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What have we learnt so far from COVID-19?

Peter C. Doherty

While COVID-19 shows us the enormous power of modern molecular medicine, it also reminds us of the basic contradictions and limitations of the human condition. As it is highly likely we will experience further such events through the twenty-first century, we should regard COVID-19 as a training run for something that could be much worse, and organize our governance, global interactions, institutions and practices accordingly.

Credit: Image courtesy of the Doherty Institute

We learn from challenges, disruption and failure. What, apart from war, could be more disruptive than a pandemic? In a sense, although COVID-19 is taking a deadly toll both socially and economically, it is, with a mortality rate of somewhat less than 1.0%, by no means the worst such situation that we could face. In fact, we should treat COVID-19 as a learning experience, analyse it very closely from every aspect and conduct an international discussion to formulate agreed policies that will protect the human family from an even more disastrous future pandemic. We live in one world with one health!

Back in 1918–1919, with a global population of around 25% of what it is today, the 1918–1919 H1N1 influenza pandemic is thought to have killed between 50 and 100 million people. While there was an early tendency to describe COVID-19 as a '100-year event', it would be very unwise to assume that this is the case. Since 2003, considering only coronaviruses of (likely) bat origin, five have crossed over to spread within human populations. Only one, the original severe acute respiratory syndrome coronavirus (SARS-CoV) has burnt out while the other viruses are still circulating. The Middle East respiratory syndrome (MERS) virus (which emerged in 2012 and has a 30% mortality rate) remains restricted to the Middle East and parts of East Asia. As we are all aware, SARS-CoV-2 is causing a continuing, global problem with more than 1.5 million deaths so far. In addition to these more familiar viruses, two other human coronaviruses (HCoVs) emerged in 2004, namely HCoV-NL63 in the Netherlands and HCoV-HKU1 in Hong Kong. Both of these viruses are now experienced across the planet as part of the 'seasonal' toll of generally mild respiratory infections. Prior to the year 2000, there were only two 'common cold' type CoVs circulating in the human family.

What has changed over the past two decades? Most important is the rapid ramp-up of mass global tourism, which becomes increasingly risky when there is travel to and from countries with a cultural history of live animal and bird markets, or where people are starving (about a billion across the planet) and killing wildlife as a food source. There are also problematic farming practises that increase the likelihood of zoonotic spillover. Extensive forest clearing, for example, can lead to a loss of larger wildlife (including top predators) and a greater preponderance of small animals, especially rodents, that are more likely come in contact with people or contaminate human food.

These are, of course, issues for national governments. But the very first lesson that we must learn from COVID-19 is that, as soon as any country detects a rapidly spreading respiratory infection caused by an unknown pathogen, this has to be made known globally and all international and national flights from that region must cease immediately. In the past, the mantra has been that 'you can't stop the spread of seasonal, or pandemic, influenza by stopping the planes'. We now know that this is untrue. Both Australia and New Zealand are essentially free of COVID-19 because, early on, we stopped the planes and, more recently, have instituted compulsory quarantine for incoming travellers.

What are the specific lessons for immunologists? The first is that, watching the 'pivot' to COVID-19 research by colleagues who have never worked with a pathogen, all any good immunologist needs is an ongoing collaboration with a competent virologist. And many virologists have also 'pivoted' from their usual 'diseases and death' infectious agents to work with SARS-CoV-2. In fact, most virologists have long worked with neutralizing and other antibodies, but what they gain from immunologists is our expertise with T cells, B cells and so forth.

A further lesson is that, if we are to screen for effective vaccines and therapies that operate to blunt the impact of a novel pandemic pathogen, researchers need easy access to, at the very least, small animal facilities operating at a biosafety level 3 (BSL3)/physical containment 3 (PC3) safety level, preferably within, or close to, their host institutions. Some universities have been extraordinarily reluctant to let infectious agents

Department of Microbiology and Immunology, The University of Melbourne, Melbourne, Australia.

e-mail: pcd@unimelb.edu.au

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anywhere near their laboratory animal facilities. That needs to change.

Perhaps the biggest lesson is that, despite the sophistication of modern molecular science and our capacity to make potential vaccine protein, or nucleic acid, 'product' very rapidly, the necessity for human safety and efficacy testing takes time. With COVID-19, that has been about 12 months. The same is true for virus-specific monoclonal antibodies, although, as with any potential therapeutic, testing is more straightforward as the product can be given to clinically affected individuals. With a vaccine, the necessity is for large test and control cohorts who are then put 'out there' in the face of natural infection. Even with accelerated SARS-CoV-2 vaccine evaluation, that has taken several months.

Some of the vaccines that are in advanced development or testing were brought forward under the global CEPI (Center for Epidemic Preparedness Initiative), which was funded from a variety of sources, including major philanthropy. Other lead vaccines, including one of the mRNA candidates, were independent of CEPI. For the future, what we need is a CEPI that nurtures the development and testing of antiviral drugs that could be available for immediate, emergency use when we are hit by a novel pathogen.

The existing anti-influenza drugs are effective against all of the influenza A and B viruses, although their utility is limited in the therapeutic (as distinct from the prophylactic) sense because the pathogenesis of human influenza is such that they need to be given soon after diagnosis. That is less of a problem in a severe pandemic situation, as both doctors and patients are very aware of the fact that a lethal influenza virus is circulating. In addition, the antiretrovirals we have for HIV and AIDS can be used both therapeutically and prophylactically as they operate across the entire viral spectrum.

What we need, therefore, are panels (more than one to avoid mutant selection) of antiviral small molecule products that effectively target all of the HCoVs. In addition, experience with the paramyxoviruses (especially the henipaviruses) and the filoviruses (most notably Ebola virus and Marburg virus) suggests that these pathogens should also be considered as crucial components for future pandemic preparedness programmes. Developing this idea in the context of the CoVs, candidate drugs could be tested against the common cold/childhood croup CoVs, both in clinical settings and by deliberate exposure in properly constituted human trial facilities. If we did that, we would have panels of therapeutics that could, under emergency use conditions, be available to combat a novel, 'high-path' variant. This would need to be done using public and/or philanthropic funding. We can't expect private companies to operate in this space if there is no possibility of financial return.

In addition, if we could be sure that a cocktail of specific antivirals will work to stop an infection — which we would learn quickly from clinical application — that could also be used to drive more rapid vaccine development by doing human challenge studies. That may sound drastic, but vaccination is always a risk/benefit equation. How will we react if, rather than targeting (in the main) the elderly, a future pandemic virus kills, say, 1–10% of fit young people and children? Vaccines will always be cheaper and easier to roll out than therapeutics when it comes to mass deployment.

Mentioning vaccines also brings us to the final lesson. Scientists and public health professionals need to refine and develop their communication skills. My personal view is that many more of us should allocate at least some of our time to public communication, and all scientists need to be trained in the basics of connecting with people who don't (as we do) see the natural world through the prism of evidence and reason. We need to learn how to become story tellers and, where possible, provide visual imagery. More generally, humanity must re-engage with what all tribal cultures understood intimately: the reality of shared fates. And, when it comes to pandemics, climate change and so forth, we have to grasp that those fates are shared by all people, everywhere across the planet.

Competing interests
The author declares no competing interests.

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