Coronavirus - Part 12 (October 2021)

(Previous editions of this update may be found on John Ling's personal website: http://www.johnling.co.uk)

The Covid-19 numbers

First, a brief preamble. How do you portray a pandemic? With obvious difficulty, because however elegant or truthful or colourful your vocabulary, it will prove to fall short. So we also rely on non-verbal statistics. And the numbers presented here, month by month during the last year, have painted a statistical picture – also inadequate but at least readers are aware of something of the magnitude of this Covid-19 disaster. Consider, for example, the almost 250 million global cases and the 5 million deaths. But these huge pandemic numbers are ungraspable as well as anonymous. Other pandemic numbers are smaller, more bite-size, like the 2,068 deaths per million population in the UK, or the national R value (reproduction number) of between 1.1 and 1.3. But they too are essentially depersonalised arithmetic.

In truth, these mathematical descriptors lack the human touch. Numbers cannot express suffering and sorrow. Statistics cannot communicate physical and mental pain. Figures cannot articulate the tribulations of dying and death. Yet each Covid-19 datum represents a real person, someone precious, made in the image of God – even when Covid-19 challenges such sentiments. So, while the following paragraphs are full of those dispassionate numbers, think individual tragedies, personal sufferings, anxious minds, crushed hearts and interminable tears. Respond to this wretched virus with a little human kindness.

Now, back to those cold, raw data. They are as gloomy as ever. On 30 October, the number of UK cases since the pandemic began broke through the 9 million barrier. During October, the UK had the highest numbers of Covid-19 cases and deaths in Western Europe. Whereas France, Germany, Spain and Italy successfully suppressed their waves of variant infections, the UK numbers have slowly risen by an average of 42,000 new cases and 150 deaths every day. Many of these infections are attributed to a rise among schoolchildren and the use of additional testing. Whatever, we remain in a largely unchanging, precarious position.

Hospitals have been coping with no serious signs of being overwhelmed with Covid-19 patients – yet. However, the winter flu season is approaching and a combined Covid-19 plus winter respiratory infections could dangerously test the NHS. Already the numbers of Covid-19 patients on the wards have begun to rise to approximately 9,000 with 950 on ventilators.

Vaccination numbers offered a hopeful glimmer. In total 49.9 million people in the UK have now had a first dose, and 45.7 million are now double-vaccinated. So 95.6 million doses have been administered to 73.3% of the UK population having been at least single jabbed. The new-look third boosters have so far been delivered to 7.3 million of the 10 million eligible residents of England. However, the original vaccination programme has lost momentum. At the end of October only about 40,000 first doses were jabbed each day, whereas in July the average was 100,000.

Globally, the grim picture persists. Total worldwide cases are approaching 250 million with global deaths advancing to 5 million. These are numerical benchmarks indeed. The USA still tops the daily infection table with an average of 100,000 cases per day, followed by the UK with 42,000 per day and then Russia and Turkey. The USA also dominates the total death table at 743,000 trailed by Brazil and India with the UK in eighth place (140,000).

As ever, this Coronavirus has created a pandemic that is both global and local, as well as statistical and personal. And tenacious. It has not finished with us yet.

The Covid-19 Report

On 12 October, the first official Report into the UK's response to the pandemic was published. It represents the unanimous conclusions of the 22 Conservative, Labour and SNP MPs who sit on either the health and social care committee, or the science and technology committee. Entitled, 'Coronavirus: lessons learned to date', this 147-page document does not make for happy reading. Helpfully, it includes 77 conclusions and recommendations.

The Report pulls no punches – the government made big mistakes. And Covid-19 hit the UK particularly hard 'because of the official scientific advice the government received, not in spite of it'. 'This happened despite the UK counting on some of the best expertise available anywhere in the world.' The government's policy, informed by the science and scientists, was to manage the pandemic in the hope of achieving herd immunity. This strategy delayed introducing the first lockdown, which in turn cost thousands of lives.

The Report focuses on several key areas. There was an adverse 'groupthink' among ministers, scientific advisers and civil servants. It resulted in dithering, so, for instance, the 2020 lockdown was too slowly implemented. The Report describes this as ranking as 'one of the most important public health failures the United Kingdom has ever experienced'.

Then there was the farrago of the NHS Test and Trace (NHST&T) scheme. It cost an estimated £37 billion yet was never fit for purpose. The Report highlights its 'slow, uncertain, and often chaotic performance' in 2020. 'It ultimately failed in its objective to prevent future lockdowns.' The failures associated with social care are also recorded. It was given insufficient priority that resulted in 'devastating and preventable repercussions for people receiving care and their families', including many thousands of deaths.

The one bright light was the success of the vaccination programme. The Report lauds it as 'one of the most effective initiatives in the history of UK science and public administration.' Although the UK's preparedness in the face of a pandemic had been widely proclaimed in advance, the practical reality was that the country's response lagged behind that of many others. 'Our inquiry found that the UK's preparedness for responding to covid-19 had important deficiencies.'

Government officials failed to challenge the scientific consensus which meant that only a limited scope of options were considered, particularly excluded were those being used successfully in East Asian countries. Moreover, there was a fatalistic 'accepting that herd immunity by infection was the inevitable outcome'. The Report also pinpoints other specific failures of judgment, for example, in sport. The government's action plan of 3 March 2020 showed it had no intention to bring in a strict lockdown. Otherwise, why was the Liverpool v. Atletico Madrid football match on 11 March allowed to take place at Anfield, and why was the Cheltenham Festival allowed to proceed for four days between 10 and 13 March? There were crowds of over 50,000 at Anfield and 250,000 at Cheltenham. 'Subsequent analysis suggested that there were an additional 37 and 41 deaths respectively at local hospitals after these events.'

Overall, the Report blames the UK's slow initial response to the pandemic which cost lives. It declares that the government was ill-prepared to tackle any forthcoming and unavoidable pandemics, as was proved by the Covid-19 failures. And there will inevitably be another pandemic coming. The hope is that the authorities will have learned the lessons of Covid-19 and be able to

respond better next time. In the meantime, we await the more detailed public inquiry to be launched in Spring 2022.

Five commonest myths about vaccination

In early October, YouTube joined Twitter and Facebook in banning misinformation about Covid-19 vaccines. Yet misinformation and many myths about these vaccines still persist, even abound, on these social media platforms and elsewhere.

Fortune magazine (2 October edition) spelled out the most common myths in an article by Dana Smith under the title, 'Five biggest myths about the COVID-19 vaccines, debunked.' Fans of the myths should bear in mind at least two caveats. First, the Covid-19 vaccines have proved to be overwhelmingly effective – reducing the risk of hospitalisation and death by about 95%. Second, they are also incredibly safe – severe side effects and deaths are exceptionally rare. Smith quotes figures of just 0.002% for adverse effects and a mortality rate of 1.6% for confirmed cases. So, here are the top five:

Myth 1: The mRNA vaccines change your DNA.
Myth 2: The vaccines negatively affect fertility.
Myth 3: The vaccines were rushed, and we don't know what the long-term side effects will be.
Myth 4: If you have already had Covid-19, you don't need a vaccine.
Myth 5: The vaccines don't protect against transmission.

Such statements are being enthusiastically spread by anti-vaxxers and conspiracy theorists, but they do not stand up to orthodox scientific interrogation – yes, they are all utterly untrue. Such myths are typically based upon a few isolated incidents and anecdotes rather than the broad sweep of hundreds of human clinical trials, millions of cases and billions of samples instigated, investigated, analysed and presented by seasoned scientists and medical personnel. In other words, follow the science, not the pseudoscience!

A new Delta variant, AY.4.2

Currently the Delta variant (B.1.617.2) is the dominant Covid-19 mutation in the UK. However, data published by the UK Health Security Agency on 15 October suggest that 6% of cases are of a new type, namely AY.4.2, also called Delta Plus. It may contain mutations that give the virus survival advantages. AY.4.2 was first identified in the UK during July 2021. It includes spike mutations A222V and Y145H. A few cases have also been identified in the USA and Denmark, but new AY.4.2 infections have since declined there.

Experts considered that AY.4.2 was unlikely to escape vaccines, or immunity, or be especially transmissible, or more contagious, or pose a serious threat to human health. Therefore it had not been allocated the status of a Variant of Concern, a VOC. However, on 22 October, because of 'a slowly increasing proportion of cases in the UK', the Health Security Agency designated AY.4.2 as a new Variant Under Investigation, officially known as VUI-21OCT-01.

Currently, there are 4 VOCs, 5 VUIs and 5 variants 'in monitoring' in the UK. They will all be kept under surveillance. Meanwhile, the major Covid-19 vaccine makers are updating and testing their products ready to roll out quickly against any new variant strains and especially against the emergence of an 'escape variant', a strain that becomes dominant and resistant to current vaccines.

Vaccines and transmission

Previous research had suggested that vaccinated and unvaccinated people were roughly equally infectious. In mid-October, results from the first study to examine directly how well the Oxford-AstraZeneca and Pfizer-BioNTech vaccines prevent the spread of the Delta variant were published. The article was entitled, 'The impact of SARS-CoV-2 vaccination on Alpha & Delta variant transmission' by David Eyre et al., and published as an online preprint at medRxiv (15 October 2021). The work, which has yet to be peer reviewed, analysed testing data from 139,164 close contacts of 95,716 people infected with Covid-19 between January and August 2021, when the Alpha and Delta variants were competing for dominance in the UK.

The Delta variant is highly transmissible. These results showed that people, who were vaccinated and subsequently infected by the Delta variant, in so-called 'breakthrough infections', were less likely to transmit the virus to their close contacts, compared with their unvaccinated counterparts. In this, the Pfizer-BioNTech vaccine was more effective than the Oxford-AstraZeneca vaccine. Moreover, though vaccination reduced Delta transmission it was only about half as effective compared with transmission limitation of the Alpha variant. Also there was a higher risk of having a 'breakthrough infection' caused by Delta than one caused by Alpha.

However, this beneficial effect against Delta transmission was small and waned rapidly to levels similar to unvaccinated individuals three months after the second dose of both vaccines. The authors concluded that, 'Booster vaccinations may help control transmission together with preventing infections.'

Vaccine complications

There are emerging reports of rare neurological complications associated with Covid-19 infections and with Covid-19 vaccinations. These are being misinterpreted and creating unfounded anxiety. A landmark study, published at the end of October, puts the matter in perspective and provides well-founded reassurance.

The study, entitled, 'Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection' by Martina Patone et al., was published in Nature Medicine (2021, 25 October).
The investigators examined the NHS records of 32 million adults in England in order to assess the frequency of rare adverse neurological events resulting in hospital admissions after a first dose of either Oxford-AstraZeneca or Pfizer-BioNTech jabs, or after a Covid-19 positive test, indicating a Covid-19 infection.

Several neurological conditions were recorded but their incidences were mostly numerically minor. The major observations were an increased risk of Guillain–Barré syndrome and Bell's palsy with the Oxford-AstraZeneca vaccine and of haemorrhagic stroke with the Pfizer-BioNTech vaccine. However, there was a substantially higher risk of all neurological outcomes in the 28 days after a positive Covid-19 test. For example, there were an estimated 38 excess cases of Guillain–Barré syndrome per 10 million people receiving the Oxford-AstraZeneca vaccine, but 145 excess cases per 10 million people after a positive Covid-19 test. The researchers concluded, 'In summary, although we find an increased risk of neurological complications in those who received COVID-19 vaccines, the risk of these complications is greater following a positive SARS-CoV-2 [Covid-19] test.'

These findings should inform healthcare professionals and policy makers in this country and internationally. In addition, the results should reassure people that the risks of adverse neurological

events following Covid-19 infections are much greater than those associated with vaccinations. In other words, being vaccinated offers the best protection for overall health.

Shots for children

Vaccinations for 12- to 15-year-olds in the UK started on 20 September. So far, at the end of October, uptake has been poor with only about 21% of that age group in England having received one shot. This is in contrast to Israel, where more than 50% of that cohort have had at least one shot. Most other European countries have also begun vaccinating their over-12s.

Now attention is turning towards the under-12s. At the end of October, advisers to the US Food and Drug Administration (FDA) recommended that a low-dose version of the vaccine made by Pfizer-BioNTech be given emergency approval for use in the nation's 28 million 5- to 11-year-olds.
The decision was made on the basis of a clinical trial that involved around 4,650 children – nearly two-thirds of the youngsters received a one-third dose of the adult vaccine and the rest received a placebo. They all had two doses, three weeks apart.

Data from the trial showed the vaccine to be effective and safe. It was nearly 91% effective in preventing symptomatic infections – this was based on 16 Covid-19 cases in children given placebos versus three cases in the vaccinated children. And there were no reports of severe cardiac illnesses, like myocarditis or pericarditis, as previous studies had reported, especially among young men. Vaccinated children also exhibited milder symptoms of minor side effects. The advisers' conclusion was that the benefits outweighed the risks. Overall, Covid-19 is far less lethal among children than adults. Of the 6.3 million US children who have caught the disease, around 440 youngsters aged 5 to 18 have so far died from it. That is noticeably low compared with some 735,000 deaths across all US age groups.

At the end of October, the FDA issued emergency approval for the Pfizer-BioNTech vaccine to be used in children aged 5 and up. A final decision from the CDC (Centers for Disease Control and Prevention) is now awaited – it is expected on 2 November. Then administrative decisions to actually use the vaccine must be made. Then individual children and their parents must decide whether to get vaccinated. In these matters, the USA is far ahead of the UK because vaccinations could begin there in November with the first children fully vaccinated by Christmas. The UK government has yet to announce any Covid-19 policy for vaccinating the under 12s.

Other countries are already vaccinating their under 12-year-old children. For instance, in the past three months Chile, China and Cuba have begun. Others are closely watching the US approach. Meanwhile, at the end of October, Moderna reported that its low-dose version of its vaccine is safe and effective for children aged between 6 and 11, but the company has yet to apply for FDA authorisation. Both Pfizer-BioNTech and Moderna are also trialling their vaccines in children under 5 and as young as six months old.

Jabs for jobs

Mandatory vaccination – this has become a recurring, and divisive, hot topic. The UK Health Secretary, Sajid Javid, has already stated that care home workers who are not prepared to get the Covid-19 vaccine should get another job. Furthermore, he has said he is not prepared to 'pause' the requirement for care staff in England to be fully vaccinated by 11 November. Meanwhile, the National Care Association has urged the government to delay the vaccination deadline to allow staff more time to get jabbed. And there are warnings that some homes will be unable to cope if workers are forced to leave their employment.

Moreover, on 14 September, Boris Johnson announced the UK government's winter strategy. It consists of a Plan A with a contingency Plan B. The latter will be activated if Plan A proves to be insufficient to prevent 'unsustainable pressure' on the NHS. The government has announced that included in Plan B could be vaccine certification, also known as vaccine passports, and less commonly as vaccine mandates.

From 1 October, the Scottish government announced that Covid-19 vaccine certificates will be needed to enter high-risk, large events, such as sports matches, music events and entrance to nightclubs. Proof of double vaccination will be via a paper copy or a QR code on a new app, though the latter has been plagued by technical problems since its launch. From 18 October, after an 18-day grace period, the scheme became legally enforceable. Its objective is to limit the spread of the virus and to increase the uptake of the vaccine.

Meanwhile in the USA, President Biden has recently urged companies to impose vaccine mandates. It has already begun. For example, United Airlines has reported that 99% of its US workforce has complied with the company's vaccine requirement. To increase vaccination rates in New York City, the mayor, Bill de Blasio, recently issued a mandate, that all of its 46,000 unvaccinated city workers, police officers, firefighter and others, must get jabbed by the end of October, or lose their pay checks. The NY carrot is an extra $500 in their pay packets.

OK, those are examples of governmental perspectives and policies. What do bioethicists think about mandatory vaccination? Are they bioethically justified? Here is the view from the UK's Nuffield Council on Bioethics. In mid-October, Danielle Hamm, Director of the Council, stated, 'We support the Government's aim to increase vaccine uptake among health and social care workers in order to protect patients, service users, and co-workers from harm. All those working in health and social care should accept a primary responsibility to prevent avoidable harm to the people they care for. But we urge the Government to gather more evidence and explore other options more thoroughly before resorting to such a coercive approach.'

And a view from the USA comes from the Association of Bioethics Program Directors (ABPD), a group of nearly 100 members based at medical centres and universities across North America. In early October, it issued a statement entitled, 'Time to Stand Up For The Morality of Vaccine Mandates'. It declared that, 'To protect the health, safety and future prosperity of humankind, mandated vaccination is now necessary. The ABPD supports the use of vaccine mandates as an essential measure against COVID-19.'

The well-known bioethicist Art Caplan, professor of bioethics at New York University Langone Medical Center, stated in an explanatory note, 'Two primary arguments drive opposition to mandates. One is that governments ought not play a role in imposing vaccination requirements. They ought not intrude on personal liberty. But this absolutism in the name of liberty makes little sense. Certain dire challenges to human health, flourishing and viability require collective action organized, coordinated and directed by governments. Legislatures and courts have long given the authority to government and its agencies to follow sound scientific and medical advice to minimize the danger posed by grave public health crises. Covid-19 with its 4.5 million deaths, untold numbers of people with disabling complications, psychosocial havoc and burdens on health systems is recognized as a very serious public health emergency. It makes sound ethical sense to permit restrictions on both liberty and personal choice including mandating vaccination for all deemed medically eligible to combat a dangerous worldwide plague.'

Caplan continued, 'The other moral objection to vaccine mandates is that they intrude on the fundamental right to bodily integrity including freedom to reject medical intervention. It is true that

the right to accept or reject medical care is a long-standing right in America and other nations. However, this right has as the ABPD statement acknowledges limits and consequences. One may reject vaccination but then be subjected to penalties including fines, loss of employment, loss of benefits, restrictions on travel, restrictions on accessing certain businesses and services and denial of entry to government positions. Rejecting vaccination may also mean that masking or testing requirements must be followed to move about in society. Individuals are free to reject safe and effective prophylactic medical care including vaccines but private and public entities are free to enact penalties in the name of protecting the public's health including those especially vulnerable to harm from Covid-19.'

Caplan concluded, 'I fervently hope the position statement from an organization representing moral expertise in matters of health care ethics will counter flawed moral objections to vaccine mandates so that the threat from Covid-19 can be greatly reduced in North America and around the world.' While there is much agreement on the purposes and practicalities of mandatory vaccination, there is no consensus. While voluntary vaccination is increasing there will always be those who, though eligible, refuse to be vaccinated. They may yet pay the price of restriction at both work and play.

Concomitant Covid-19 and flu vaccinations

The prospect of one appointment with two jabs was welcome. But that has not been the reality for most over 50s in the UK. On the other hand, it is comforting to learn that double jabbing, or more formally, concomitant administration, is safe. Such a simple and cheaper dual scheme would also reduce the burden on healthcare systems.

The clinical trial involved 679 adult volunteers at 12 sites in the UK who were due for their second dose of either the Pfizer-BioNTech or Oxford-AstraZeneca vaccine. Half had a flu vaccine in the other arm and half had a placebo. Three weeks later the volunteers were give the alternative jabs. After six weeks, the reported side effects were mostly mild or moderate with no appreciable difference between the two groups. Antibody responses were also similar. Maybe in the future such vaccines will be combined as a single injection as with, for example, the MMR.

These results were published as 'The Safety and Immunogenicity of Concomitant Administration of COVID-19 Vaccines (ChAdOx1 or BNT162b2) with Seasonal Influenza Vaccines in Adults: A Phase IV, Multicentre Randomised Controlled Trial with Blinding (ComFluCOV)' by Rajeka Lazarus et al., online in The Lancet (30 September 2021). Their conclusion was, 'Concomitant vaccination raises no safety concerns and preserves the immune response to both vaccines.'

mRNA vaccines for flu and other diseases

Messenger RNA (mRNA) vaccines have become the new kids on the block in the fight against Covid-19. The huge success of the Moderna and Pfizer-BioNTech mRNA-based vaccines has not only proved the efficacy of this novel technology, it has also started biotech companies thinking about wider applications. Recalcitrant diseases, such as tuberculosis, HIV and malaria, plus rare illnesses, like Duchenne muscular dystrophy and cystic fibrosis, are in their frames. However, seasonal influenza is currently top of their to-do lists. At least a dozen vaccines have been produced. Three are now in Phase 1 clinical trials and the rest are in preclinical testing.

Trials are being conducted by the Big Three – Moderna, Sanofi-Translate Bio and Pfizer. For example, in late September, Pfizer dosed its first participants aged between 65 and 85. The trial will 'evaluate the safety, tolerability, and immunogenicity of a single dose quadrivalent mRNA vaccine against influenza in healthy adults.'

However, known hurdles are acknowledged. For instance, though existing seasonal flu vaccines offer only 40 to 60% protection against infection there is, as yet, no guarantee that mRNA vaccines will fare any better. Will the mRNA be capable of delivering haemagglutinin glycoproteins, the main antigen found in flu vaccines? Also, producing mRNA vaccines effective against the several varieties of flu may be more complex than against lone Covid-19. And whereas Covid-19 vaccines initially faced no established challengers, competitive flu vaccines are already common – nine are currently available in the USA. Then again, will adverse side effects be a problem, as often reported after mRNA Covid-19 jabs?

These and other questions will be answered soon because the market for seasonal flu vaccines is both global and annual. Commercially, that seems like a pot of gold worth pursuing. After all, the two mRNA-based Covid-19 vaccines are expected to reach global sales of at least US$50 billion during 2021.

Molnupiravir, the promising drug

The US pharmaceutical firms Merck and Ridgeback Biotherapeutics have developed and tested molnupiravir, the first oral antiviral Covid-19 treatment. In early October, they announced that molnupiravir can cut hospitalisations and deaths among Covid-19 patients by about 50%. The study involved 775 people who had recently tested positive for the virus but were not seriously ill. Of those given a five-day course of molnupiravir, 7.3% ended up hospitalised or died, compared with 14.1% of patients in the placebo group who were hospitalised or died. The results look promising, though they have yet to be peer reviewed. Molnupiravir is still experimental and has yet to complete clinical trials, though authorisation for its emergency use from the US Food and Drug Administration (FDA) is about to be requested.

Standard, current practice is that molnupiravir is given twice a day to patients who have recently been diagnosed with Covid-19. Such an oral medicine would encourage treatment earlier and easier and effectively at home. Just three steps – symptom, prescription, swallow. Indeed, during Phase 3 clinical trials, molnupiravir was so effective in patients with severe Covid-19 that the independent committee overseeing the study stopped it prematurely. And there is additional evidence that the drug can suppress the transmission of the virus.

A simple medication has been a goal of Covid-19 healthcare scientists since the pandemic began. Other antivirals exist. For instance, remdesivir is another, but it must be administered intravenously or by injection, unlike the preferable oral route for molnupiravir. Like remdesivir, molnupiravir is a nucleoside analogue, which means it mimics some of structures of RNA. But the two drugs work in entirely different ways. Remdesivir halts the formation of RNA chains, whereas molnupiravir, once incorporated into RNA chains, forces genetic errors in the virus. When sufficient mutations have occurred, and because these are random, the virus cannot evolve a resistance strategy fast enough, so the viral population disintegrates – this is known as lethal mutagenesis. And so the body's immune system can fend off Covid-19.

What about adverse side effects? Could molnupiravir become incorporated into DNA and become mutagenic? What about molnupiravir and children? Preliminary data released by the companies showed that adverse events occurred in 35% of those who received molnupiravir and in 40% of those who received the placebo. Only time and more trial results will tell if serious effects exist. Already there is a serious disadvantage to molnupiravir – it currently costs $700 for a five-day course of treatment. That effectively excludes it from low- and middle-income countries.

Even so, the UK government has recently bought 480,000 courses of molnupiravir. They are likely to be delivered before the end of November, if the drug is approved. Alongside that purchase the Health Secretary, Sajid Javid, announced that the UK has also bought 250,000 courses of Pfizer's antiviral treatment, code named PF-07321332/ritonavir. Though licensed as an antiviral for HIV/AIDS, it has yet to pass its final Phase 2 and 3 trials for Covid-19, though scientists are confident it will be effective. It is expected to be available in February 2022.

In the meantime, pharmaceutical companies across the world are busy in the hope of developing effective Covid-19 antivirals, preferably of the oral variety. The potential markets and the financial rewards are vast.

Ivermectin, the doubtful drug

Ivermectin tablets have been called a Covid-19 'miracle' drug. It has been promoted mainly by anti-vaxxers in numerous countries, particularly in Latin America, but also by people, driven by a lack of vaccine, who are seeking some alternative form of treatment. Inevitably, large pro-ivermectin Facebook groups have sprung up. But the promise of the drug, with respect to Covid-19, has recently been examined and found wanting.

As a common, over-the-counter drug, licensed since 1981, ivermectin has been used as an anti-parasitic medicine to treat humans and animals. It is effective against, for example, worms and head lice. More recently there have been calls to repurpose it against Covid-19. Several studies have allegedly supported this strategy. One such key investigation was led by Dr Ahmed Elgazzar from Benha University in Egypt, and published as a preprint on the Research Square website in November 2020 as 'Efficiency and Safety of Ivermectin for Treatment and prophylaxis of COVID-19 Pandemic.' The study of some 400 Covid-19 patients in hospital purportedly showed that when they 'received ivermectin early [they] reported substantial recovery' and that there was 'a substantial improvement and reduction in mortality rate in ivermectin treated groups' by more than 90%. Those are unexpectedly massive effects which drew critical attention. Critics raised serious concerns about plagiarism, data manipulation and numerous other irregularities. On 14 July 2021, Research Square withdrew this preprint 'due to ethical concerns.'

This is not the first study to conflict ivermectin and Covid-19. Other, seemingly positive, reports have previously been retracted. And there is concern that currently-published reports of ivermectin's effectiveness could be flawed, statistically biased, poorly designed and poorly controlled. And some conspiracy theorists maintain that ivermectin does indeed work and that drug companies are deliberately depriving the public of a cheap Covid-19 medicine.

To date, the most favourable assessment is that the curative case for ivermectin has yet to be proved beyond reasonable doubt. Results from larger, more high-quality trials are needed. They are coming. In the meantime, get a vaccine!

Covid toe

Of all the serious side effects associated with Covid-19 infections, be they respiratory, muscular, long Covid, or even death, one of the least dangerous and debilitating must be Covid toe. It is described as an outbreak of chilblain-like lesions (CLL) and redness on the hands and feet that has been reported extensively during the early phase of the Covid-19 pandemic, though less commonly during the Delta variant wave. The condition can sometimes last for months, yet its underlying pathophysiology is unclear.

An observational study was conducted during April 2020 at Saint-Louis Hospital, Paris, France. All 50 patients who were referred there with CLL during this pandemic period were included in this study. Those with a history of chilblains or chilblain lupus were excluded. The aim was to study skin and blood endothelial and immune system activation in patients with CLL in comparison with healthy controls.

The researchers reported that, 'CLL were characterized by higher IgA tissue deposition and more significant transcriptomic activation of complement and angiogenesis factors compared with SC [seasonal chilblains].' They also observed 'a systemic immune response associated with IgA antineutrophil cytoplasmic antibodies in 73% of patients, and elevated type I interferon blood signature in comparison with healthy controls.' In other words, the results suggested that Covid toe may be caused by the immune system's response to attacking the Covid-19 virus as well as an endothelial dysfunction. The condition appears to be self-limiting though local or systemic anti-inflammatory treatment could probably help reverse the cutaneous manifestations.

This study by Laure Frumholtz et al., was published in The British Journal of Dermatology (online, 5 October 2021) under the title, 'Type I interferon response and vascular alteration in chilblain-like lesions during the COVID-19 outbreak.'

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