breathing becomes difficult. This, however, may be too late. The critical point, symptoms or no, is when the O_2 saturation drops below 92%. If every household had a pulse oximeter—a simple device, costing tens of pounds or dollars, that clips on the finger, it would make the identification of those at risk more accurate and more timely and would almost certainly result in patients being admitted for intensive therapy before it was too late. The blood tests that determine systemic involvement could then also be done faster. I recommended this in May 2020. Nothing happened [9].

What, then, is Covid-19? Is it overwhelming viral damage? Almost certainly not. It is an abnormal reaction of the body's immune system to the viral infection, which we call a cytokine storm syndrome. What we see in Covid-19 has numerous parallels in previously noted conditions; these include hereditary conditions (HLH, or haemophagocytic lymphohistiocytosis, can be hereditary or acquired), other infections (including other coronaviruses) or administered drugs or immunological preparations. A major textbook has been written about the syndrome, CSS for short [10]; interestingly its publication preceded the coronavirus pandemic. The mechanism is a massive upsurge in the so-called immune cascade, with the release of inflammatory chemicals such as interleukins, and it is these that cause the damage. Rheumatology specialists see similar immunological issues in inflammatory joint diseases and have learned that they may be controlled by agents that neutralize these inflammatory substances. I have seen one case of CSS and a small iatrogenic outbreak was seen in 2008 during a trial of an antibody therapy [11].

The treatment of CSS is steroids and specific so-called biological agents. To date both interleukin-1 and interleukin-6 (IL-1 and IL-6) have been implicated, and both have biological antagonists in current use in rheumatology practice. Their introduction for Covid-19 was delayed by the supposed need to do trials on the basis that the virus was new, whereas what it causes was not. It was also apparent that the timing of steroid and biological use was critical; too early, and they might impair the immune system's direct response to the virus, but too late (as with rheumatic diseases) and the immune cascade had become unstoppable and/or resulted in irretrievable damage.

A component of CSS, and something seen in sepsis, is abnormal coagulation of the blood. This results in thrombotic complications—coronary artery occlusion, stroke, renal damage etc. It may also cause a rash through cutaneous vasculitis. This last is seen in the acute rheumatic condition of Kawasaki disease in children. I remain astounded that the parallels with Covid-19 were not immediately identified; indeed some newspaper reports echoed the puzzlement of government scientists—but my attempts to explain this fell on deaf ears.

While considerable effort was directed at trying to find antiviral agents (of which ivermectin, a widely available antiparasitic drug, may be one) such therapy would not necessarily prevent infection from triggering CSS. Had treatment of Covid-19 concentrated on effect, rather than cause, success could have been brought forward by several months, but even after 9 months there is still no defined or agreed investigation and treatment protocol in the UK. So this is an example of two faults; first, that the experts planning management were not versed in the immunological aspects—they were the wrong experts—and second, that there was insistence on trials for the wrong reasons.

It might be argued that initial small-scale trials seemed to show that certain things did not work. This was true of vitamin D and the IL-6 blocker, tocilizumab. Later, larger trials suggested they had benefit after all—indeed in the middle of February 2021 the BBC News feed ran an article stating "A drug normally used to treat arthritis can be a life-saver for some of the sickest hospital patients with Covid, new research shows".[1] The research may be new, but its conclusion was predicted by me in May 2021, placed before the powers that be, yet

[1] https://www.bbc.co.uk/news/health-56024772

subjected to trials despite both drugs being in use for CSS caused by other triggers. Cron and Behrens' textbook has 12 references to tocilizumab. The apparent failure of earlier trials was almost certainly due to their trial administration at the wrong time. On the other hand, hydroxychloroquine appeared to work in an initial small trial, but was later shown to be ineffective—in my view another example of the right drug (at least in theory) being administered at the wrong time. Is the wholesale administration of existing drugs used for a different purpose ethical? The answer depends on the situation: in desperation you do not wait for trials, you just do it. If a ship is sinking you do not stop to ensure that every lifejacket has a quality control sticker on it. In the case of steroids and tocilizumab the lifejackets had actually been tested. I did try to explain, but no one was listening…

6. RISK FACTORS

It was rapidly realized that some elements of the population have a higher risk than others of developing Covid-19; the elderly, those with obesity and/or diabetes and those from certain ethnic minorities in particular. The approach to the last of these has been bizarre, perhaps fueled by today's "woke" attitude to ethnic issues and an underlying preconception that the risk was related to racism and deprivation. There was no systematic attempt to shield ethnic minority healthcare workers by withdrawing them from front-line Covid-19 care (and it could hardly be argued that NHS consultant staff who died from Covid-19 were deprived). I attempted to remind Government that there was longstanding evidence that changes in susceptibility were often due to genetic factors. In the case of CSS the hereditary form of haemophagocytic lymphohistiocytosis is commonest in people from Bangladesh, and there is good evidence that small mutations on chromosomes 3 and 19 allow the virus to infect cells more readily by causing a change in the ACE-2 surface receptors [12–14]. In the Spanish flu pandemic there were differing fatality rates between different ethnic groups. Yet the specialist committee set up to investigate the ethnic minority issue, full as it was with worthy social scientists, did not contain a single relevant clinician and my efforts to get one included (I even offered myself) were futile. Thus the scientific evidence was sacrificed on the altar of political correctness.

I believe that some cultural factors may increase transmission, whether these are because homes are in multiple family occupation or because of practices such as mass prayer or social gatherings. But acquisition of SARS-CoV-2 is a separate issue from the development of Covid-19.

7. THE ROLE OF THE MEDIA

While the laying-out of numbers may enable people to understand the gravity of the situation, the press conferences at which this was done were very emotive, almost as if the politicians and scientists wished to frighten the populace into submission. Initially individual fatalities were not only reported on by name, but with the addition of potted life histories and family interviews. This was morally unacceptable and unethical, as was the invasion of intensive therapy units by camera crews. Media presentations should be unemotional and unambiguous. The figures themselves were, and are, not put into context, and their impact was thereby exaggerated. Furthermore there was substantial confusion over terminology. As I have indicated, positive "test" results for SARS-CoV-2 were wrongly shown as positive "cases" of Covid-19, and only absolute figures were shown. When in December 2020 the number appeared to rise dramatically, the number of tests being done had risen *pari passu*, hence the actual percentage of tests yielding a positive result remained fairly steady. Comparing the percentage figure with other countries showed that, far from there being a precipitate, disproportionate rise in the UK, the percentage was similar to those in other EU countries, if not lower. There was also ongoing controversy about the effect on the figures of false positive tests and it was apparent that even the Government's scientists did not understand the statistics. The numbers of deaths reported failed to make clear that they were deaths *with*, and not necessarily *from* SARS-CoV-2 infection. The accounting method is probably responsible for the apparent high death rate compared to other countries, because *any* death where Covid-19 was noted anywhere on the death certificate was recorded as a Covid death. There was specific instruction to pathology laboratories that post-mortems were not to be done on Covid-19 patients. Thus there is no absolute proof that the recorded number of deaths is accurate. Given that there are many recorded instances of patients being admitted to hospital for other reasons and acquiring the coronavirus in hospital, it is impossible to say how many died from the virus, because of the virus being a final precipitant, or despite the virus. Other countries have a more rigid definition, hence in comparison the inclusion of deaths that are "not proven" overstates the figures. Furthermore the media chose to report numbers to five significant figures, thereby implying an accuracy that was completely spurious.

From a personal viewpoint I find the media seriously wanting. I approached several national correspondents with comments, or with questions I thought they should put at the Government press conferences. I had a single

response from a regional correspondent, on whose interview with a medical professional I had commented favourably, and nothing at all from anyone else.

8. THE ROLE OF THE EXPERTS

It became apparent that the expert committee, known as SAGE for short, comprised scientists, public health doctors and epidemiologists who were, in the context of severe disease, not experts at all. There were also far too many of them—the main SAGE committee has 86 members—as indeed there are on all of the subgroups, most of which do not have any clinical focus. For a disease with severe clinical manifestations this omission is egregious. There was an extreme reluctance to respond to questions or criticism, of which there was a great deal from other experts. In my own case it was more than reluctance; it was refusal. Initial forecasts based on modeling were wildly inaccurate, fueling dissent, not least when one expert broke the lockdown rules. The argument became entrenched into what was almost a war between lockdown sceptics and lockdown zealots, with the motives, if not the scientific analyses, of the respective sides being impugned. When reasonable concerns, or questions about interpretation of data, were raised by outsiders (among which I include myself) they were simply ignored. As with media correspondents I sent numerous e-mails and letters to departmental figures, including the Secretary of State, and had no response, let alone a rebuttal of my proposals. Neither did I have any acknowledgement later, when my hypotheses and proposals for treatment proved to be correct and I pointed this out. A SAGE committee member recently admitted in a letter that many senior figures automatically filed e-mails in their spam or junk folders.

The failure to include acute care physicians, and specialists in immunological diseases, was a grave error.

9. LOGISTIC FAILURES

The Test and Trace programme was, predictably, a failure. It relied on people using the system (without phone tracking, which can be turned off, it is useless) and if they did use it, using it correctly. The first rule when introducing change is to examine where it might go wrong. This was not done. While the setting-up of the Nightingale hospitals was a logistic triumph unparalleled in peacetime their rôle was rapidly shown to be limited—firstly, because mechanical ventilation in severe Covid-19 is medically the wrong thing to do; and secondly because these new hospitals had to be staffed, when the NHS's own staffing situation was precarious. The first came out in the wash; the second was predictable.

10. VACCINATION

The only unequivocal positive is in the development of the vaccination programme, which was remarkable if now bedevilled by "anti-vaxxer" mis- and disinformation. The roll-out has been impressive; the regulatory procedures were speeded up to an unimaginable degree; bureaucracy was minimized. However, the speed of introduction has fueled the anti-vaccination enthusiasts who claim, among other things, that the speed of the vaccine roll-out has compromised safety by telescoping the approval process undertaken by the regulatory agencies. Might it not be that the normal speed is too slow? And have such arguments used a cost–benefit analysis to balance risk from vaccination against risk from Covid-19? It is particularly concerning that the ethnic minority groups most at risk of developing Covid-19 are the groups that appear most resistant to being vaccinated.

11. CONCLUSION

This is a personal view. My blog [2] shows that although my initial analysis was faulty in that I expected at the beginning that the pandemic was simply a flu variant, and that there was unnecessary panic, many of my subsequent hypotheses were correct and my proposals for treatment were likewise sound. I have thus found it intensely frustrating that my efforts to communicate with those in charge have completely failed—this frustration made worse by the belief that early and aggressive treatment of Covid-19 should not have been delayed through a spurious insistence on trials because what the virus did was identical to a known syndrome with established therapy. Many deaths might have been avoided.

Something that I have found saddening is that in the majority of pandemics of the 20th century clinical and political management was found wanting in ways identical to the errors in management of the present SARS-CoV-2 pandemic. It is as if no one has learned from the past. One ignores history at one's peril.

The economic effect of the anti-SARS-CoV-2 measures worldwide is enormous. Has the benefit of world management by lockdown outweighed the cost to businesses, livelihoods, mental health and the medical care of non-Covid conditions? Should we have let it rip, and find its own level? No doubt in the fullness of time a conclusion will be drawn.

REFERENCES

1. M. Honigsbaum. *The Pandemic Century: A History of Global Contagion from the Spanish Flu to Covid-19*. London: Penguin Books (2020).
2. The Rye Observer's Covid-19 update. At https://bamjiinrye.wordpress.com

3. D. Defoe. *A Journal of the Plague Year: being observations or memorials of the most remarkable occurrences, as well publick as private, which happened in London during the last great visitation in 1665*. London: E. Nutt, J. Roberts, A. Dodd, J. Graves (1722) (authorship was given as "Written by a CITIZEN who continued all the while in *London*. Never made publick before").
4. S. Pepys. *The Diary* (ed. H.B. Wheatley). London: George Bell & Sons (1895).
5. M. Abbas, T. Robalo Nunes, R. Martischang et al. Nosocomial transmission and outbreaks of coronavirus disease 2019: the need to protect both patients and healthcare workers. *Antimicrobial Resistance Infection Control* **10** (2021) 7.
6. P. Nuki. Covid eradication is unlikely…the future of the virus is more likely to follow the flu or measles. *Daily Telegraph* (20 February 2021).
7. See Welsh Parliament Research Service: Testing for Covid-19 using the rt PCR test, p.3 (15 December 2020) https://business.senedd.wales/documents/s500005944/Research%20brief.pdf
8. The website https://ourworldindata.org/ carries a regularly updated graph of percentage positive tests by country.
9. Described in a report on BBC News: J. Gallacher. Covid: How a £20 gadget could save lives (21 January 2021) https://www.bbc.co.uk/news/health-55733527
10. R.Q. Cron, E.G. Behrens. *Cytokine Storm Syndromes*. Springer (2019).
11. H. Attarwala. TGN 1412. From discovery to disaster. *J. Young Pharmacists* **2** (2010) 332–336.
12. D. Ellinghaus et al. The ABO blood group locus and a chromosome 3 gene cluster associate with SARS-CoV-2 respiratory failure in an Italian–Spanish genome-wide association analysis. medRxiv doi:10.1101/2020.05.31.20114991 (2020).
13. H. Seeberg, S. Pääbo. The major genetic risk factor for severe COVID-19 is inherited from Neanderthals. *Nature* **587** (2020) 610–612.
14. E. Pairo-Castineira, S. Clohisey, L. Klaric et al. Genetic mechanisms of critical illness in COVID-19. *Nature* **591** (2021) 92–98.