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The Who, How and Why of COVID-19

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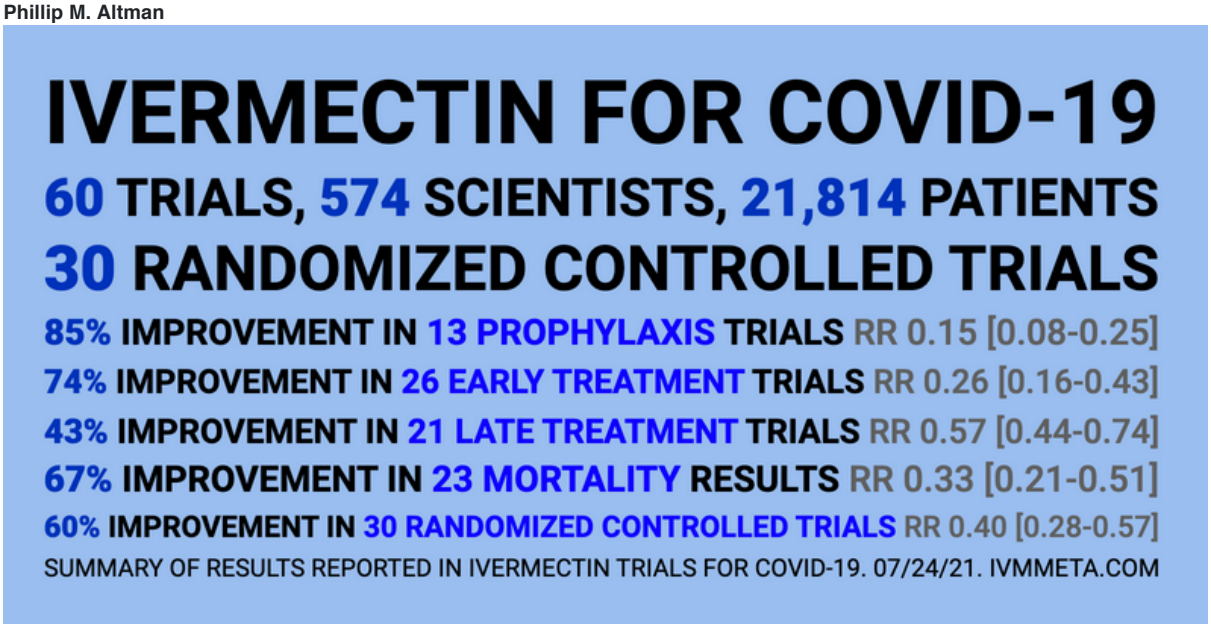

There is a considerable amount of misinformation, including bias by omission, in the mainstream media regarding COVID-19. As a pharmacologist involved in drug development, clinical trials and drug registration for 40 years – here are a few facts you need to know.

From where did Covid-19 come?

Coronaviruses can cause the common cold but there is little doubt that the coronavirus COVID-19 is a genetically engineered virus designed to be highly contagious. According to viral evolutionists, unique nucleic sequences have been inserted in this coronavirus, sequences which could not spontaneously arise by chance in nature. Since the beginning of this pandemic some leading infectious disease researchers and physicians and the World Health Organisation (WHO) have tried to claim COVID-19 came from the Wuhan wet market despite the absence of a single piece of evidence to support this proposition. Despite an intense search, no animal has been found to contain the virus.

There are many international patents which paved the way for the construction of COVID-19 based on work in association with the US National Institute of Health (NIH) and the US National Institute of Allergy and Infectious Disease (NIAID) using dangerous "gain-of-function" research.

Social media has de-platformed and censored anybody claiming the virus probably arose from the Wuhan Institute of Virology. Experts and the media are finally walking back the natural origin bat/wet market theory and admitting it is probable COVID-19 leaked from the Wuhan Institute of Virology in China. The implications of this are enormous as many people involved directly or indirectly in creating the virus (such as Drs. Anthony Fauci, Ralph Baric and Peter Daszak) now are involved in vaccine development and/or helping to set US government policy and shape public opinion while standing to gain financial benefit. Moore importantly, they count

among some of the loudest critics of therapeutic measures other than vaccines to counter COVID-19.

These simple facts are the foundation for much of the misinformation and poor public health policy we are now experiencing. Until we clearly understand how this disaster happened we will be doomed to repeat the catastrophe.

The new vaccine technology

The new genetic vaccine technology used in the mRNA-based vaccine of Pfizer (and Moderna) and the DNA- based adenovirus AstraZeneca and J&J vaccines have never been previously approved for use as any new pharmaceutical. These vaccines could be called 'genetic vaccines' because they deliver genetic material for your cells to use as a template in manufacturing the identical spike protein which is found on the surface of COVID-19 virus. It is this manufactured spike protein, released into the blood from your cells following vaccination, which triggers your body to produce antibodies to protect you from a COVID-19 infection.

Have the COVID-19 vaccines been fully approved?

No.

Due to the urgency of the pandemic, vaccines have been provisionally approved in the US and Australia pending the generation of further safety and efficacy information. The following COVID-19 vaccines (*listed below*) have been released in Australia under "provisional approval" which includes strict conditions such as the requirement to provide further long-term efficacy and safety information from ongoing clinical trials and post-marketing assessment from the reporting of adverse reactions.

Effective date	Sponsor	Name	Type
25 January 2021	Pfizer Australia Pty Ltd	COMIRNATY - BNT162b2 [mRNA]	mRNA
15 February 2021	AstraZeneca Pty Ltd	COVID-19 Vaccine AstraZeneca	Viral vector
25 June 2021	Janssen-Cilag Pty Ltd	COVID-19 Vaccine Janssen	Viral vector

Unresolved questions about the new vaccines

What is the duration of protection from infection following vaccination?

What is the chance of transmitting infection if one is fully vaccinated?

What is the risk/benefit of vaccinating individuals who have had COVID-19 and have developed natural immunity on their own?

Which vaccine is best for older people or young people?

Should all children, babies or pregnant mothers be vaccinated?

Are there circumstances where specific vaccines should not be used (contraindications)?

How effective are the new vaccines against emerging strains of Covid-19 such as the Delta variant?

How effective are the new vaccines?

The new mRNA vaccines were provisionally approved on the basis of a single randomised, controlled clinical trial involving about 40,000 volunteers. Regulatory bodies, such as the US Food and Drug Administration in the US and the Therapeutic Goods Administration in Australia, usually require many clinical trials for approval. However, this was an exceptional set of circumstances. Gaining approval after only a single clinical trial means that it becomes extremely important to gain additional post-market safety and efficacy data.

Now that millions of doses have been used, experience to date strongly suggests the genetic vaccines can prevent, to a large degree, more serious COVID-19 symptoms, hospitalisation and death, especially in those individuals with co-morbidities (age, diabetes, compromised lung and cardiovascular function).

It has been widely reported that the mRNA vaccines were about 95 per cent effective, but the question is: "effective at doing what"? In fact, the trials of the genetic vaccines did not find any difference in the death rates for vaccinated and unvaccinated groups (there were too few COVID-19 cases) and, furthermore, the primary criteria for being "effective" was a positive COVID-19 test *and* a symptom(s), including even a mild ones like a cough or fever. While this clinical trial result is one metric to indicate the level of immune efficacy, the selected criteria did not permit any reliable estimate of the level of protection against progressing to serious clinical conditions, being admitted to hospital or dying from COVID-19. This was because the numbers in these categories were too small to be statistically meaningful.

What does the daily reporting of "cases" tell us?

COVID-19 tests use long-established Polymerase Chain Reaction (PCR) technology. This test is so sensitive it can be set to detect even a single molecule of the target substance.

PCR tests measure a short nucleic acid sequence which is present in COVID-19 whether or not this is in the form of an intact COVID-19 virus or a fragment of a dead virus from a previously infected person. The test cannot tell if there is the presence of a live virus, nor can it determine the viral load (the amount of virus) in a positive test. Then why is the number of positive PCR tests the key metric driving public health policy in this pandemic, which is causing such massive economic and social damage? It makes no sense.

Given more than 99 per cent of people who are infected by COVID-19 experience either no symptoms or mild symptoms, shouldn't our health policy be driven by the number of seriously ill subjects, patients admitted to hospital, or the number of deaths due to COVID-19 (not "with" COVID-19)?

Let's keep a sense of perspective. There are normally more deaths expected due to ordinary pneumonia/influenza each year than have died with COVID-19 since the pandemic began.

How safe are the new mRNA and DNA vaccines?

Safety is a relative term in pharmacology. Anti-cancer drugs are highly toxic but they can also save your life. There is always, with any drug, an assessment of risk vs benefit. The benefit side of the equation is becoming clearer with widespread vaccine usage, but the risk side of the equation is far from clear because there has been no detailed, publicly available overall analysis of the incidence of adverse drug reactions (ADRs) that are likely or, probably, related to the vaccines.

The evaluation of ADRs includes a detailed analysis of the subject's medical history, the circumstances surrounding the ADR, the temporal relationship to the drug and co-administered drugs, and consideration of the mechanism of action of the suspect drug. There are various guidelines and definitions used to estimate whether or not there is a causal relationship. It takes experts considerable time to assess with any

precision which serious adverse effects observed are actually due to a drug's administration.

In the past, safety concerns have led to the withdrawal of certain vaccines following widespread usage, and regulatory agencies routinely monitor the safety of vaccines via various ADR systems. There is a specific ADR system used by the US Centres for Disease Control (CDC), the Vaccine Adverse Event Reporting System (VAERS).

As a general rule, as few as ten per cent of ADRs are reported. This observation, coupled with the government's perceived need to overcome vaccine hesitancy in the population, work to minimise ADR reporting and underestimate the true incidence of any particular ADR. This frustrates an accurate assessment of risk.

For mRNA vaccines, it has been reported that nearly one-third of those deaths reported in the ADR system occurred within two days of vaccination. These reports and thousands of hospitalisations following vaccination need full investigation to determine if there is any causal association. To date the public has not been appraised of any comprehensive, reliable and detailed analysis of the type and incidence of adverse reactions likely to be associated with genetic vaccines given the worldwide experience.

Claims that the vaccines are "completely safe" should be considered premature until further safety data becomes available. Until that time, the risk-benefit proposition in healthy young people, those previously infected with COVID-19, infants, children and the pregnant remain unresolved.

Every vaccine is different. The use of more traditional vaccines, like Novavax in the near future, may present a relatively more attractive risk-benefit position, but only time will tell.

Masks

There is much misinformation about face masks.

First, there is no credible evidence in the literature that cloth models or the ubiqitous blue-paper surgical masks prevent to any significant degree the spread of airborne viruses. N95 masks *can* be effective, but they need to be fitted so there are no air gaps. If you do use a paper surgical mask of the common blue type, do not reuse it, do not place it on hard surfaces, do not put it on and off repeatedly — it is designed for aseptic single use. Surgeons use masks to prevent the infection of open surgical sites. They are not used to prevent the surgeon from getting an infection. There has been a dramatic increase in bacterial pneumonia worldwide associated with the use of masks mandated by governments. As to wearing masks outdoors, most authorities consider outdoor transmission of COVID-19 as improbable.

Recommending that very young children wear paper or cloth masks, given the incredibly low relative risk, has been the subject of experts' criticism due to the deleterious effects on their physical and mental health. Apart from anything else, small children tend not to wear masks correctly and are most unlikely to follow aseptic procedures.

Delta variant

Various medical bureaucrats and politicians have exaggerated the threat posed by the Delta variant now sweeping the world. Multiple sources report the Delta variant to be more infectious but less deadly. Claims that the Delta variant is a "beast" that will kill thousands are not supported by current knowledge and contribute without justification to the creation of unnecessary fear.

Challenges of a vaccine-centric strategy

There are several problems in relying almost exclusively on vaccines to deal with the COVID-19 pandemic. Theoretically, putting all one's eggs in a single basket seems to be a risky strategy when there is so much yet to be learned about the safety and efficacy of these vaccines, and because so much depends on a successful outcome.

At this point in time we should be spending more effort in considering preventative and/or drug treatment strategies for ambulatory patients through to seriously ill COVID-19 subjects. The advice to those who have been determined as COVID-19-positive is to isolate. No treatment is actively recommended – just wait until you feel better or become so ill you need to be hospitalised.

Alternative therapeutic strategies – hydroxychloroquine and ivermectin

Given the sweeping global impact of COVID-19, it would seem prudent to hedge our bets and pursue alternative therapeutic strategies in parallel with mass vaccination. Some conventional drugs, including corticosteroids to counter the inflammatory effects of COVID-19, as well as newer approaches, such as antibody infusions and remdesivir (an expensive and provisionally approved antiviral drug) have been shown to have limited efficacy but they fall short of a complete solution.

Certain other candidate therapies, including hydroxychloroquine and ivermectin, have been studied in many clinical trials and used in national programs in India, Mexico and South America with reported success. But there exists broad censorship across social media, mainstream media and the professional literature which is preventing the sharing of clinical trial results and the academic exchange of views. Up until recently this censorship has been further entangled in the stifling of debate regarding the origin of the COVID-19 virus.

On March 24, 2020, our TGA restricted the prescribing of hydroxychloroquine, citing concerns about media reports of increased "off-label use" (prescribing for other than officially approved uses) which might confront patients for whom it is essential in the treatment of malaria and certain chronic autoimmune diseases (including rheumatoid arthritis and lupus erythematosus). This ruling denied Australian doctors the option to prescribe hydroxychloroquine for their patients in relation to COVID-19. A surprising and unprecedented move, the TGA edict came with a warning about the "well-known serious risks to patients, including cardiac toxicity (potentially leading to sudden heart attacks)…." Even though this old drug has been widely used for decades, continues to be used by millions of people around the world, and is on the World Health Organisation (WHO) List of Essential Drugs there has been no prior enforcement of any such restrictive prescribing.

The TGA's ban also raised concerns about interference in the sacred doctor-patient relationship. It is not uncommon for medications to be used "off label", with doctors employing their discretion in prescribing a drug which they deem most suitable. In Queensland, early in the pandemic, prescribing hydroxychloroquine for COVID-19 was criminalised , with heavy fines and up to six months' imprisonment available to be imposed. This, too, is a step without precedent.

The TGA has issued a detailed statement regarding the basis for its action (August 26, 2020) and the clinical evidence upon which the policy decision was based, including a review by the National COVID-19 Clinical Evidence Taskforce and reference to the previous and disappointing interim results of international trials of hydroxychoroquine. Also cited were regulatory actions in relation to hydroxychloroquine by the US FDA and the UK Medicines and Healthcare Products Regulatory Agency (MHRA). However, since that time considerable additional clinical evidence has been generated in regard to hydroxychloroquine. (**Note:**the sister drug to hydroxychloroquine, chloroquine, is not marketed in Australia.)

More recently, another drug, ivermectin, used to treat parasitic infections such as scabies, has been studied in clinical trials against COVID-19 and received attention as a possible useful therapeutic. Some published clinical trial data suggests ivermectin might be preferred to hydroxychloroquine because it may have an additional role in the late treatment of COVID-19.

Ivermectin is a compound with known antiviral and anti-inflammatory properties which appears to act by interfering with entrance into cells and their replication of mRNA viruses such as COVID-19. It was originally derived from unique natural compounds found in a bacterial culture near a Japanese golf course in 1975. Since its approval more than 40 years ago it has had a dramatic impact on human health worldwide, first being used in treating river blindness. Its effective, broad spectrum, safe, well tolerated and easily administered characteristics were employed to treat a variety of parasitic worm infections which blighted the lives of billions of poor and disadvantaged peoples in the tropics. Its discovers, Prof. Satoshi Omura and Irish biologist William Campbell, were awarded the Nobel Prize in Medicine in 2015, reflecting the magnitude of their achievement.

A comprehensive meta-analysis of 18 randomised and controlled clinical trials regarding the efficacy of ivermectin in the prophylaxis and treatment of COVID-19 has been published in a prestigious medical journal, *The American Journal of Therapeutics 28 (*e299-e318, 2021), which announced statistically significant reductions in mortality, progression to serious disease and time to clinical recovery as well as preventing COVID-19 infections (prophylaxis). Another comprehensive meta-analysis of 24 randomized controlled trials involving 3406 participants reached similar conclusions (*American Journal of Therapeutics 28*, e434-e460). Randomised (where subjects are randomly allocated to a treatment group) and controlled (a comparison treatment group) clinical trials are considered the most reliable and least-biased clinical trials, while meta-analyses can be a powerful tool with which to analyse clinical trial data as it does not depend on the individual results of any one study but, rather, the sweep of results from a much larger group of

patients under a defined set of rules, even though under somewhat diverse, but well defined, conditions.

A discussion of the safety and efficacy assessments of hydroxychloroquine and ivermectin, important as it is, is beyond the scope of this essay. However, it should suffice to say that there exists considerable international expert support, particularly for ivermectin, for the prophylaxis and treatment of COVID-19 based on the results of published randomised, controlled clinical trials.

Widespread social and professional media censorship of the debate and data concerning therapeutic management using hydroxychloroquine and ivermectin has not assisted an informed position regarding these drugs. According to the TGA's latest advice (July 5, 2021):

There is currently insufficient evidence to support the safe and effective use of ivermectin, doxycycline and zinc (either separately, or in combination) for the prevention or treatment of COVID-19. More robust, well-designed clinical trials are needed before they could be considered an appropriate treatment option. The National COVID-19 Clinical Evidence Taskforce, consisting of a large group of clinical experts, is continuously updating treatment recommendations based on the best available evidence. They have not made any recommendations for the use of ivermectin, doxycycline or zinc outside of properly conducted clinical trials with appropriate ethical approval.

The use of ivermectin for COVID-19 in Australia is prevented by effectively blocking its supply and dispensing. The public trusts expert bureaucrat medical and public health opinion (which involves the TGA and expert committees), so opposing voices challenging current official advice on COVID-19 treatment struggle to have an impact in our current environment of information suppression, a gag never before seen.

I refer specifically to the Australian voices of Prof. Robert Clancy (Emeritus Professor of Immunology, Univ. of Newcastle) and Nobel Prize winner Prof. Thomas Borody, also echoed by Craig Kelly MP (Member for Hughes, NSW), who have argued to broaden the treatment strategy for COVID-19, expanding it from an approach dependent almost exclusively on mass vaccination to one involving the treatment, especially the *early* treatment, of ambulatory symptomatic subjects with repurposed drugs such as ivermectin.

On the one hand, it seems the TGA can lower the data bar for the interim approval of the new vaccines but it appears not to be so compromising in relation to the level of data required for a drug like ivermectin. This seems to be somewhat out of character because there have been circumstances in which the TGA has demonstrated considerable flexibility where it was important to do so.

I specifically refer to a case with which I was involved – botulinum toxin (now marketed as Botox). Botulinum toxin is one of the most deadly neurotoxins known to man but was approved without a single randomised controlled clinical trial for the rare condition termed blepharospasm (uncontrolled eye blinking). That was a good, but surprising, decision by the TGA. By comparison, there is an enormous amount of randomised, controlled clinical safety and efficacy data to support ivermectin.

Conclusions

As the vaccine rollout continues in the fight against COVID-19 we are gathering important new information with which to assess and define the safety and efficacy of the new vaccines and the risk-versus-benefit in various subgroups of the population. But until we can accurately define many unresolved questions regarding vaccine safety and efficacy, it would seem unwise to pursue a one-size-fits-all strategy. It would appear prudent to cover our bets by exploring the usefulness of drugs such as

ivermectin which have shown encouraging results, are cheap, have been used safety for decades and are readily available. We should not waste any more time.

Disclaimer: The information contained above does not represent health advice

a pharmacologist