

Notes on COVID-19

Part 5: 2020-04-24 to 2020-04-xx

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2020-04-xx

2020-04-24 Swedish epidemiologist Anders Tegnell, author of Sweden's policy/strategy talks to Nature: <https://www.nature.com/articles/d41586-020-01098-x>

2020-04-24 (Publication date 2020-04-25) The editor of The Lancet, Richard Horton, details the timeline and the facts of the WHO's response to the information about the “pneumonia of unknown cause” (as it called it in its disease outbreak news on 2020-01-05). He comments on the US President's decision not to fund WHO further and calls it “a crime against humanity.” [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30969-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30969-7/fulltext)

2020-04-24 Reuters have talked to a collection of doctors and researchers who query the effectiveness of invasive ventilation, and have had success with non-invasive breathing assistance even in difficult cases <https://www.reuters.com/article/us-health-coronavirus-ventilators-special-report-as-virus-advances-doctors-rethink-rush-to-ventilate-idUSKCN2251PE> The link was recommended by Nature in its Briefing email.

2020-04-25 A letter published in Nature Medicine by Chorin et al. reports clinical observations of administering hydroxochloroquine with azithromycin to 84 Covid-19 patients. They report it affected the corrected QT interval (QTc) in many of them, and in 11% it became sufficiently prolonged to put them at high risk of cardiac arrhythmia and sudden cardiac arrest <https://www.nature.com/articles/s41591-020-0888-2> . A trial in Brasil of chloroquine was reported in JAMA by Silva Borba et al. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765270> They found “*In this phase IIb randomized clinical trial of 81 patients with COVID-19, an unplanned interim analysis recommended by an independent data safety and monitoring board found that a higher dosage of chloroquine diphosphate for 10 days was associated with more toxic effects and lethality, particularly affecting QTc interval prolongation. The limited sample size did not allow the study to show any benefit overall regarding treatment efficacy.*” The trial was halted because of the significant adverse findings: “*The preliminary findings from the CloroCovid-19 trial suggest that higher dosage of chloroquine should not be recommended for the treatment of severe COVID-19, especially among patients also receiving azithromycin and oseltamivir, because of safety concerns regarding QTc interval prolongation and increased lethality.*” The trial intended to enroll 440 patients, but was halted before even a quarter were enrolled. The paper was commented by Fihn, Perencevish and Bradley <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765269>

2020-04-25 The justification for asking people to wear masks in order to inhibit the spread of droplets possibly containing virus when they speak is given in Anfinrud et al in the NEJM on 2020-04-15 <https://www.nejm.org/doi/full/10.1056/NEJMc2007800>

2020-04-26 In Bielefeld. The way the data are collected and presented changed on 2020-04-20, due to new criteria introduced by the state of NRW. The numbers of hospitalised and in ICU are no longer being given.

Date	Total cases	Diff(=new)	Ill	Recovered	Died
• 2020-04-25	358	8	101	254	3

• 2020-04-24	350	1	101	246	3
• 2020-04-23	349	9	102	245	2
• 2020-04-22	340	2	107	231	2
• 2020-04-21	338	0	106	230	2
• 2020-04-20	338	n/a	107	229	2

2020-04-26 The Australian state of NSW has looked at 18 cases of Covid-19 in schools in March and April. 735 students and 128 staff were “close contacts” of these 18. Two children *may* have contracted Covid-19 from one of these cases at their schools; no teacher or staff member contracted Covid-19 from any of these cases. <http://ncirs.org.au/covid-19-in-schools> (with link to full report).

2020-04-26 Spinato et al surveyed patients with mild Covid-19 to find whether they had experienced alterations in sense of taste or smell. 202 people completed the telephone survey <https://jamanetwork.com/journals/jama/fullarticle/2765183> They used standard survey devices, namely ARTIQ and SNOT-22. Just under two-thirds reported altered taste and/or smell. There are reasons not to be surprised by this “*Previous strains of coronavirus have been demonstrated to invade the central nervous system through the olfactory neuroepithelium and propagate from within the olfactory bulb. Furthermore, nasal epithelial cells display the highest expression of the SARS-CoV-2 receptor, angiotensin-converting enzyme 2, in the respiratory tree.*”

2020-04-26 Serological tests just aren't that good yet

<https://www.nytimes.com/2020/04/24/health/coronavirus-antibody-tests.html>

2020-04-27 A TheG interview of Christian Drosten, head of the German reference laboratory on virology, by Laura Spinnery, who has just written a book on the 1918 influenza pandemic which a colleague has recommended as very good.

<https://www.theguardian.com/world/2020/apr/26/virologist-christian-drosten-germany-coronavirus-expert-interview> Most of the interview is about epidemiology, not virology. A key point is that controlling resurgence of Covid-19 without further lockdown will require contact tracing, and because of the characteristics of the disease that can only be effective if there is electronic help, of the sort that Apple and Google and other countries are now introducing.

2020-04-28 The US National Academies' Rapid Expert Consultations recounted on 2020-04-14 in Notes Part 3 are a device developed during the Deepwater Horizon emergency, a decade ago, which proved fruitful as recounted in <https://www.nationalacademies.org/news/2020/04/lessons-from-a-crisis> . The process consists of an expert being asked to produce a report in 24 hours.

2020-04-28 An article in the BMJ on what we learned from the case of the Diamond Princess, the cruise ship with many Covid-19 cases on board that was quarantined in Nagasaki

<https://www.bmj.com/content/369/bmj.m1632> Although the lockdown protocol was criticised, it seems to have done a reasonable job of limiting transmission; transmission after lockdown was largely confined to roommates of infected persons, and the crew, who were necessarily visiting many cabins. Besides, it provided the first quantifiable study of asymptomatics and their role in

Covid-19.

2020-04-28 Sheila Bird, statistician, former programme leader at the MRC Biostatistics Unit, member of the Royal Statistical Society Covid-19 task force, and a former member of the task force for swine flu, has scathingly criticised the gathering and presentation of UK RT-PCR test statistics <https://www.bmj.com/content/369/bmj.m1664> She said, first, that the present classification of results does not allow useful statistical inference; second, that results should be presented by the date of the swab test, not by the date the result was available; and, third, that multiple tests on individuals should be agglomerated. The second point is obvious. As is the third: if you have someone who presented at the hospital with symptoms, who initially tested negative, then positive, then twice negative before discharge, this manifestly does not represent the same situation as testing four people once, with three testing negative and one positive; yet the data as reported does not distinguish these two situations. A PHE response says that the data at <https://coronavirus.data.gov.uk> are reported by date of test. However, a look at the site gives the “[n]umber of new cases reported today”, which suggests that Bird is correct on this point and the PHE response not.

2020-04-28 Some news in the BMJ on the state of play with regard to vaccines, published 2020-04-27 <https://www.bmj.com/content/369/bmj.m1679>

2020-04-28 Readable blog commentary from Richard Lehmann on the BMJ site <https://blogs.bmj.com/bmj/2020/04/27/richard-lehmans-covid-19-reviews-27-april-2020/> In his paragraph “Dialogue concerning the two world systems”, he compares China, which prioritised saving the individual life and appears to have succeeded, with Britain, which “[o]n 12 March declared in favour of “herd immunity”, and nothing that has happened since shows serious intent to prevent the cull which that implies.” He also refers to a result of ICNARC that the mortality rate of those in the UK going on to invasive mechanical ventilation is 67%. But ICNARC's report, available from <https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports> , seems to say that, of known outcomes, it is closer to 50%-50% (Table 7, p17).

2020-04-28 Jeffrey Aronson's introduction to exponential growth/decay, with a reference to simple/compound interest, and to varying values of R, for those who have forgotten their school mathematics <https://blogs.bmj.com/bmj/2020/04/24/jeffrey-aronson-when-i-use-a-word-exponential-finance-increasing-decreasing/>

2020-04-29 Thomas Holtz at the Universität Ilmenau has developed an alternative nowcast estimate of the effective reproduction number R_e <https://stochastik-tu-ilmenau.github.io/COVID-19/germany> (in German) based on the estimation method of Fraser <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0000758> . There is also a model developed at the Helmholtz Centre for Infection Research in Braunschweig (Brunswick as it used to be known in both English and German) <https://gitlab.com/simm/covid19/secir/-/wikis/Report> . The Helmholtz estimates are based on the model in Khailaie et al <https://www.medrxiv.org/content/10.1101/2020.04.04.20053637v1> Both of these projects currently estimate R_e to be less than 1, where it needs to be, whereas RKI in its Tuesday briefing suggested it

was round about 1 on Monday April 27 <https://www.theguardian.com/world/2020/apr/28/germans-urged-to-stay-home-amid-covid-19-infection-rate-fears>

2020-04-29 The paper by Fraser to which I just referred points out that the Kermack-McKendrick paper which introduced SIR also introduced the time-to-infection model which he uses, in order to separate within-household infection processes from between-household infection processes. Fraser is now a Professor at Oxford, associated with the Big Data Institute. His group has come to the conclusion that Covid-19 can be stopped through effective contact tracing, which must be “sufficiently fast, sufficiently effective and happens at scale.” <http://www.coronavirus-fraser-group.org/> They suggest therefore via mobile app, similar to the opinion of Christian Drosten noted above. They refer to their article in Science, published on 2020-03-31, <https://science.sciencemag.org/content/early/2020/04/09/science.abb6936> , which says this cannot be accomplished for this disease by manual contact tracing.

2020-04-30 Results of a large RCT of remdesivir appear to have shown that use of the drug for ten days in severely ill patients allowed 31% faster recovery (defined as: “being well enough to come off oxygen despite remaining in hospital; being well enough for hospital discharge although not quite back to normal health; or being out of hospital and returned to normal activity levels.” <https://www.theguardian.com/world/2020/apr/29/remdesivir-coronavirus-drug-experimental> Also, in the group receiving the drug, 8% died, whereas 11% died in the control group, but this is not said to be statistically significant. The results were announced by Anthony Fauci, who said treatment with remdesivir will become the standard of care. All the renowned experts to whom TheG talked welcomed the results. The work has not yet been peer-reviewed but nobody seems to be doubting it. There is some disappointment that it doesn't seem to stop you dying <https://www.theguardian.com/world/2020/apr/30/remdesivir-the-antiviral-drug-is-being-touted-as-a-possible-coronavirus-treatment-but-will-it-work>

The report by Wang et al of the inconclusive Chinese trial, which was stopped early because of a lack of recruits, is at <https://www.thelancet.com/lancet/article/S0140673620310229> , followed by a comment on the study by John David Norrie [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31023-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31023-0/fulltext)

2020-04-20 Robert May, Lord May, Baron of Oxford, has died <https://www.theguardian.com/science/2020/apr/29/robert-may-former-uk-chief-scientist-led-chaos-theory-lord-dies-aged-84> He was the UK government's Chief Scientific Advisor 1995-2000. With his collaborator Roy Anderson he established the important role of outbreak analysis using R_0 , which concept Adam Kurcharski in The Rules of Contagion (Wellcome Collection, Profile Books, 2020) on p54 attributes (following Heesterbeek) to an idea in the appendix to a paper of George MacDonald on mosquitos as vectors and what could be done about them, and its formalisation twenty years later by Klaus Dietz. May became known in the 1970's for a paper on growth of fish populations of which the mathematics exhibited chaos-theoretic properties <https://de.wikipedia.org/wiki/Chaosforschung> (in German, not referenced in the English page on Chaos Theory, which is mostly pure mathematics). He also studied financial contagion (“booms” and “busts”).

2020-04-30 There has been worry about the excess deaths caused by Covid-19, as fewer people needing critical care, for example new instances of cancer, seek or are able to get treatment. Damian Carrington reported in TheG on a study from Harvard's TH Chan School of Public Health, which concluding that a small increase in PM2.5 leads to a significant increase in the death rate from Covid-19 <https://www.theguardian.com/environment/2020/apr/07/air-pollution-linked-to-far-higher-covid-19-death-rates-study-finds> (I have not read the original report, but it stands to reason, with all that is known about pollution and respiratory-system ailments). Turning that around, lockdown/stay-at-home in Europe has lowered such pollution. A new research organisation called the Centre for Energy and Clean Air <https://energyandcleanair.org> has published a report saying there have been 11,000 fewer deaths in Europe in the last weeks, due to cleaner air and lack of pollution. Compared with the same period in 2019, NO₂ is down by 40% and PM2.5 down by 10%. A report in TheG <https://www.theguardian.com/environment/2020/apr/30/clean-air-in-europe-during-lockdown-leads-to-11000-fewer-deaths> says that these two forms of pollution are “normally” responsible for 470,000 deaths in Europe annually. The following CECA blog post links to the CECA report, which I have not yet read <https://energyandcleanair.org/air-pollution-deaths-avoided-in-europe-as-coal-oil-plummet/> Echoing this finding, TheG reports a comment by L J Smith, a respiratory-medicine consultant at King's College hospital in London: *“We have seen many fewer patients admitted with exacerbations of asthma and COPD [chronic obstructive pulmonary disease] over the last month and there is no doubt that a fall in air pollution is part of the reason. It’s allowed us to question what we have previously accepted as normal. If air pollution returns to its previous levels my waiting room will once again start filling up with children and adults struggling to breathe.”*

2020-04-30 On a similar theme about the altered environment, the International Energy Agency said that electricity from renewables is the only energy source resilient to the shock caused by Covid-19. They expect energy from renewables to grow by 5% this year, whereas gas to drop by 5% and coal by 8%. Global demand for energy will drop by 6%, they think, with 11% across the EU and 9% in the US. And global emissions will drop by 8%, including 3bn tonnes of CO₂. <https://www.theguardian.com/business/2020/apr/30/covid-19-crisis-demand-fossil-fuels-ia-renewable-electricity>