Notes on COVID-19

Part 8: 2020-05-24 to 2020-05-31

Peter Bernard Ladkin
2020-05-31

2020-05-26 The WHO has dropped hydroxycholoroquine from its "solidarity" trial of possible drugs for Covid-19 on 2020-05-25 in light of the Lancet study published last week https://www.theguardian.com/world/2020/may/25/who-world-health-organization-hydroxychloroquine-trial-trump-coronavirus-safety-fears

2020-05-26 Kuo et al have studied the genes of Covid-19 patients and noted that those with two copies of the e4 variant of ApoE had more than twice the risk of severe Covid-19 as those with two copies of the e3 variant. The former have a risk of dementia up to 14 times that of the latter. News report https://www.theguardian.com/world/2020/may/26/research-reveals-gene-role-in-both-dementia-and-severe-covid-19 and the paper is open-access at https://academic.oup.com/biomedgerontology/advance-article/doi/10.1093/gerona/glaa131/5843454 "*In older adults, we found that pre-existing dementia is a major risk factor (OR = 3.07, 95% CI: 1.71 to 5.50) for COVID-19 severity in the UK Biobank (UKB) [1]. In another UK study of 16,749 patients hospitalized for COVID- 19 [2], dementia was among the common comorbidities and was associated with higher mortality. Additionally, impaired consciousness, including delirium, is common in severe cases [3]. The ApoE e4 genotype is associated with both dementia and delirium [4], with the e4e4 (homozygous) genotype associated with a 14-fold increase in risk of Alzheimer's disease [5] compared to the common e3e3 genotype, in populations with European ancestries. We therefore aimed to test associations between ApoE e4 alleles and COVID-19 severity, using the UKB data*."

2020-05-28 David Hunter thinks Rt needs to be down to about 0.25 in the UK to get the virus to decline at the same rate as it spread. No one thinks Rt is anywhere near that low. https://www.theguardian.com/commentisfree/2020/may/28/coronavirus-infection-rate-too-high-second-wave

Hunter suggests R0 may in fact be 4 or higher, and refers to a Harvard Magazine article in which Havard epidemiologist Michael Mina opines R0 is likely higher than 2-3. The article refers to a paper by Ke et al of Los Alamos National Laboratories in Emerging Infectious Diseases journal. A preprint appears to be here https://www.medrxiv.org/content/10.1101/2020.02.07.20021154v1 Harvard epidemiologist Marc Lipsitch finds this a "minority view" but "credible".

Hunter goes on to enumerate the consequences of a continuing high prevalence of Covid-19 in the population. Continuing social restrictions, and likely a second wave when colder weather returns.

2020-05-28 The Covid-19 Symptom Study https://covid.joinzoe.com/about has apparently shown that "*in the last week of March, Liverpool and Cheltenham were among the areas with the highest number of suspected cases. an estimated 5-6% of the population, aged 20 to 69, having symptoms in those two regions.*" https://www.bbc.com/news/uk-52797002 (2020-05-26). Liverpool had hosted the Champions' League football match against Athletico Madrid on 11 March, and Cheltenham the Cheltenham Festival on 16-19 March. The study is led by Tim Spector of King's College, London.

2020-05-29 The Financial Times reports on excess death rates in various countries, as a widely-recognised indicator of the toll of an epidemic https://www.ft.com/content/6b4c784e-c259-4ca4-

9a82-648ffde71bf0 GB has an excess death rate of 891 per million over the 5-year average. Only Spain is higher at 921 per million.

2020-05-29 Lombardy's first case was by no means Mattia Maestri from Codogno, the well known "Patient 1". There was a 64-year-old woman visited her GP with what turned out to be Covid-19 on 20 January https://www.theguardian.com/world/2020/may/29/why-was-lombardy-hit-harder-covid-19-than-italys-other-regions

2020-05-30 In the local newspaper today (Neue Westfalische; paywall; I receive the printed version) there are statements from virologist Christian Drosten as well as epidemiologist Hendrick Streeck, who studied the Heinsberg outbreak about the infectivity characteristics of Covid-19. Apparently most infections come through superspreading events. The reference is to a podcast from Drosten https://www.ndr.de/nachrichten/info/podcast4684.html (in German). David Hunter also mentioned this phenomenon in his TheG article linked above. The "rule of thumb" appears to be that about 10% infect 80%. This suggests that track-and-trace and controlling outbreaks may very well keep the virus in check and inhibit a "second wave". The figures appear to derive from a report from – where else – LSHTM, Endo et al https://wellcomeopenresearch.org/articles/5-67 from 2020-04-09. According to CMMID, whence this paper derives, the first version was available 2020-03-11, so it has been around two and a half months https://cmmid.github.io/topics/covid19/ The phenomenon was confirmed recently by an Israeli study by Miller et al https://www.medrxiv.org/content/10.1101/2020.05.21.20104521v1 from 2020-05-22, in preprint, and there is a preprint from Hong Kong, Adam et al, saying the same https://www.researchsquare.com/article/rs-29548/v1 With high-quality coauthors, I take it as very likely that these three independent studies are right. It is no surprise to see Drosten quoting their results.

He also said that incubation time and infectivity time are noticeably shorter than originally supposed (I don't know yet whence these derive). Quarantine only needs to be 7 days.

There was an news article in Science about it also, on 2020-05-19, which interviewed Kucharski on the LSHTM CMMID work and their estimate of dispersion factor (k) to be 0.1 https://www.sciencemag.org/news/2020/05/why-do-some-covid-19-patients-infect-many-others-whereas-most-don-t-spread-virus-all

2020-05-30 Raharusun et al performed a retrospective cohort study from Indonesian records and found that "*[w]hen controlling for age, sex, and comorbidity, Vitamin D status is strongly associated with COVID-19 mortality outcome of cases.*" https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3585561 Note, this report is a preprint, but SSRN is well known. It is known that Vitamin D levels do correlate with susceptibility to poor outcomes in other respiratory diseases, and studies linked in previous Notes have noted this (see, for example, Mitchell's discussion in The Lancet Diabetes and Endocrinology linked on 2020-05-23 in Notes Part 7). Thanks to Risks Forum Digest contributor R. G. Newbury for the reference https://catless.ncl.ac.uk/Risks/31/91#subj19

2020-05-30 Anakinra is a recombinant IL-2 receptor antagonist. It has been suggested it could help in suppressing the cytokine storm that can follow infection with SARS-CoV-2, even after the virus is no longer heavily shed. Huet et al report in The Lancet Rheumatology on a prospective cohort

study with a retrospective control group in Paris hospitals https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30164-8/fulltext . Main composite outcome was admission to ICU for invasive ventilation or death. There were 52 in the group which received anakinra and 44 in the retrospective control group. Main outcome occurred in 13 (25%) of the anakinra group and 32 (73%) of the historical control group. Good news for treatment. Of course the authors say "*[c]onfirmation of efficacy will require controlled trials*". But if anakinra is that effective at mitigating the inflammatory post-reaction, it is ethically questionable whether one could or should perform such a trial. Anakinra does appear to have side effects, apparently sometimes an increase in liver aminotransferases, which correlates with Type 2 diabetes. The comment by Cron concludes that "*[t]his study is the most definitive evidence to date that anakinra can benefit patients with COVID-19-associated cytokine storm syndrome. The significant reduction in mortality associated with anakinra use for COVID-19 in this study is encouraging in these challenging times*." https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30165-X/fulltext

2020-05-30 Burki has a news article on testing for Covid-19 in The Lancet Respiratory Medicine https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30247-2/fulltext Martin Hibberd of LSHTM notes that a saliva test is preferable to swab testing for a number of reasons, inter alia that it enables workplace testing. He points out that effective testing is one of three prongs of a control strategy that avoids lockdown: "*Testing alone will not be sufficient; you also have to ensure that you have a strong system for contact tracing, and that people comply with the regulations", stresses Hibberd. If all three components work in tandem, then the virus can be controlled. Hibberd gives the example of South Korea and Singapore. "If you look at those countries, there is one clear lesson", he said. "If you can identify and quarantine most of the positive cases, then you do not have to lockdown everyone else.*"

2020-05-30 Zhu et al report on a Phase 1 trial of a Chinese Covid-17 vaccine in The Lancet on 2020-05-22 https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)31208-3.pdf Comment by Lee and McGeer on 2020-02-28 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31239-3/fulltext They mention that a Phase II trial is starting in China.

2020-05-30 Oran and Topol summarise research and reports into asymptomatic cases https://www.scripps.edu/science-and-medicine/translational-institute/about/news/sarc-cov-2-infection/ For example, Lavezzo et al report on the outbreak in Vò https://www.medrxiv.org/content/10.1101/2020.04.17.20053157v1 dated 2020-04-18 43.2% of infected were asymptomatic. On the Diamond Princess cruise ship, it was 46.5%. On the USS Theodor Roosevelt aircraft carrier, 58.4%. On the Charles de Gaulle, 47.8%.