FINANCIAL REVIEW

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How to reboot international travel without a vaccine

A vaccine is the best option to get international travellers airborne again, but if it doesn't eventuate there may well be alternative options.

After COVID-19, travel will never be the same again. Passengers arriving in Rome line up for a test at the airport. **AP**

Jill Margo *Health editor*

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While the world waits for a vaccine to reboot international travel, there's a fair chance other drugs could do it first. Compared with vaccines, these drugs are getting very little public attention, although researchers across the globe are feverishly working on them.

“We have to rethink our options in case the best option is not available,"says Professor Brendan Crabb, director of Melbourne’s Burnet Institute.

Just as travellers to malaria-affected areas take anti-malarial drugs for protection, so drugs could be used for temporary protection against COVID-19, says Professor Brendan Crabb. **Burnet Institute**

“This time next year we could be sitting here, back at square one with vaccines, but with new drug options and a drawer full of diagnostic tests we can use any time of the day.

“I expect we will be light years ahead of where we are today in monitoring and tracking the virus, with more user-friendly, digitally connected tools.”

While a vaccine would provide long-term protection, with these other drugs only short-term protection is expected.

Just as travellers to malaria-affected areas take anti-malarial drugs, so these drugs could be used for protection against COVID-19. There is also a parallel with people at risk of HIV who take antiviral drugs to protect themselves from infection.

Antivirals are a prime contender to protect travellers. So are biologicals – drugs made of antibodies rather than chemicals. Then there are compounds called adjuvants, which are usually mixed with vaccines to boost the body’s general immune response.

Crabb says such drugs would be the pointy end of a larger strategy that includes self-administered rapid blood or saliva tests and the usual public health measures of hand hygiene, temperature taking, distancing and masks.

This week US President Donald Trump gave biological therapy a big push. He was advocating the use of convalescent antibodies that, as the name suggests, are antibodies from people who have recovered from COVID-19.

Their antibodies are given to people with severe COVID-19, who don’t have any. The hope is that some of the donor’s immune response will be transferred.

But what interests Crabb, are single laboratory-produced antibodies, each engineered to substitute those that the body would produce itself. These monoclonal antibodies can be produced in the millions, each a perfect

replica of the other.

They have radically changed cancer treatment over the past decade, particularly malignant melanoma.

“These antibodies are vastly superior to convalescent antibodies. The idea is to take them and not get infected for several months,” he says.

Australia has a lot of expertise in monoclonal antibodies, but it is scattered around the country. Melbourne’s Walter and Eliza Hall Institute is collaborating with other groups to try to identify antibodies that can block the COVID-19 infection.

Sydney’s Garvan Institute is researching this too. “These monoclonal antibodies are even more specific and potent than direct-acting antiviral drugs," says Garvan's executive director, Professor Chris Goodnow.

Monoclonal antibodies are heat-seeking missiles with extraordinary specificity to lock onto whatever target you train them on, says Professor Chris Goodnow. **Peter Secheny**

“They are a natural product of our body, a heat-seeking missile with extraordinary specificity to lock onto whatever target you train it on. I think it’s realistic to use them for travel because they are absolutely defined pharmaceutical products and there is an endless source of them.

"They can be engineered so that one shot can provide protection for three months, and they have a well-characterised safety profile. But the main downside is that no company in Australia can produce the quantities at the scale we would require.”

In New York, the company that made a cocktail of antibodies for Ebola is now in phase three clinical trials with a cocktail for COVID-19.

The Garvan Institute has a pair of antibodies that target a different part of the virus. Ultimately, Goodnow says a cocktail of several may be needed to cover all aspects of this tricky virus.

Antiviral drugs work differently. They target the virus in people who are already infected and work better early on, before the virus has had a chance to multiply significantly and cause real damage.

The antiviral Remdesivir was developed for Ebola but diidn't work well and was outperformed by monoclonal antibodies.

Now Remdesivir has been taken off the shelf and is being used with some success in shortening the hospital stays of people with COVID-19. It’s the first antiviral to be approved for this disease and targets the virus’ ability to replicate.

"But it is not very potent and doesn’t initiate a huge fall in viral load, " says Goodnow.

"If we can get cheap antivirals to take for the duration of our time abroad, we'll be away," says Professor Tony Cunningham. **Kate Geraghty**

"The hope is that if Remdesivir was taken prophylactically, before a person was exposed to the virus, it would be strong enough to protect against an initial encounter because it would only have to deal with a low number of viral particles.

"I think it is the best direct acting antiviral candidate for travellers, at the moment."

Professor Tony Cunningham, director of the Centre for Virus Research at the Westmead Institute for Medical Research and the University of Sydney, says a huge number of candidate antivirals are being researched, including the possibility of repurposing existing ones.

"If we could get a couple of antivirals for COVID-19, maybe people could

travel while on the drugs. The analogy to HIV is a good one. If you acquire the virus, then immediately the drugs swing into action and kill it at its point of entry," he says.

A combination of two drugs is used in PrEP, pre-exposure prophylaxis for HIV. Two are used to counter genetic mutations in the virus and to stop the development of resistance.

"Because of our past experience, antivirals may be faster than vaccines, but then vaccines are now moving a lot faster and, because we are desperate, the bar is lower," Cunningham says.

"While we are keeping our fingers crossed for a vaccine that has 60 per cent efficacy next year, the FDA [US Food and Drug Administration] will accept 50 per cent. It might not stop transmission, but it will certainly slow it. Our flu vaccines, in those over 65, are no more than 50 per cent efficacious."

Biologicals could potentially open up travel but could be expensive and complicated to deliver. He says antivirals are more convenient and can be taken by mouth.

"If we can get cheap antivirals to take for the duration of our time abroad, we'll be away," says Cunningham.

Given the time we are in, all things are on the table.

— Stephen Turner, professor in the department of microbiology at Monash University

Professor Stephen Turner, from the department of microbiology at Monash University, points to the use of Tamiflu, an antiviral that attacks the flu virus to keep it from multiplying and to reduce symptoms.

He says some people take it before flying. Although it won't prevent infection, it will limit the growth and transmission of the virus. It can also stop them getting sick.

Turner also raises the possibility of using adjuvants, immune stimulants usually mixed with vaccines. While they work generally rather than specifically, they boost frontline immunity.

Professor Stephen Turner sees adjuvants as a possible "first line of defence". **JOE ARMAO**

“These compounds mimic what triggers the immune response after infection. With this, they induce a transient inflammatory response, which in the main should be antiviral," he says.

“So, they could be a first line of defence, and could be protective.”

Turner says travellers might potentially be able to spray it up their nose to stop the initial replication of the virus. As this may work only for a week, they could carry the spray with them.

“Given the time we are in – all things are on the table. I don’t see this outside the realm of possibility, I just don’t think it will happen very quickly.”

He notes a TB vaccine is now being trialled in Melbourne healthcare

workers to see what sort of protection it can provide. Having been used in

millions with tuberculosis, it has a good safety profile.

Professor Tania Sorrell, director of the Marie Bashir Institute for Infectious Diseases and Biosecurity, says the principles of providing protection for travel “are very appealing", especially if they protect individuals and reduce spread to others.

Ethical issues will arise if the drugs are not available to the entire population.

— Professor Tania Sorrell, director of the Marie Bashir Institute for Infectious Diseases and Biosecurity

"But there is much to be done on the journey to make them a reality. One thing is getting antibodies to the respiratory tract, in high concentrations, for long enough to be effective.

"Trials will be critical to prove benefit. If drugs are going to be used by millions for prolonged periods, uncommon side effects will surely arise."

She says if you test negative on the day of departure, it doesn’t mean you will be negative the next day.

"If we don't protect our neighbours, we won't protect ourselves," says Professor Tania Sorrell.

"In theory, you need to take your prophylaxis for two weeks both before departure and after return from a hotspot to cover the incubation period.

"And ethical issues will arise if the drugs are not available to the entire population. The scale of our public health problem is enormous.

"It's very important we treat ourselves as a global community, because if we don't protect our neighbours, we won't protect ourselves. Nevertheless, this concept of having drugs or antibodies for prevention is exciting."

Should a vaccine fail to arrive, another option is to test everyone every week for live virus, with cheap disposable saliva tests.

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"This way we would eradicate the virus," says Goodnow. "It would be an escalation of what we are doing now by many orders of magnitude.

"I don't think it should be not considered. There are technologies that could deliver it, if we made the investment.

"Look at the cost to the economy of this virus. The return on that investment would be huge."

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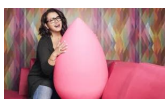

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