Happy MLK Day-in line with his I Have a Dream speech, I have a dream that we will vaccinate >100,000 million people by April and that we will start to see the end of the pandemic and we can start to slowly get back to a "new normal". With all I see and hear about what is going on in DC I recall a quote by the great Israeli philosopher Martin Buber:

"It is not neutrality that we need, but rather cohesion, a cohesion of mutual responsibility and mutual influence. We are not required to blur the boundaries among the factions, circles, and parties, but rather share a recognition of the common reality and to share the test of mutual responsibility."

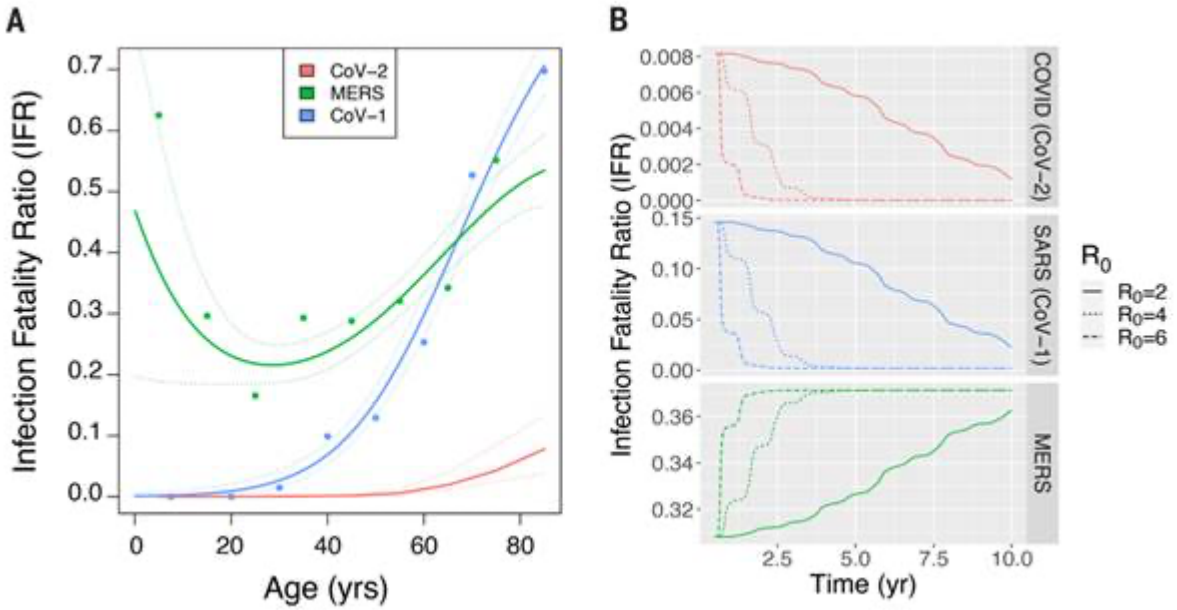
In these times of uncertainty let us all recommit to build greater respect, community purpose, and foster hope.

Now back to COVID-19. Today I review I think a very important immunological model governing the transition from a pandemic to an endemic. The second article is analyzing a very large dataset on the clinical characteristics and outcomes of hospitalized women giving birth with and without COVID-19. The last article is a very nice study on in-flight transmission of SARS-CoV-2 despite predeparture testing.

Have a wonderful day

Ed

Immunological Characteristics Govern the Transition of COVID-19 to Endemicity
Science published online November 12, 2021
doi:10.1126/science.abe6522 (2021)
Their analysis of immunological and epidemiological data on endemic human coronaviruses (HCoVs) shows that infection-blocking immunity wanes rapidly, but disease-reducing immunity is long-lived. Their model, incorporating these components of immunity, recapitulates both the current severity of CoV-2 and the benign nature of HCoVs, suggesting that once the endemic phase is reached and primary exposure is in childhood, CoV-2 may be no more virulent than the common cold. [we can only hope!] Reanalyzing data from a previous study, they found that the first infection with common cold coronaviruses occurs on average at 3 to 5 years of age. After that age, people may become infected again and again, boosting their immunity and keeping the viruses circulating. But they do not become very ill.



The overall infection fatality ratio (IFR) of emerging coronaviruses once they reach endemicity is strongly influenced by the IFR of young children in the initial epidemic. See above.

Comment: The timing of how long it takes to get to this sort of endemic state depends on how quickly the disease is spreading, and how quickly vaccinations are rolled out. Bottom line in my opinion, depending on how fast the virus spreads (Ro [new variant]), and on the strength and longevity of the immune response it would take a few years to decades of natural infections to become endemic without a vaccine. However, vaccines completely alter that calculus. The faster people can be immunized, the better. An efficient vaccination rollout could shorten the timeline to a year, or even less, for SARS-CoV-2 to become an endemic infection. Still, vaccines are unlikely to eradicate SARS-CoV-2. The virus over time I think will become a permanent, albeit less virulent virus. It is more likely that the vaccines will prevent illness — but not necessarily infection and transmission. [to be determined] If so that means that SARS-CoV-2 will continue to circulate. The vaccines we have right now are unlikely to provide "sterilizing immunity." The model rests on the assumption that the new coronavirus is similar to the common cold coronaviruses. But that assumption may not hold up. Another possible scenario is that the virus may come to resemble the seasonal flu, which is mild some years and worse in others. New variants of the coronavirus that may evade the immune response will only complicate the picture. Vaccine composition may need to be changed just like we do for influenza vaccines. As a reminder, influenza is associated with 20,000-70,000 deaths per year. These results reinforce the importance of behavioral containment during pandemic vaccine rollout, while prompting us to evaluate scenarios for continuing vaccination in the endemic phase.

Clinical Characteristics and Outcomes of Hospitalized Women Giving Birth With and Without COVID-19

JAMA Intern Med published online January 15,2021
doi:10.1001/jamainternmed.2020.9241

Women giving birth and discharged between April 1 and November 23, 2020, were identified by International Statistical Classification of Diseases and Related Health Problems Tenth Revision (ICD-10) codes within the Premier Healthcare Database, an all-payer database encompassing approximately

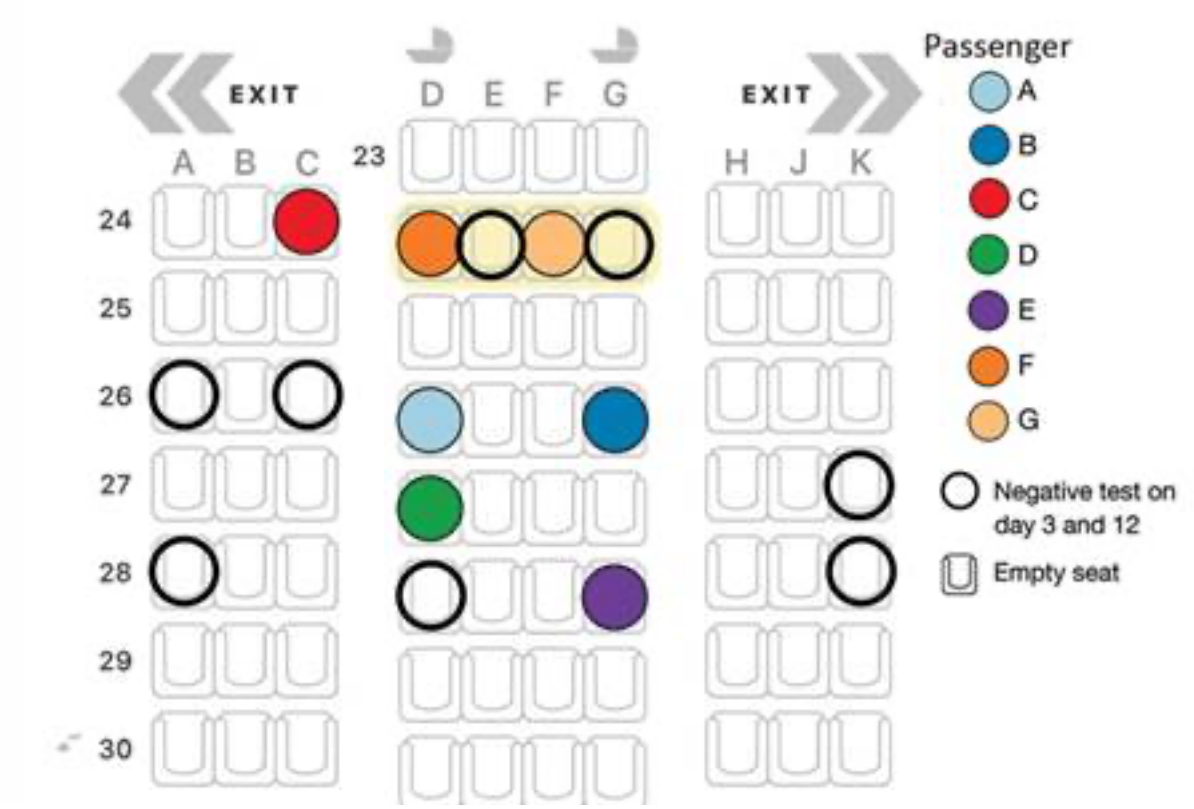
20% of US hospitalizations. Race and ethnicity were self-reported, and COVID-19 status (*ICD-10* code U07.1), comorbidities, and in-hospital outcomes were identified using ICD-10 and billing codes. Discharge disposition and in-hospital death were reported in all patients. Data were collected and deidentified by Premier Inc, which curates the Premier Healthcare Database, then analyzed at Brigham and Women's Hospital.

Among the 406,446 women hospitalized for childbirth over the 8 months of the study, 6380 (1.6%) had COVID-19. Compared with pregnant women without COVID-19 (n = 400 066), the women with COVID-19 were younger and more often Black and/or Hispanic and with diabetes and obesity. Of the 6380 women with COVID-19 who gave birth, 6309 (98.9%) were discharged to home, 212 (3.3%) needed intensive care, 86 (1.3%) needed mechanical ventilation, and 9 (0.1%) died in the hospital. Although in-hospital mortality was low, it was significantly higher in the women with COVID-19 than in those without COVID-19 (141 [95% CI, 65- 268] vs 5.0 [95% CI, 3.1-7.7] deaths per 100 000 women). Rates of myocardial infarction and venous thromboembolism (VTE) were higher in the women with COVID-19 who gave birth than in those without COVID-19 (myocardial infarction: 0.1% vs 0.004%; VTE: 0.2% vs 0.1%; $P < .001$). COVID-19 was associated with higher odds of preeclampsia (adjusted odds ratio [aOR], 1.21 [95% CI, 1.11-1.33]) and preterm birth (aOR, 1.17 [95% CI, 1.06-1.29]) but not with significantly higher odds of stillbirth (aOR, 1.23 [95% CI, 0.87-1.75]). Use of chest imaging, intensive care treatment, and mechanical ventilation was higher among the women who gave birth with COVID-19 compared with those without COVID-19. Among women with COVID-19 who gave birth, age (OR, 1.91 [95% CI, 1.31-2.77] per 10 years), morbid obesity (OR, 3.85 [95% CI, 2.05-7.21]), diabetes (OR, 4.51 [95% CI, 2.10 9.70]), kidney disease (OR, 21.57 [95% CI, 7.73-60.10]), eclampsia (OR, 116.1 [95% CI, 22.91-588.50]), thrombotic events (OR, 45.10 [95% CI, 17.13-118.8]), and stillbirth (OR, 7.88 [95% CI, 2.39-25.98)] were associated with higher odds of mechanical ventilation use or in-hospital death.

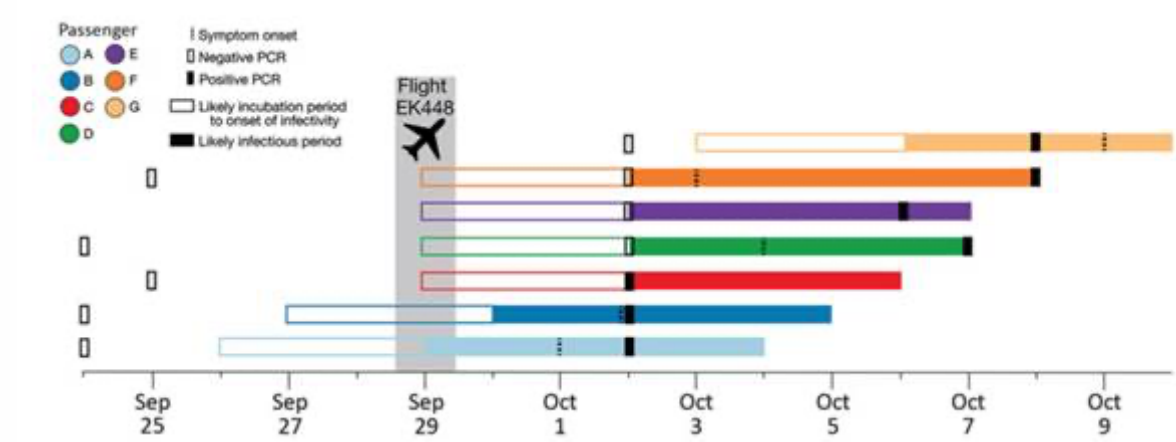
Comment: The higher rates of preterm birth, preeclampsia, thrombotic events, and death in women giving birth with COVID-19 highlight the need for strategies to minimize risk. Limitations include potential misclassification by *ICD-10* codes, lack of confirmatory testing and imaging findings, information on disease severity, the inability to distinguish asymptomatic from symptomatic COVID-19 cases, low event rates, and residual confounding. Given this large national cohort of US women hospitalized for childbirth, they found that absolute rates of death and adverse events in those diagnosed with COVID-19 were low, as might be expected in a young population, but given the large number of women in this dataset they were able to determine higher rates of preterm birth, preeclampsia, thrombotic events, and death in women giving birth with COVID-19 which would have been missed in smaller datasets.

Genomic Evidence of In-Flight Transmission of SARS-CoV-2 Despite Predeparture Testing
MMWR published online January 12,2021
In response to the growing international risks associated with importation of SARS-CoV-2, on March 20, 2020, New Zealand closed its borders to all but New Zealand citizens, permanent residents, and persons with an exemption. On April 9, 2020, to better control importation risks, New Zealand implemented a system of managed isolation and quarantine (MIQ) at the border. Persons arriving in New Zealand were required to stay in a government assigned MIQ facility for at least 14 days before entering the New Zealand community. In June 2020, a system of testing persons who were returning to New Zealand and staying in MIQ facilities was instituted; nasopharyngeal swabs were taken on approximately the third and the twelfth day of the quarantine period and from anyone in whom symptoms developed or those identified as close contacts of persons with severe acute SARS-CoV-2 positive test results.

On September 29, 2020, flight EK448, which originated in Dubai, United Arab Emirates, with a stop in Kuala Lumpur, Malaysia, landed in Auckland, New Zealand. During the required 14-day MIQ period, 7 passengers who had traveled on the flight received positive SARS-CoV-2 test results. The 7 passengers had begun their journeys from 5 different countries before a layover in Dubai; predeparture SARS-CoV-2 test results were negative for 5. These 7 passengers had been seated within 4 rows of each other during the ≈18-hour flight from Dubai to Auckland. Because recent studies have reported conflicting findings of the risks associated with in-flight transmission, the investigators undertook a comprehensive investigation to determine the potential source of infection of these travelers.



While in MIQ, all 86 passengers on the flight underwent PCR diagnostic testing for SARS-CoV-2 on day 3 and again on day 12 if the previous test result was negative. Cabin crew members departed New Zealand soon after their arrival and were therefore not tested. They determined seating plans by consulting the flight manifest for the Boeing 777–300ER aircraft and confirmed them by administering a questionnaire to passengers, asking where they actually sat.



Genomic sequencing was performed on the 7 isolates. The sequences obtained were assigned to lineage B.1 and were genetically identical, apart from 1 mutation for the sample from passenger D.

Comment: Evidence of in-flight transmission on a flight from the United Arab Emirates to New Zealand is strongly supported by the epidemiologic data, in-flight seating plan, symptom onset dates, and genomic data for this group of travelers who tested positive for SARS-CoV-2 (passengers A–G). Among the 7 passengers, 2 (A and B) were probably index case-patients infected before the flight, 4 (C, D, E, and F) were probably infected during the flight, and the remaining passenger (G) was probably infected while in MIQ. All 7 passengers were seated in aisle seats within 2 rows of where the presumed index case-patient(s) were seated. The data do not definitively exclude an alternative exposure event, such as virus transmission at the Dubai airport before boarding. That 3 passengers had positive test results on day 3 of their 14-day quarantine period indicates some of the complexities of determining the value of predeparture testing, including the modality and timing of any such testing as is being implemented now for overseas flights to the US. I strongly believe proof of immunization should also be added to the prescreening criteria.