Reflections on and predictions for the Covid-19 pandemic as 2020 gives way to 2021. Part 2

By JOHN DWYER | On 3 January 2021

If there is a "brotherhood of man" now is the time for it to manifest itself as we respond to the enormous challenge involved in overcoming the inequity that could stop us winning the struggle with a deadly virus. Of course in helping the less fortunate we will be helping ourselves.

Vaccines – The news is good

There are more than 100 companies developing vaccines to the SARS-2 virus that causes Covid-19 disease. While Donald Trump claims that it was his determination to have a Covid vaccine developed in a year ('Operation Warp Speed') that has resulted in the Pfizer and Moderna vaccines now being available, it is in fact the availability of new technologies that have allowed candidate vaccines to be developed far more rapidly than was the case with earlier vaccine production.

Much of the work on the Pfizer vaccine was actually done in Germany. Four companies in China have developed and been distributing vaccines for a number of months as has Russia. While efficacy data has not been published to western medicine standards by either China or Russia there is no doubt that both countries have the scientific skills needed to produce effective vaccines. They are already being used in a number of poorer countries ravaged by the epidemic.

The vast majority of the vaccines developed have one target in mind. To infect any of our cells the virus uses one strategy without which infection is impossible. This 'all one's eggs in the one basket' strategy involves a projection from the surface of the virus known a 'spike' protein. This structure can bind, key in lock fashion, to a specific receptor present on the surface of cells lining our mouth, nose, eyes and bronchial tree. Once bound the spike cuts a hole in the surface of the cell to be invaded. If you neutralise this mechanism the virus is harmless.

Two approaches, (one traditional, one very new) for producing antibodies that bind to (neutralise) this spike protein have dominated efforts to produce a vaccine. The traditional approach involves purifying the spike protein isolated from the virus and mixing that with agents known to stimulate an immune response.

The new approach involves taking the *genetic instructions* that the virus uses to generate a spike protein ('messenger RNA') and injecting those instructions into human cells. We are used to making proteins from such a blueprint so have no trouble making the crucial spike protein.

However, once we pop the finished product out of the cell where it was manufactured, our immune system quickly recognises that this is indeed a foreign protein (non-self) and responds by producing antibodies to the spike. This then prepares us to attack the spike protein on the surface of the SARS-2 virus should it ever enter our body. Very clever. The Pfizer vaccine now being rolled out in the US and Europe, as well as the Moderna vaccine which is about to be distributed, both use this approach

Science can on occasions can be a cruel master. Spare a thought for the scientists at the University of Qld. and our CSL who developed an effective vaccine that could have been produced here only to have the whole enterprise collapse because of a small error of judgement.

Vaccine scientists know that after infection with the SARS virus some of the 'spike' protein referred to above can degrade in the bodies fluids. Degradation stops our immune system from recognising the spike and producing effective antibodies. Antibody production would be more efficient if the target was stabilised.

In *film noir,* imagery think of a victim held on either side by two strong men as a third was about to start a punch up! There is a protein that stabilises a part of the AIDS virus that must bind to human cells for entry. It's known as gp 41. The UQ scientists decided to use this protein as a clamp around the spike protein of the SARS virus to stop it changing its structure and not being appropriately recognised by our immune system. It worked like a charm but when individuals were vaccinated using this clamp technology they also made antibodies to the clamp. This resulted in a disastrous situation for the investigators as all vaccine recipients, if tested for the presence of HIV, would return a false-positive result. This outcome made the vaccine commercially non-viable and the project has been scrapped.

In 1975 I was working on a project for the WHO in Senegal. I remember clearly a distressing incident when local physicians found that a huge consignment of desperately needed Polio vaccine had arrived from America only to lie in scorching heat on a dock for a week. Without refrigeration, the vaccine was destroyed.

I mention this as there has been much attention given to the fact that the Pfizer vaccine must be kept at very low temperatures to remain stable. Even in developed countries, this is a challenging requirement, for most developing countries it is an impossible ask. The very similar Moderna vaccine is less demanding but still presents a challenge for mass distribution. Both these vaccines are expensive at about $A40 a shot. Both need a second dose 3- 4 weeks after the first.

It is my feeling that with time the Oxford University/AstraZeneca vaccine will become the most valuable and widely used vaccine. It would probably have been the first to be commercially viable had not investigators testing the vaccine in South Africa and Brazil not had data management problems when the testing regimens being used turned out not to be identical.

Subsequent better-standardised testing however has revealed at least a 95% effectiveness in providing protection. This vaccine is stable needing only standard refrigeration and it costs about $A10 per shot. It is far more suitable for mass vaccinations in poor countries. We are purchasing millions of doses for Australia with sleeves up time for March a real possibility.

<u>Vaccine questions</u>

While there are many important questions about Covid vaccines currently unanswered we are confident that the three leading western vaccines are safe and will stop the vaccinated from getting seriously ill if they meet up with the SARS-2 virus.

When they are available to us, probably in March, we will, as have other countries, prioritise vaccinating the older fragile population who are clearly most likely to suffer serious illness or death if infected and our front line health care workers. Around the world, thousands of doctors and nurses caring for Covid patients have died following infection.

When we start vaccinating the general population it will be crucial that the majority of us are vaccinated over a relatively short period. The much sought after 'herd immunity' will require about 70% of us to be concurrently protected. There are two reasons for this. As with all vaccines, antibody levels will fall over time and we don't want a lot of us having waning levels while still others are just getting vaccinated. We need a situation where there are not enough susceptible hosts for the virus to readily multiply.

The other reason is associated with a current weakness associated with the available vaccines. *They don't prevent infection.* Covid related illness occurs when the virus gets into our tissues in organs

such as our lungs which can be damaged in the struggle between the virus and our immune system. After immunisation antibodies, available to our tissues, will kill the virus before this can happen.

Those antibodies we will have after vaccination, however, are not found in our saliva, tears, and respiratory secretions so even though vaccinated and personally protected we can still have the live virus in our secretions and infect others. This is no big deal if we are all protected from virus-induced disease but will be a problem in the early stages of the vaccination program. The fact that the vaccinated can remain infectious means that for the next year or so travel will still be associated with the need for quarantine.

There are specialised antibodies that are found in our secretions but to have anti-covid antibodies in our secretions before meeting the virus so that it is killed before it can get into our tissues, we need a vaccine preparation that can be delivered to the specialised immune system that lines our 'inner skin" the membranes that line our mouth, nose, eyes, bronchial tree and intestines

Work is in progress to try and develop a vaccine that can be delivered as a nasal spray.

Another huge issue is the vaccination of children. There is every reason to believe that this will not be a problem and immunising children, who can be efficient spreaders of the virus even while having no symptoms, is important. While most children are not ill when infected for a small percentage this not the case. In the US, 3% of Covid patients admitted to hospital are children. Current research is looking at the safety and efficacy of vaccinating children between the age of 12 and 18. If there are no problems with that age group researchers will move to test children less than 12 years of age.

We already have data that indicates it is safe to vaccinate pregnant women. The Covid virus does not find its way into breast milk.

We will learn over the coming months just how long immunity lasts after vaccination. Natural infection appears to provide the recovered with protection from a second infection for at least six months. It is very likely that we will need booster doses before each winter as we do with the Influenza vaccine.

We can afford to buy the vaccines we need, we have the logistics capability to deliver the vaccine to all Australians, our economy can recover but while pursuing these outcomes there is an enormous humanitarian challenge to which the 'haves' of this world must respond.

At least 4 billion people who are the 'have nots' of this world cannot afford the vaccine and don't have the infrastructure to deliver the vaccine even if it was available. If there is a "brotherhood of man" now is the time for it to manifest itself as we respond to the enormous challenge involved in overcoming the inequity that could stop us winning the struggle with a deadly virus. Of course in helping the less fortunate we will be helping ourselves.