From Coates to COVID-19 and Climate Change

Sir Albert Coates Memorial Oration, Federation University Ballarat, 16 November 2022

Through a substantial part of his extraordinary life, Albert Coates (1895-1977) was recognized as a great surgeon, an entertaining and informed lecturer and mentor and an Australian medical leader. What elevated Lt/Col Coates to hero status was his fearlessness, determined resolve, outstanding technical competence, and empathy as a top army doctor caring for POWs on the Burma/Thai railroad. I should like to have said much more about this effective, decent and modest man, but there isn't time. There is an excellent 2009 biography by Walter Gherardin *Against the Odds: Albert Coates, a heroic life*.

Born in 1895, Albert Coates experienced three major global crises, WW1, the 1918/19 influenza pandemic, and WW2. Maybe three is the magic number. Now, the same age (82) as Coates was when he left us, I've lived through WW2, the continuing HIV/AIDS pandemic and COVID-19. Added to that, the human family is facing what many regard as the greatest and most dangerous challenge in the story of us, the inexorable progression of anthropogenic climate change.

When it comes to an acute crisis rather than the building threat of climate change, the modern Australian Nation has never been in greater danger than it was in 1942. Easing into retirement in 2019, I began writing the 'war and peace' story of my two tennis-playing, citizen-soldier, maternal uncles, an effort that was delayed by COVID-19 and my being recalled to active service as a public science communicator. Like Albert Coates, Charlie Byford (he didn't make it home) was a POW on that terrible railroad. Jack Byford survived (with relapsing malaria and PTSD) after fighting as an infantry private on the Kokoda track, in East New Guinea, and in the last battle of the war, at Balikpapan in Borneo. Published this August, researching *Empire War Tennis and Me* greatly enhanced my understanding of Australia's Pacific war, with some of that surfacing in this discourse.

Now, 80 years later, those who served in 1939-45 have mostly left us. Born in 1940 my generation, who recall these men and women as relatives, teachers and young adults, is also shrinking fast. Reflecting on the citizen-soldiers of WW1 (Coates served in both) and WW2 and the social environment that molded them, I decided to develop this Oration from a mildly military perspective.

When we're talking generally about COVID-19 or climate change, inherent in that discussion is the nature and effectiveness of our national defence. We aim to 'win the war' against a pandemic pathogen and, like an army in the field, prefer not to contemplate the possibility of defeat.

At a different level, we may say that an individual has won, or lost, the battle as they 'fought valiantly' to 'defeat' a malignant cancer. That's an interesting one. Cells become cancerous and develop into tumours of different types when they escape from normal growth control. The economic model our types of societies commit to is endless growth. In medicine, we call that cancer. And the cancer cell is the ultimate dumb victor: when it 'succeeds' and kills its host, us, it also dies! Something to ponder on there, especially with regards to climate change?

Trying to explain viral immunity to the broader community, I wrote about the protective 'neutralizing antibody' molecules induced by vaccination or prior infection as 'clone soldiers' that, spilling over from the blood into the nasal cavity, hopefully block the virus 'enemy' as it seeks to invade, and take over cells in our respiratory epithelium. Then, if the virus breaks through the protective antibody barrier, the 'killer' T lymphocytes that eliminate those cellular 'virus production factories' are the 'cloned assassins', or elite

commandos that infiltrate sites of conflict (in our body tissues and organs) and bring the battle to a close.

We know what we mean by the term 'army', but how well does this describe the forces we massed against COVID-19? The Australian 'army' of health care workers, from ambos and nurses, to GPs, and respiratory medicine and ICU specialists is, of course, diverse and under a number of separate, and often poorly-linked commands, from private and public hospital administrations, to operations run by for-profit and non-profit deliverers of services, to small-group and individual providers and so forth. The link that brings many of these together is presumably mutually supportive needs, established practices and, of course, funding.

When it comes to the overall command structure in a health emergency, the closest thing to that is presumably the State Health Departments. Informed by various expert standing committees, there can also be a co-ordination/oversight role from the Commonwealth reflecting that the Federal Government is, in the end analysis, the major source of funding. But, while we formed a national army after 1901, health services, insofar as they were conceived at all at that time, were left with the States.

Not being a public health doctor, I learned a lot about how this works during the COVID-19 pandemic. Listening to senior colleagues and group leaders at our Institute describe (in morning zoom meetings) what they were doing, including the various frustrations they were facing, I gained a new understanding of the complexity and challenges of this health care environment

As I describe in my 2021 book *An Insider's Plague Year*, our Institute is unique in that we have various State (Melbourne Health) and federally funded operations under the same roof as the *University of Melbourne Department of Microbiology and Immunology*. The *WHO Collaborating Centre for Reference and Research on influenza* is one of 6 globally that identify the virus strains for the annual influenza vaccines. Led locally by an outstanding scientist, Kanta Subbarao, the WHO influenza network is a modeI for international co-operation and pandemic preparedness. At least in Melbourne, much of their effort, plus that of many of our basic scientists, pivoted fast to work on COVID-19.

I know the University and the global influenza cultures reasonably well, but it was a revelation to hear regularly from the top professionals in *VIDRL*, the state virus reference and diagnostic laboratory; the *MDU* that performs the same role for bacterial and fungal infections but switched some of its gene sequencing capacity to do the genomics of SARS-COV-2; and *VIDS*, the infectious disease specialists who work at Royal Melbourne Hospital, and took a heavy clinical load as cases peaked and staff were furloughed due to infection or contact.

I should also make the point that our job was to provide laboratory and clinical services and solicited advice. The use of the term 'Doherty Modelling' has led some to think that we were responsible for the various lockdowns. I'll say more about modelling later, but the role of our epidemiologists was simply to lay-out possible scenarios to help those with authority make useful decisions.

Both with the military and with the public health response, the ultimate responsibility and power rests with elected political leaders. As we are all aware, the authoritative face of the COVID-19 response had the Prime Minister and State Premiers performing regularly with their Chief Medical Officer (CMO, Federal) or Chief Health Officer (CHOs, the States). And, of course, they spoke to us via our TV sets, a technology that was not available for the 20th century crises that Albert Coates endured.

In his later years, Sir Albert Coates chaired the Board of the now defunct Fairfield Infectious Disease Hospital, where he worked with Matron Vivian Bulwinkel, the sole survivor of the Bangka Island Massacre when, in 1942, 22 Australian nurses were driven into the sea and machine-gunned. Some of the senior medical leaders through COVID-19, including our Director Sharon Lewin, trained early on at Fairfield.

The CHOs represented the professionals of the various state Health Departments, including medical doctors with specialist public health training. The degree to which they had any control over those departments varied, and much of the time they were speaking to us with an authority based in our best understanding of the science as they explained why a particular strategy was being followed.

That generally positive interaction between the doctors and the politicians reflected a way of operating that emerged years back with HIV/AIDS. Part of the reason Australia did so well with this (compared to the USA) is that we took a pragmatic approach with politicians acting on the medical advice. In part that reflects, I think, the broad character of the Australian people where, we do take a collective view that emphasizes the public good. The one element that was not repeated at the federal level was the bipartisan inclusion, by Health Minister Neal Blewett, of opposition health spokesman and medical doctor Peter Baume (later Jim Carlton) in the AIDS discussion. As everywhere, our politics has become more polarised.

We had our first case of COVID-19 in late January 2020 – he was diagnosed with the PCR test that Mike Catton and Julian Druse at VIDRL developed within a few days of the publication of the gene sequence on January 15 – and the country was immediately on alert. The VIDRL team isolated the SARS-CoV-2 virus and the decision was made immediately to distribute that globally to any legitimate group that requested it. We were the first to do so.

Why was that important? Growing live virus in tissue culture cells is essential for the 'benchmark' virus neutralization test, and it's also necessary for mandated preclinical studies for vaccine and antiviral drug development where laboratory animals are challenged with the pathogen. Back in 2002/3, we'd had the greatest difficulty in obtaining the original SARS-CoV-1 virus.

As an illustration of how science has changed over the past 100+ years, though doctors back then knew that a virus was the cause of the 1918/19 flu pandemic, the first influenza viruses were not isolated until the early 1930's. AIDS raged for almost two years before Francoise Barre'-Sinousi (she is a member of our scientific advisory board) identified the causative human immunodeficiency virus (HIV). The first case of Sudden Acute Respiratory Syndrome caused by the SARS-CoV-1 virus was detected (in China) in November of 2002, and the virus was isolated in March 2003. Once that happened, it was soon realised that very sick patients were (unlike the situation with influenza) highly infectious late in the disease. That led to the adoption of strict barrier nursing (protective clothing, masks and gloves) and the disease soon burnt out. In all, a total of 8469 people are known to have been infected, with an 11% mortality. With COVID-19, though retrospective analysis suggests that the SARS-COV-2 virus could have been circulating for 1-2 months before, the first official notification of the problem in Wuhan was in December 2019, the virus was isolated immediately and the gene sequence was soon published.

Returning to the Australian public health response to COVID-19, though the informed professional community was saying from the outset that 'this is not influenza', the response globally was conditioned by our long experience of influenza. The 1918/19 influenza pandemic began in the latter half of 1918 and devastated the armies on the

western front. Estimated to have killed some 50 million people, the German military commander General Ludendorf later said that influenza effectively compromised their capacity to continue fighting. Having to travel by ship, the flu did not get to Australia until 1919, and the global pandemic was essentially over by 1920.

Since then we have, of course, learned how to make reasonably effective flu vaccines. If, instead of a CoV we'd been dealing with an influenza virus, we could have been getting vaccine 'out there' and into people's arms within a matter of months. And we already had antiviral drugs, like *Tamiflu*, that, if given early after a rapid PCR diagnosis (the strategy developed for COVID-19), works well to bring the infection to an end. In the future, we might envisage that making flu-specific RATs and antiviral drug available to the broader community would blunt any future influenza pandemic.

One of the mantras within the global influenza community has long been that: 'you can't stop the flu by stopping the planes.' Well, when Australia and New Zealand locked down and stopped the planes, we also stopped the 'flu. Perhaps it would have already been too late but, if China had stopped outgoing international flights (they did ground domestic flights) as soon as they knew they had a problem, would that have slowed virus spread? If the global community has learned anything from this, the lesson should be that we stop passenger planes flying from an afflicted area as soon as we know there's a problem. Added to that, there must be immediate and full disclosure via the WHO of the nature and scope of the disease outbreak.

The second mistake that we made from the virology aspect was to think that, as SARS-CoV-2 has both a much larger genome than flu and a potential mechanism for molecular proof reading, it would throw off mutant viruses much more slowly. As we now experience a further round of infection with the BQ.1 and XBB variants, which are clearly immune escape variants in the Omicron lineage, we all understand how wrong that was.

The severe lockdowns in Australia were no doubt influenced by the idea that, as with influenza, having reasonable vaccines available would bring the problem to an end. And the SARS-CoV-2 vaccines were indeed great when it came to blocking infection and severe disease caused by the Wuhan strain. Now these vaccines are doing little to prevent infection, though priming T cell mediated immunity (which is much less subject to mutational escape) may still be keeping vaccinated people who are capable of generating a strong immune response out of hospital.

And a further problem is we thought initially that COVID-19 was, like influenza, primarily a viral pneumonia. Human flu viruses pretty much only infect the respiratory tract. But, while there may be horrible 'ground glass opacities' in the lungs of COVID-19 patients, SARS-CoV-2 also travels throughout the body in the blood (systemic spread) and infects other body organs like the heart and kidneys. Additionally, COVID-19 can present as a 'coagulopathy', with microclots in the tiny blood vessels in the lung blocking gaseous exchange and the potential for an enhanced incidence of heart attacks and strokes, both acutely and in the long term.

Despite those caveats, our public health response worked reasonably well from the aspect of protecting people against infection. So far, we've had about 15,000 deaths mostly, though not exclusively in the immunocompromised elderly. The great majority of these have happened since we progressively weakened the public health controls. It's a very crude measure but, if we simply use relative population size to compare our performance with that of the USA and the UK we might, in both cases, have expected 60-70,000 deaths from, or with, COVID-19. Was it worth it? We need solid, in-depth academic analysis from

economists, sociologists, educators, civil rights lawyers, mental health experts and various medical professionals to inform that continuing debate, locally and globally

Currently, our Federal Government is developing a new national public health initiative under the rubric of an Australian CDC. What that means will likely become clearer over the next couple of months. For someone with my background, the term CDC refers to the *US Centres of Disease Control and Prevention* that, located in Atlanta, Georgia, is the central laboratory for the USPHS, the *United States Public Health Service* (USPHS). Many of the medical doctors who work at the CDC, in the USPHS and in the massive medical research complex at the *National Institutes of Health* (NIH, Bethesda) -where Tony Fauci is located - are members of the *Public Health Service Commissioned Corps*. The PHSCC is one of 8 uniformed Federal Corps. They can be required to wear what looks like a naval uniform once a week. Additional to the Army, Navy, Airforce, and Coast Guard, we can add the Space Force (founded in December 2019) and NOAA, the National Oceanographic and Atmospheric Administration, which runs the US weather service and is a central government agency (along with NASA) researching climate change.

The CDC and the NIH have both put out great information through the COVID-19 pandemic, and much of the best research on what's happening with COVID-19 has been done in universities on extramural NIH grants. But much of the public health response across the USA has, as here, been run out of the States. Some, like Washington State, have used protocols that are not so different from ours and have had relatively low death rates. Others 'let the virus rip' with the predictable results we are now seeing here.

When we discuss Health Care in the USA, we don't normally think in terms of a national health service. However, the Veterans Administration (VA) runs a network of hospitals and provides life-long medical care for full-time members of the 8 commissioned corps. Though heavily biased towards men, the VA databases have provided some of the best information on what has been happening at the population level with COVID-19. The other great resource has been the UK National Health Service where, with central control and financial incentives, hospitals across the country are effectively linked as clinical research nodes. Some of the best population studies have come from Public Health England and Public Health Scotland. Personally, what I'd like to see happening with the CDC discussion in Australia is the emergence of robust mechanisms for better coordination, data-linkage, and sharing of reagents, resources and information across the country.

A prominent feature of WW1 and WW2 is that both conflicts drove technological advances and the rapid development and deployment of new 'weapon systems. With COVID-19, we saw mRNA and Adenovirus vectored vaccines that had been in development for decades suddenly come to the fore and, at least initially, work spectacularly well, though with some side effects that are still being sorted out. On the downside, despite the sophistication of those approaches, we have also had a harsh lesson in how a virus that is evolving across the whole human family can rapidly escape from immune control. Like the British and Dutch in SE Asia before WW2, we greatly underestimated the enemy!

As unicellular organisms, bacteria use different biochemical pathways to us. A completely novel bacterial pathogen that came out of nature could likely be countered by existing broad-spectrum antibiotics. Viruses, on the other hand, are obligate intracellular parasites that can only replicate within the living cells of other species, from bacteria (bacteriophages) to people. This means that antiviral drugs generally target molecular pathways that are unique to a particular virus, or class of viruses. The influenza antiviral

Tamiflu, for example, can be used to block the replication of all influenza A, B and C viruses, while the influenza vaccines are redesigned yearly to counter the latest mutant strains.

What needs to happen over the next few years is for humanity - and it will require the input of national governments, philanthropic donors and the pharmaceutical industry - to (as is the case with HIV/AIDS) develop at least two, perhaps three, drugs that target different molecular pathways (the HIV/AIDS strategy) in the classes of virus that potentially threaten us. Apart from influenza, the potential 'public enemy number 1' list includes the CoVs, the henipaviruses (Hendra and Nipah virus) and the filoviruses (Ebola and Marburg viruses). Multiple variants of each of these virus families are known to be carried by fruit and insectivorous bats. That realisation, which only goes back to the 1990s, has led to surveillance programs that seek to enhance preparedness by isolating and characterizing novel (to us) viruses in bats. With no solid evidence to support it, some believe that SARS-CoV-2 is one such strain that escaped from a laboratory. That is, of course, almost impossible to disprove.

On the other hand, virologists who work with the CoVs are generally convinced that the gene sequence of the original Wuhan SARS-CoV-2 strain indicates that it has not been manipulated in any way, and accept the evidence that the initial cases clustered around the Wuhan seafood/live animal market. We do know, of course, that the SARS-CoV-1 virus transmitted from bats to civet cats, and finally to humans in a live animal market. Anyone who has looked at how influenza viruses jump from avian reservoirs into us is in no doubt that live bird markets pose a major threat.

In the military context there is, of course, an absolute perception that the more we know about a potential enemy the better. That is, of course, the basis the intelligence services work from. If we hark back to WW2, the Imperial Japanese Navy (IJN) positioned a major carrier task force in striking distance of Hawaii without the Americans being aware of what was happening. Then, four of the six aircraft carriers that launched the 7th of December 1941 attack on Pearl Harbor sailed on to waters north of Australia to bomb Darwin on 19 February 1942. The payback phase began when, from 4 to 7 June 1942, due to inspired guesses by US intelligence analysts, all four of those IJN carriers were sunk at the Battle of Midway.

Today, of course, any large-scale movement of surface ships, and perhaps those below the surface for all we know, will immediately be detected by satellites that constantly monitor the globe. Apart from any military role, a further essential role that satellite systems fulfil in ways that are ever more sophisticated is to track greenhouse gas emissions and their consequences. Such functions range from relaying the readouts from diver buoys that report temperature, acidity and so forth at different levels of the ocean to measuring the extent and depth of ice sheets and glaciers. On land, they monitor the progress of desertification and deforestation. A recently developed capacity to measure local methane emissions could have major implications for Australia.

When it comes to predicting future events in both pandemics and climate change, these seemingly diverse areas of human enquiry come together in the 'thought experiments' of the mathematical modellers. Apart from climate and weather modelling (recognized by the 2021 Nobel Prize for Physics) COVID-19 introduced us all to the epidemiologists who, contracted by government, provide predictive models to inform public health decision-making.

The mathematical skill sets required for climate and epidemiological modelling are comparable. While many epidemiologists are MDs with later specialist training, others

crossed-over from physics. Medicine also recruits such people to work with laboratory-based researchers as 'computational biologists', or 'informatics' specialist, as we try to make sense of the enormous data sets generated by contemporary molecular technology and robotics. We're talking here about genomics, proteomics, metabolomics and so forth. We also compete with commercial interests (banks, the gambling industry) when it comes to hiring talent.

With massive amounts of data coming in constantly from satellites, sophisticated computational analysis is also essential for generating the data sets that underly the assumptions basic to climate modelling. With COVID-19, those assumptions became more robust as we saw what was happening with the rapid evolution of SARS-CoV-2, especially as regards infectivity and immune escape.

Currently, much of the climate modelling is based on a 100 km grid. A point made recently https://www.youtube.com/watch?v=hLQ5AqldAx0 is that, if we are to achieve much better long term predictions of both extreme events and prevailing weather for particular regions of the planet, that needs to come down to a 10km grid. This would require ramping up the computing speed from 10^{15} to 10^{18} fps (floating point operations) per second and cost, say 200 million euro per year. Why is that important? If we don't, for example, make more accurate predictions around, say, the persistence of low cloud cover and wind strength, we could commit to expensive infrastructure solutions that will simply not do the job

A major, and horrific, technological development, the atomic bomb, brought the war in the Pacific to an abrupt end on August 14, 1945. Reading the war diaries for my Uncle Jack's infantry battalion (the 2/31st), I learned that Earl Mountbatten (the C-in-C for the South Asian region) visited after the cessation of hostilities and told them that the alternative war plan would have delayed the invasion of Japan's main island till March 1946. Following the experience of Okinawa, it was predicted at least a million military and civilian lives could be lost, additional to the killing of all POWs.

After peace was declared and WW2 ended, the allies - determined to avoid the mistake made after WW1 when massive reparations were demanded of Germany – helped what became West Germany and Japan rebuild. The problem is, though, with both COVID-19 and climate change, we can't just declare peace and go back to normal, though many seem to be convinced that we are at this stage with the pandemic. Others are still telling themselves that climate change is some sort of hoax: what would be the point of that?

War leaves many with enduring physical compromise and/or PTSD. Both COVID-19 and the extreme weather-related events (like fires and floods) we've been experiencing so regularly are associated with massive economic loss, persistent psychological damage and unresolved medical problems like Long COVID. The pandemic has shown us both the strengths and limitations of science. With climate change, when did we last make it rain or stop raining?

While we pursue technological innovation, like generating unlimited energy from nuclear fusion, we must also be brutally honest with ourselves and squarely confront the challenges facing us. That's what extraordinary people, like Albert Coates, and ordinary people, like my two uncles, did during WW2. We face the greatest challenge that has ever confronted humanity: to change the way that we operate on this planet, our only home.

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