Notes on COVID-19

Part 26: 2021-04-16 to 2021-06-18

Peter Bernard Ladkin
2021-06-18

2021-04-16 Virologist Julian Tang and colleagues have written in the BMJ about the predominating importance of aerosol transmission of the virus. Key prophylaxis is better ventilation in indoor environments, and ensuring a face mask fits well enough to filter out aerosols. Tang, JW, Marr LC, et al, Covid-19 has redefined airborne transmission *BMJ* 2021; 373 2021-04-14 doi: https://doi.org/10.1136/bmj.n913 (Cite as: *BMJ* 2021;373:n913) https://www.bmj.com/content/373/bmj.n913 Similar points to these wer made in the Position Paper of the German Association for Aerosol Research (Gesellschaft für Aerosolforschung, GAeF) on 2020-12-17 (Position paper of the Gesellschaft für Aerosolforschung on understanding the role of aerosol particles in SARS-CoV-2 infection, GAeF 2020-12-17. Available from https://ae00780f-bbdd-47b2-aa10-e1dc2cdeb6dd.filesusr.com/ugd/fab12b_0b691414cfb344fe96d4b44e6f44a5ab.pdf , accessed 2021-04-15) and recently emphasised in an open letter to German Chancellor Merkel from GAeF officers (2021-04-11) (Asbach C, Scheuch G, et al, Offener Brief; Ansteckungsgefahren aus Aerosolwissenschaftlicher Perspektive, in German, available at http://docs.dpaq.de/17532-offener_brief_aerosolwissenschaftler.pdf , accessed 2021-04-15)

2021-04-16 Nicola Davis on TheG LiveBlog 2021-04-15 at 11:47 GMT+1 says that comparative background rates have been established for CSVT in Covid sufferers versus those having been vaccinated. https://www.theguardian.com/world/live/2021/apr/15/coronavirus-live-news-former-world-leaders-urge-biden-to-waive-vaccine-ip-rules-olympics-could-still-be-cancelled

" *.... a database of 81 million people primarily in the US ..... CVST is around eight to 10 times more common among people who have had Covid, than those who have had a vaccine against the disease…….. a rate of 39 cases of CVST per million patients in the two weeks after diagnosis with Covid, with about 30% of cases occurring in people under the age of 30…….. the rate was just over four cases per million among ..... people who had received an mRNA vaccine..... in the two weeks after vaccination. ..... the EMA .... said that there have been around 5 cases of CVST per million people who have had the Oxford/AstraZeneca vaccine.*"

Note that the researchers looked at CSVT, not CSVT+thrombocytopenia. They also apparently did not look at splanchic thrombosis+thrombocytopenia. Also, the EMA appear to have revised their risk numbers downwards since the statement last week. Last week, it was 1 in 100,000; now it is half that.

The research comes from Uni Oxford, from people in psychiatry and cognitive neuroscience, not associated with the ChAdOx team. The preprint, as well as expert commentary organised by the Science Media Centre, is referenced below, entry of 2021-04-22.

2021-04-16 Qureshi, Greenhalgh and Bourouiba have written a piece on the importance of "minimising shared air" in indoor environments, with a particular view towards the return to presence schooling. Qureshi Z, Greenhalgh T, and Bourouiba L, The return to school is welcome, but we must minimise shared air, 2021-03-09 https://blogs.bmj.com/bmj/2021/03/09/the-return-to-school-is-welcome-but-we-must-minimise-shared-air/

2021-04-16 Jacqui Wise has a useful history of AstraZeneca's communication and other troubles. Wise J, Covid-19: How AstraZeneca lost the vaccine PR war, 2021-04-14, BMJ 2021;373:n921 doi: https://doi.org/10.1136/bmjn921 https://www.bmj.com/content/373/bmj.n921

2021-04-16 Paul Hunter has an editorial in the BMJ about thrombosis and the AZ vaccine, which includes a survey of the discovery and concerns, and references to the medical literature on the phenomenon. Hunter PR, Thrombosis after covid-19 vaccination, BMJ 2021;373:n958 2021-04-14, doi: https://doi.org/10.1136/bmj.n958 https://www.bmj.com/content/373/bmj.n958

2021-04-16 Andreas Greinacher and colleagues have published their study of thrombotic thrombocytopenia in 11 patients in Austria and Germany. Greinacher A, Thiele T, et al, Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination, 2021-04-09, N. Eng. J. Med., DOI: 10.1056/NEJMoa2104840, https://www.nejm.org/doi/full/10.1056/NEJMoa2104840 They call it "*immune thrombotic thrombocytopenia*" and say that vaccination with ChAdOx1-nCoV19 can result in it. Maybe so. The mechanism is not known, although it is "*mediated by platelet-activating antibodies against PF4*", which "*clinically mimics autoimmune heparin-induced thrombocytopenia*."

2021-04-16 Nina Schultz and colleagues have published a study of five patients in Norway presenting with thrombosis and accompanying thrombocytopenia after AZ vaccination. Schultz NM, Sørvoll IH, et al, Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination, 2021-04-09, N. Eng. J. Med., DOI: 10.1056/NEJMoa2104882, https://www.nejm.org/doi/full/10.1056/NEJMoa2104882 They wish to call it "*vaccine-induced immune thrombotic thrombocytopenia*", but it is not yet known whether it is indeed induced by the vaccine, rather than just being associated with it.

2021-04-16 Kate-Lynn Muir and colleagues describe a case of thrombotic thrombocytopenia occurring in a patient in Omaha, Nebraska, after receiving the Janssen vaccine- Muir K-L, Kallam A, et al, Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination, N. Eng. J. Med., 2021-04-14, DIO: 10.1056/NEJMc2105869, https://www.nejm.org/doi/full/10.1056/NEJMc2105869

2021-04-16 Jacqui Wise summarises the Greinacher and Schultz work in Wise J, Covid-19: Rare immune response may cause clots after AstraZeneca vaccine, say researchers, BMJ 2021;373:n954

2021-04-12, DOI: https://doi.org/10.1136/bmj.n954 , https://www.bmj.com/content/373/bmj.n954

2021-04-17 Viktoria Muster and colleagues in Graz describe a case of pulmonary embolism with thrombocytopenia in a patient vaccinated with ChAdOx1-nCoV19 in The Lancet. Muster V, Gary T, et al, Pulmonary embolism and thrombocytopenia following ChAdOx1 vaccination, The Lancet 2021-04-14, doi: https://doi.org/10.1016/S0140-6736(21)00871-0 , https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00871-0/fulltext

2021-04-17 Markus Naumann and colleagues in Augsburg had a case of secondary immune thrombocytopenia with, at first, ocular symptoms caused by superior opthamlmic vein thrombosis, thrombocytopenia, and finally a stroke. Bayas A, Menacher M, et al, Bilateral superior ophthalmic vein thrombosis, ischaemic stroke, and immune thrombocytopenia after ChAdOx1 nCoV-19 vaccination, The Lancet 2021-04-14 DOI:https://doi.org/10.1016/S0140-6736(21)00872-2 , https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00872-2/fulltext

2021-04-17 The controversy continues over whether droplets/fomites or aerosols are the primary transmission factor for Covid-19. A number of authors writing in The Lancet point out that the secondary evidence for airborne transmission (aerosols) is overwhelming. Greenhalgh T, Jimenez JL, Prather KA, Tufekci Z, Fisman D, Schooley R, Ten scientific reasons in support of airborne transmission of SARS-CoV-2, The Lancet 2021-04-15, DOI:https://doi.org/10.1016/S0140-6736(21)00869-2 , https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00869-2/fulltext This note responds to Heneghan CJ, Spencer EA, et al, SARS-CoV-2 and the role of airborne transmission: a systematic review, preprint 2021-03-24, https://f1000research.com/articles/10-232/v1 , of which the conclusion states "*SARS-CoV-2 RNA is detected intermittently in the air in various settings. Standardized guidelines for conducting and reporting research on airborne transmission are needed. The lack of recoverable viral culture samples of SARS-CoV-2 prevents firm conclusions over airborne transmission.*" Greenhalgh & colleagues point out inter alia that "*[m]easles and tuberculosis, two primarily airborne diseases, have never been cultivated from room air.*"

2021-04-20 David Hunter points out in TheG on 2021-04-20 how LAT and PCR testing, effectively arranged, can control the pandemic, even with Type II error rates as reported https://www.theguardian.com/commentisfree/2021/apr/19/lateral-flow-tests-uk-covid

2021-04-22 Oxford researchers Prof Harrison, Prof. Geddes and Dr. Taquet from the Department of Psychiatry and Prof. Husain from the Department of Clinical neurosciences, not associated with the ChAdOx vector vaccine development work, have analysed data from the US TriNetX health records network on Cerebral Venal Thrombosis (CVT, also known as Cerebral Venous Sinus Thrombosis, CVST, or in my previous notes as Cerebral Sinus Vein Thrombosis, CSVT), and also on Portal Vein Thrombosis (the portal vein is attached to the liver, so part of the splanchnic venous system) in Covid-19 patients, people vaccinated with the mRNA vaccines from Moderna or BioNTech, as well as "background" rates. The point estimates for CVT are 39 per 1m after Covid-19, 0 per 1m after influenza, and 4.1 per 1m after vaccination with either of the mRNA vaccines. They cite the estimate from the EMA of CVT at 5.0 per 1m after ChAdOx1-nCoV19 vaccination (Vaxzevria. No

figures are available in this dataset since this vaccine is not available in the US). They also give a "background" figure ("*incidence observed across the entire health records network*") of 0.41 per 1m people. For PVT, the point estimates are a lot higher: 436.4 per 1m after Covid-19, 98.4 per 1m after influenza, and 44.9 per 1m after vaccination with an mRNA vaccine.

There are, of course, the usual issues surrounding the datasets, as well as issues with observation and recording the data (these conditions are not easily differentially diagnosable and so occurrences may well have been missed). However, if the data and results are roughly accurate, then occurrence of CVT after mRNA vaccination is about 10 times background, after Vaxzevria vaccination about 12.2 times background, and after Covid-19 about 95 times background. These figures should surely put paid to any vaccine hesitancy.

Taquet M, Husain M, et al, Cerebral venous thrombosis: a retrospective cohort study of 513,284 confirmed COVID-19 cases and a comparison with 489,871 people receiving a COVID-19 mRNA vaccine, preprint, OSFhome, Version 2 of 2020-02-15 https://osf.io/a9jdq/

There are commentaries in the Science Media Centre from a variety of British experts on 2021-04-15 at https://www.sciencemediacentre.org/expert-reaction-to-preprint-looking-at-incidence-of-rare-cerebral-venous-thrombosis-cvt-following-covid-19-infection-compared-to-incidence-after-vaccination-or-influenza/

2021-05-04 There was a review article on one of the deleterious consequences of Covid-19, cytokine storm, in the NEJM on 2020-12-03, which I somehow missed. Fajgenbaum DC and June CH, Cytokine Storm, N Engl J Med 2020; 383:2255-2273 2020-12-03 DOI: 10.1056/NEJMra202613 . Available at https://www.nejm.org/doi/full/10.1056/NEJMra2026131 .

2021-05-04 The RECOVERY trial has published its results on the use of tocilizumab for adult patients admitted to hospital with hypoxia and systemic inflammation. (Preliminary results were reported in February. See Notes Part 23, entry 2021-02-12). Just over 4,000 patients were enrolled between 2020-04-23 and 2021-01-24, just over 3,300 of them receiving corticosteroids. Patients receiving tocilizumab were more likely to be discharged within 28 days, and less likely to reach the composite endpoint of mechanical ventilation or death (35% versus 42% for the control group). That is a huge 20% improvement. Given the variable results on the use of tocilizumab in previous, much smaller trials, this result should settle the question. It helps. Recovery Collaborative Group, Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial, 2021-05-01, DOI:https://doi.org/10.1016/S0140-6736(21)00676-0

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00676-0/fulltext

The comment by Gupta and Leaf notes that the release of the pro-inflammatory cytokine interleukin-6 (IL-6) has been implicated in severe Covid-19 (for the cytokine storm, see above), and tocilizumab is an IL-6 inhibitor. They discuss the history of tocilizumab research for Covid-19 patients. The REMAP-CAP trial showed positive results, but was limited to more severely ill patients. The RECOVERY trial was general, and showed improvement across all groups. They

report the results a little differently from above, writing " *The primary outcome, all-cause mortality within 28 days of random assignment, occurred in 35% of patients allocated to usual care and 31% of patients allocated to tocilizumab.*" Gupta S and Leaf DE, Tocilizumab in COVID-19: some clarity amid controversy, 2021-05-01, DOI: https://doi.org/10.1016/S0140-6736(21)00712-1 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00712-1/fulltext

The full paper of the REMAP-CAP trial of tocilizumab has also recently appeared. The REMAP-CAP investigators, Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19, 2021-04-22, N Engl J Med 2021; 384:1491-1502 DOI: 10.1056/NEJMoa2100433 https://www.nejm.org/doi/full/10.1056/NEJMoa2100433

2021-05-04 The first report of the SIREN study of the effectiveness of the BNT162b2 vaccine in over 23,000 health-care workers in the UK has been published. The study is ongoing. The results were that "*[a] single dose of BNT162b2 vaccine showed vaccine effectiveness of 70% (95% CI 55–85) 21 days after first dose and 85% (74–96) 7 days after two doses in the study population.*" Hall VJ, Foulkes S et al, COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study, 2021-04-23, DOI: https://doi.org/10.1016/S0140-6736(21)00790-X https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00790-X/fulltext The comment by Lesham and Lopman discuss the importance of these results for transmission of the virus and herd immunity, amongst other things. Lesham E and Lopman BA, Population immunity and vaccine protection against infection, 2021-04-23, DOI:https://doi.org/10.1016/S0140-6736(21)00870-9 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00870-9/fulltext

2021-05-04 A prospective cohort study of vaccine efficacy using the EAVE-II database and hospital admission records, including details of 5.4m people in Scotland, about 99% of the population, has been published. Between 2020-12-08 and 2021-02-22 somewhat over 1.3m people were vaccinated. "*The first dose of the BNT162b2 ... vaccine was associated with a ... effect of 91% (95% CI 85–94) for reduced COVID-19 hospital admission at 28–34 days post-vaccination. Vaccine effect at the same time interval for the ChAdOx1 vaccine was 88% (95% CI 75–94)..*" Vasileiou E, Simpson CR et al, Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study, 2021-04-23 DOI: https://doi.org/10.1016/S0140-6736(21)00677-2 , https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00677-2/fulltext The comment by Dean emphasises the importance of such large, real-world studies. Dean N, Hospital admissions due to COVID-19 in Scotland after one dose of vaccine, 2021-04-23, DOI:https://doi.org/10.1016/S0140-6736(21)00765-0 , https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00765-0/fulltext

2021-05-04 A study of the TMPRSS2 inhibitor camostat mesilate has been published in EClinicalMedicine, a Lancet journal. This protease is a key component of the means of entry of SARS-CoV-2 into cells, where it reproduces. So inhibiting this mechanism is something worth

trying. Unfortunately, the study showed no benefit (but also no harm). Gunst JD, Staerke NB, et al, Efficacy of the TMPRSS2 inhibitor camostat mesilate in patients hospitalized with Covid-19-a double-blind randomized controlled trial 2021-04-22 DOI: https://doi.org/10.1016/j.eclinm.2021.100849

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00129-2/fulltext

2021-05-04 Martin Bazant and John Bush of MIT have published a mathematical study of means to inhibit indoor air transmission of Covid-19. Bazant MZ and Bush JWM, A guideline to limit indoor airborne transmission of COVID-19, Proc. Nat. Acad. Sc. 2021-04-27 118 (17) e2018995118 DOI: https://doi.org/10.1073/pnas.2018995118 https://www.pnas.org/content/118/17/e2018995118

2021-05-06 An editorial in the NEJM by Douglas Cines and James Bussel discusses the issues around the immune thrombotic thrombocytopenia occurring rarely shortly after vaccination with one of the SARS-CoV-2 vaccines, as well as giving links to the other articles published recently in NEJM on the subject (see above, 2021-04-16 and 2021-04-17). Cines DB and Bussel JB, SARS-CoV-2 Vaccine-Induced Immune Thrombotic Thrombocytopenia, N. Eng. J. Med, 2021-04-16, DOI: 10.1056/NEJMe2106315 https://www.nejm.org/doi/full/10.1056/NEJMe2106315

2021-05-08 A study of the effectiveness of the BNT162b2 vaccine in the Israeli vaccination campaign has been published in The Lancet. The analysis period was 2021-01-24 to 2021-04-03 and during this period just over 4.7m people received two doses of BNT162b2. Results: it was well over 90% effective against infection, and over 96% effective against severe Covid-19; hospitalisation; death. It's good stuff! Haas EJ, Angelo FJ et al, Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data, The Lancet 2021-05-05, DOI: 10.1016/S0140-6736(21)00947-8 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00947-8/fulltext

2021-05-08 The W.H.O. and US CDC have finally changed their advice on Covid-19 infection to emphasise the role of airborne transmission (via aerosols). Zeynep Tufekci, Professor at UNC Chapel Hill and a regular contributor to the NYT, discusses the history of the increasing acknowledgement of airborne transmission, in an elegant essay. Tufekci, Z, Why Did It Take So Long to Accept the Facts About Covid?, NYT 2021-05-07 https://www.nytimes.com/2021/05/07/opinion/coronavirus-airborne-transmission.html

2021-05-16 A Danish cohort study looked at somewhat over 8,000 SARS-CoV-2-positive individuals in Denmark from 2020-02-27 to 2020-05-31 who were not admitted to hospital, compared with some 80,000 SARS-CoV-2 negative individuals, to see what kind of sequelae might be associated with mild-to-moderate disease in those who did not need hospital care. Risk ratios

seem to me to be a useful indicator. SARS-CoV-2-positives were prescribed more bronchodilatory agents, RR 1.32; and more triptans, RR 1.55. They were more at risk, but not much, of dsypnoea, RR 2.0, and venous thromboembolism, RR 1.77. They made 1.18 more GP visits and 1.10 more outpatient hospital visits than the SARS-CoV-2-negative cohort. Those results seem to me to be quite encouraging. Lund LC, Hallas J, et al, Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: a Danish population-based cohort study The Lancet Infectious Diseases, 2021-05-10, DOI: 10.1016/S1473-3099(21)00211-5 , https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00211-5/fulltext

Comment by Huang L and Cao B, Post-acute conditions of patients with COVID-19 not requiring hospital admission, 2021-05-10, DOI: 10.1016/S1473-3099(21)00225-5 https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00225-5/fulltext

2021-05-16 The Economist has performed some data crunching to estimate the number of excess deaths worldwide during the Covid-19 pandemic. Their conclusion is that there have been between 7m and 13m excess deaths, considerably more than the total of "officially reported" deaths at just over 3.3m. https://www.economist.com/briefing/2021/05/15/there-have-been-7m-13m-excess-deaths-worldwide-during-the-pandemic , dated 2021-05-15.

2021-05-16 The World Health Assembly asked the WHO in May 2020 to initiate an independent review into the world response to the Covid-19 pandemic. The Panel was chaired by Ellen Johnson Sirleaf and Helen Clark, and has reported. Johnson Sirleaf and Clark summarise the findings in Johnson Sirleaf E and Clark H, Report of the Independent Panel for Pandemic Preparedness and Response: making COVID-19 the last pandemic, The Lancet, 2021-05-12, DOI: 10.1016/S0140-6736(21)01095-3

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01095-3/fulltext

Summary: we didn't do very well as a world; the International Health Regulations (2005) sometimes got in the way; there were huge disparities between appropriate national responses and nations with poor results. Recommendations include more and better sharing of expertise and resources. The report identifies "strengths" on which to build, such as rapid genome sequencing, astonishingly rapid development of vhttps://theindependentpanel.orgaccines, and the admirable devotion of health professionals and others to caring for the sick, over a long period of time.

The Report is not the only document the Panel produced; there are a host of accompanying documents. All at https://theindependentpanel.org

2021-05-17 I had heard that Vaxzevria was now being recommended for everyone in Germany. I went to the RKI Epidemioligisches Bulletin No. 19 of 2021, dated 2021-05-12, https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2021/Ausgaben/19_21.pdf which says on p24 "*Aufgrund.....empfiehlt die STIKO, die beiden Vektor-basierten Impfstoffe (Vaxzevria und COVID-19 Vaccine Janssen) für Personen im Alter ≥ 60 Jahren zu verwenden.*" Translation: "*because of..... the StIKo recommends the two vector-based vaccines ... be used for persons of 60 years of age or older.*" In other words, the recommendation stays as it has since 2020-03-30

https://www.rki.de/DE/Content/Kommissionen/STIKO/Empfehlungen/AstraZeneca-Impfstoff-2021-03-30.html (in German) . The StIKo is the "Ständige Impfkommission", the Standing Committee on Vaccination, which is an independent expert panel with 18 members, convened at the RKI, which makes recommendations on vaccines.

2021-05-17 An article by Nicholas Wade in the Bulletin of the Atomic Scientists discusses in detail whether the SARS-CoV-2 virus came from the wild or whether it escaped from a research laboratory. He points out that some opinions published by scientists arguing for the "wild" hypothesis in 2020 were premature. The "Bat Lady", Ms. Shi, at the Wuhan Institute of Virology, had been performing so-called "gain of function" (GOF) research on beta coronaviruses, funded by NIAID to the Ecohealth Alliance, and subcontracted to the Wuhan Institute. The President of the Ecohealth Alliance is Peter Daszak, one of the signatories of a Lancet letter of 2020-02-19, which contains the words "*We stand together to strongly condemn conspiracy theories suggesting that COVID-19 does not have a natural origin.*" The quoted statement is somewhat disingenuous, in that everyone reasonable deprecates "conspiracy theories", but wondering whether the virus might have accidentally escaped from a local laboratory performing GOF research on beta coronaviruses seems to be a reasonable hypothesis to consider, and not to fall under the rubric "conspiracy theory". Laboratory leaks do happen, for example, the "*SARS1 virus has .... leak[ed] from laboratories in Singapore, Taiwan, and no less than four times from the Chinese National Institute of Virology in Beijing."*

Nicholas Wade, The origin of COVID: Did people or nature open Pandora's box at Wuhan?, Bulletin of the Atomic Scientists, 2021-05-05.

https://thebulletin.org/2021/05/the-origin-of-covid-did-people-or-nature-open-pandoras-box-at-wuhan/

It seems to me that there are three main takeaways from the article. First, that GOF research is not necessarily taking place in the safest of environments. Second, that a wider discussion of the safety of GOF research is warranted. Third, opening some of the "sealed" records of the Wuhan laboratory could resolve the issue.

2021-05-19 Jamie Lopez Bernal and colleagues surveyed data on 156,000+ people aged 70 and over to assess the effectiveness of one dose of either ChAdOx1-nCoV19 or BNT162b2 vaccine, received between 2020-12-08 and 2021-02-19, against symptomatic Covid-19. Amongst participants age 80 or over, one dose of BNT162b2 led to 70% reduction @ 10-13 days; after the second dose 89% @ 14 days. Amongst the 70-and-overs, one dose of BNT162b2 yielded 61% protection @ 28-34 days; ChAdOx1 60% @ 14-20 days, rising to 73% @ 35 days. Hospital admission and mortality was also considerably reduced. Bernal JL, Andrews N et al, Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study, 2021-05-13, *BMJ* 2021;373:n1088, doi: 10.1136/bmj.n1088 , https://www.bmj.com/content/373/bmj.n1088

2021-05-19 "*Adults infected with covid-19 three weeks after receiving one dose of the Pfizer-*

BioNTech or Oxford-AstraZeneca vaccine were 38-49% less likely to pass the virus on to their household contacts than people who were unvaccinated, a preprint released by Public Health England has shown." Mahase E, Covid-19: One dose of vaccine cuts risk of passing on infection by as much as 50%, research shows, *BMJ* 2021;373:n1112, 2021-04-28, doi: 10.1136/bmj.n1112, https://www.bmj.com/content/373/bmj.n1112

2021-05-24 TheG asked NHS trusts in England about nosocomial Covid-19 infections. 80 trusts out of 123 replied (about two-thirds). "Probable" nosocomial infection was counted if a patient contracted Covid-19 8 to 14 days after admission, and "certain" if it was contracted 15 days or more after admission. Generally, the figures are for the dates between 2020-03-01 and 2021-03-01, but some answers differed somewhat from those dates. 32,307 people "probably" or "certainly" contracted Covid-19 nosocomially in that time, and 8,747 died (the deaths did not distinguish between "*from Covid*", "*with Covid*" or from an exacerbated condition). https://www.theguardian.com/world/2021/may/24/up-to-8700-patients-died-after-catching-covid-in-english-hospitals

2021-05-27 Following on from former government advisor Dominic Cummings's recounting before the parliamentary science and technology and health special committees of HMG's handling of the coronavirus pandemic in 2020, there have appeared two devastating commentaries in TheG from Devi Sridhar and Deepti Gurdasani https://www.theguardian.com/commentisfree/2021/may/27/government-covid-strategy-herd-immunity-westminster

2021-05-29 The RECOVERY trial has established that convalescent plasma is not effective in treating Covid-19 patients. RECOVERY Collaborative Group, Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial, The Lancet 397 Issue 10289, pp2049-2059, published on-line 2021-05-14. DOI: 10.1016/S0140-6736(21)00897-7 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00897-7/fulltext

Comment by Liu STH and Aberg JA, Convalescent plasma in patients hospitalised with COVID-19, The Lancet 2021-05-14, DOI: 10.1016/S0140-6736(21)01064-3 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01064-3/fulltext

2021-05-29 In the COLCORONA trail, an RCT of the antiinflammatory colchicine was performed on just over 4400 subjects, by a team led from Montréal, between March and December 2020. Those eligible had a positive RT-PCR test for Covid-19 and were not hospitalised. Primary endpoint was hospitalisation or death. Primary endpoint occurred in 4.6% of the colchicine group and 6.0% of the placebo group; serious adverse events in 4.9% versus 6.3%; pneumonia in 2.9% versus 4.1%; diarrhoea in 13.7% versus 7.3%. Nevertheless, say the researchers, the differences were not statistically significant. Tardif J-C, Bouabdallaoui N, et al, Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase 3, randomised, double-blinded, adaptive,

placebo-controlled, multicentre trial, The Lancet Respiratory Diseases, 2021-05-27, DOI: 10.1016/S2213-2600(21)00222-8 https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00222-8/fulltext

2021-05-29 A retrospective cohort study of 46 children with PIMS-TS (paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2; it used to be called MIS-C) at Great Ormond Street hospital is encouraging. None died, and most symptoms resolved over 6 months. Penner J, Abdel-Mannan O, et al, 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: a retrospective cohort study, The Lancet Chile and Adolescent Health, 2021-05-24, DOI: 10.1016/S2352-4642(21)00138-3 , https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00138-3/fulltext

2021-05-29 The BMJ has published a short editorial on the prospects of there being effective SARS-CoV-2 antivirals later in 2021. I found it very useful for its brief summary of the current state, and its pointers to the more detailed medical-scientific literature. Smith D and Gill D, Antivirals against SARS-CoV-2 by autumn? B*MJ* 2021;373:n1215 doi: 10.1136/bmj.n1215 https://www.bmj.com/content/373/bmj.n1215

2021-05-30 In The Observer on 2021-05-30 there is an astonishing piece of reporting from India about how people returning from the Kumbh Mela festival spread Covid-19 in their home towns and villages. https://www.theguardian.com/world/2021/may/30/kumbh-mela-how-a-superspreader-festival-seeded-covid-across-india Readers will likely have seen pictures from the festival, which made plain that it was an event with very large numbers of people who generally neither adhered to distancing nor to mask-wearing. There are five stories of individuals who attended, and who brought back Covid-19 and infected others. Two of the stories are astonishing for the level of denial. A politician and ex-Minister from Kashmir who attended with 11 family members, came back home, experienced symptoms and five days later started deteriorating. The first hospital suspected Covid (“suspected”??) but his son didn't agree and was taking him to another hospital but he died on the way. Eight days later his elder brother, who had not attended the festival, also died with Covid-like symptoms. A health official said that four members of the family had tested positive; a test and trace official said that at least 22 contacts had tested positive. His son still doesn't believe he died from Covid-19. A holy man from a large monastery in Uttah Pradesh attended for many weeks and started showing symptoms. His colleagues suggested he return to the ashram. He did, and he died. An ashram colleague said more than a dozen people who had contact with him after he returned also got ill, and some were hospitalised, but not many were tested. The prevalent belief in the ashram appears to be that Covid-19 is not real. The head says they drink cow urine and coronavirus will not affect them.

2021-06-06 On May 30th, The Economist posted an article by its data scientists noting that excess deaths in Wuhan due to the first wave (there has been no subsequent wave in China) are significantly larger than the official Covid-19 death count.

https://www.economist.com/grapic-detail/2021/05/30/covid-19-deaths-in-wuhan-seem-far-higher-than-the-official-count The official toll is 3,869. However, the article cites researchers associated with China's Centre for Disease Control and Prevention as established that there were 5,954 excess deaths between 2020-01-01 and 2020-03-31 compared with 2019, suggesting that, as in other cases around the world, the mortality was somewhat higher. Lu J, Zhang L, et al, Excess mortality in Wuhan city and other parts of China during the three months of the covid-19 outbreak: findings from nationwide mortality registries, BMJ 2021;372:n415 2021-02-24, doi: 10.1136/bmj.n415 https://www.bmj.com/content/372/bmj.n415 The Economist used data provided in the Appendix to that article to estimate that the excess death count in that period is more likely to be rather larger, around 13,400. The article discusses the methodology to some extent.

2021-06-09 Charlotte Summers in TheG on 2021-06-09 underlines how essential medical oxygen is for the treatment of those with respiratory problems, and bemoans the lack of reliable global supply. She suggests that rectifying this lack should be high priority.
https://www.theguardian.com/commentisfree/2021/jun/08/oxygen-shortages-killing-vaccines-drugs

2021-06-11 The NEJM published an article by doctors and communication scholars on 2021-05-12 suggesting the use of epidemiologic surveillance models also for infodemiology. As an example, they use the misrepresentation in *The Federalist* magazine on 2020-10-12 of a CDC study on mask use, that "*masks and face coverings are not effective in preventing the spread of Covid-19.*" This false statement was taken up by a Fox News commentator, and then repeating by then-President Trump during a televised presidential debate with Joe Biden. Scales, Gorman and Jamison illustrate how a "surveillance system" could have countered this infodemiological "superspreader event" by issuing timely corrections and references to reliable information. Jamieson works at the Annenberg Center at U. Penn. in Philadelphia, observes they have a misinformation classification system, indicates how it would classify the example above, and illustrates how a response might progress according to that classification. It is plausible. Scales D, Gorman J and Jamieson KH, The Covid-19 Infodemic — Applying the Epidemiologic Model to Counter Misinformation, N. Eng. J. Med., 2021-05-12, DOI: 10.1056/NEJMp2103798 ,
https://www.nejm.org/doi/full/10.1056/NEJMp2103798

The concern I have is that such systems require resources, which exist at the state level, which will be owned and/or controlled by somebody, and when such resources are in place they can surely equally be used to propagate misinformation on, say, the state's behalf, and, further, to counter critiques of that misinformation. The authors do not point out what particular characteristics "correct information" might have that would vitiate such an attempt to propagate misinformation through the same mechanisms. There are additional things one could do, such as attach a provenance analysis (say, in GSN, or Bloomfield-Rushby Assurance 2.0) to informational assertions. But that involves effort, and might well not work. If a state collects detailed data, say, from hospitals, analyses it, and then presents false results, the provenance analysis looks identical to the case in which correct results were presented. There would be no indication that the results have been deliberately faked.

It may well be that such "infodemiological surveillance systems", classification systems, and provenance analyses will only work well (in the sense of suppressing misinformation) in an informational environment which is already largely accurately factual. Or in a (seriously) free and

open speech environment in which everything in sight can be laid out.

2021-06-12 A clinical report of a 41-year-old patient in Munich who had an “unremarkable clinical history” and then suffered portal vein thrombosis, shortly after being vaccinated with a vector vaccine for Covid-19. The event happened during hospitalisation triggered by persistent headaches. Öcal O, Stecher S-S and Wildgruber M, Portal vein thrombosis associated with ChAdOx1 nCov-19 vaccination, The Lancet Gastroenterology and Hepatology, 2021-06-08, DOI: 10.1016/S2468-1253(21)00197-7 https://www.thelancet.com/journals/langas/article/PIIS2468-1253(21)00197-7/fulltext

2021-06-12 Autopsy results have shown that Covid-19-induced respiratory failure is highly associated with pulmonary microvascular thrombosis (references 7, 8 in Berger & Connors, op. cit.). A Brazilian trial of various forms of anticoagulant therapy and prophylaxis in Brazilian hospitals has shown a benefit of prophylactic-dose heparin in patients before they become critically ill. Lopes RD, Melos der Barros e Silva, PG, et al., Therapeutic versus prophylactic anticoagulation for patients admitted to hospital with COVID-19 and elevated D-dimer concentration (ACTION): an open-label, multicentre, randomised, controlled trial. The Lancet v397 i10291 pp2253-63, 2021-06-12 DOI: 10.1016/S0140-6736(21)01203-4
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01203-4/fulltext

The results in context are perhaps more easily read in the Comment by Berger JS and Connors JM, Anticoagulation in COVID-19: reaction to the ACTION trial, The Lancet 2021-06-12, DOI: 10.1016/S0140-6736(21)01291-5 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01291-5/fulltext

2021-06-14 The Royal Pharmaceutical Society has published a survey article on the accuracy and usefulness of lateral-flow tests for Covid-19, with pointers to significant studies which have been done and practical advice on limitations. Julia Robinson, How reliable are lateral flow COVID-19 tests?, 2021-05-13 updated 2021-06-01, The Pharmaceutical Journal, PJ, May 2021, Vol 306, No 7949;306(7949) DOI: 10.1211/PJ.2021.1.83246

https://pharmaceutical-journal.com/article/feature/how-reliable-are-lateral-flow-covid-19-tests

2021-06-18 The RECOVERY trial has shown that Regeneron's monoclonal antibody combination of casirivimab and imdevimab is an effective drug combination for patients with severe Covid-19 who do not generate antibodies. It reduces the death rate from 30% down to 24%. No preprint yet available, apparently. (Not really needed for such an announcement; RECOVERY has the very highest reputation for the quality of its results.) Researchers and commentators point out that this is the first positive result for a *therapy* for Covid-19. A possible downside is that this therapy is expensive.

https://www.theguardian.com/world/2021/jun/16/new-drug-cuts-deaths-among-patients-with-no-covid-antibodies

https://www.sciencemag.org/news/2021/06/monoclonal-antibodies-cut-risk-dying-covid-19-only-some-patients

2021-06-17 William Hanage is scathing in TheG this morning about the UK's early response to the pandemic in 2020. He singles out the care-home issue. Hanage says “*Office for National Statistics estimates 42,000 care home residents in England and Wales have died of Covid. This outcome was entirely predictable in the absence of meaningful infection control……..until the middle of April last*

year UK hospitals were discharging patients into care homes without requiring that they be tested for Covid first, sparking goodness knows how many introductions, outbreaks and deaths…. Before mid-April, testing was also limited to those with symptoms – which was disastrous, given the potential for unwitting transmission from currently asymptomatic people. Hancock claimed that asymptomatic transmission was not appreciated at the point that decisions were being made, but that is nonsense. " He notes that SAGE reported concern about asymptomatic transmission in its meeting minutes of January 28. The "*decisions*" were being made in February and March. Further, "*[t]he recent experience of the pandemic in northern Italy had made it clear that a serious surge of infections was headed towards the NHS, and planning for that meant that beds needed to be freed up*" which was the rationale for discharging elderly patients into care homes. However, "*[t]his surge was the consequence of delaying locking down until after a large wave had become inevitable. Hancock claims that to have taken action earlier would have meant "overruling scientific consensus" – which Stephen Reicher, a member of the independent Scientific Pandemic Insights Group on Behaviours (SPI-B), described as "quite simply untrue"*." These observations support in part the evidence of former advisor Cummings to the joint meeting of the Health and Science and Technology Select Committees of Parliament on 2021-05-26, and equally suggest that some of the evidence of Health Minister Hancock on 2021-06-10 was misleading. Hanage's title puts it more stridently: "*The evidence is clear – there was no excuse for Hancock's care homes strategy*".

2021-06-18 Reuters reported on 2021-06-16 that the CureVac mRNA vaccine turned out only to be about 47% efficacious in preventing Covid-19. The trial involved about 40K participants in Europe and Latin America. Of the cases, 124 were sequenced for variants. Only 1 was "original", and 57% were VoC.https://www.reuters.com/business/healthcare-pharmaceuticals/curevacs-covid-19-vaccine-misses-efficacy-goal-mass-trial-2021-06-16/

Curevac press release: https://www.curevac.com/en/2021/06/16/curevac-provides-update-on-phase-2b-3-trial-of-first-generation-covid-19-vaccine-candidate-cvncov/

CureVac has partnered with GlaxoSmithKline on vaccine development and production https://www.theguardian.com/world/2021/feb/03/glaxosmithkline-curevac-deal-develop-multi-variant-covid-vaccine