

TGIF! Today another country has been added to the distribution of the COVID-19 Briefing – Australia.

Today I start with a review on the current science concerning the Delta variant trying to separate fear from fact. Comments are always welcomed. Next, I summarize a letter sent to the CDC by the National Nurses United, the largest union of registered nurses, requesting universal masking be reinstated.

Under Journal Review the first two articles advocate for mandatory COVID-19 vaccinations of HCP. The third article is on viral infection and transmission in a large outbreak of the Delta variant. The last article suggests a possible relationship between reactivation of EBV and prolonged COVID-19 symptoms.

Have a terrific weekend

Ed

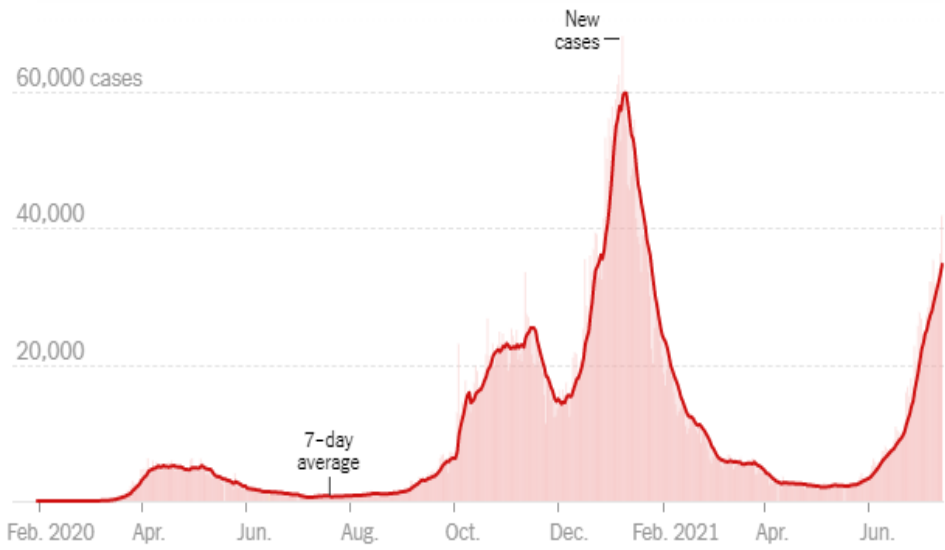
VII: Delta Variant: Fear and Noise Versus Science

In recent weeks Delta has become the “talk of the town.” To be clear, Delta should be taken seriously, but as has been the case the media has created what I call a lot of noise and fear. Let us explore what we know understanding the science could change.

First there are two basic questions to ask about any variant of SARS-CoV-2: Is it more contagious than earlier versions of the virus and second is it more severe? First the Delta variant is the most contagious version of SARS-CoV-2 accounting for more than half of new infections in the United States. Data collected by Public Health England indicates that the Delta variant is up to 60 percent more transmissible than the Alpha variant, which was itself at least 50 percent more transmissible than the wild type of the virus. (See article below on estimated viral load) Next when a variant is more transmissible, it will lead to a rise in the number of infections, especially among the unvaccinated. If, however, a variant is more severe, it causes worse symptoms for the average person who gets infected and leads to a greater percentage of cases that result in hospitalization or death. So just because a variant is more contagious, does not mean it is more severe. The news media uses the words like worse or more dangerous which can create fear and may be misleading.

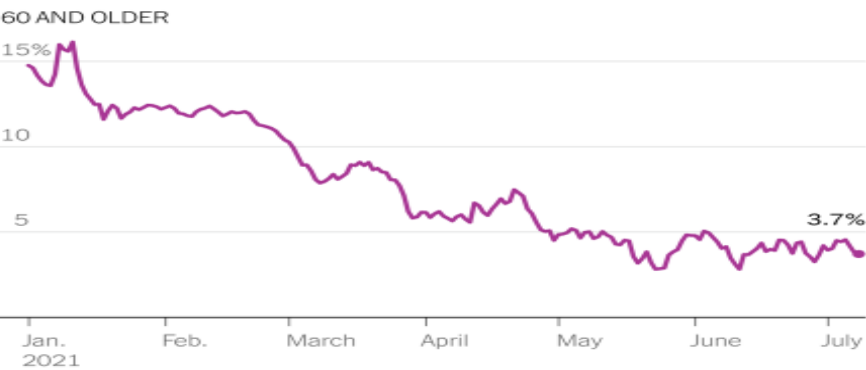
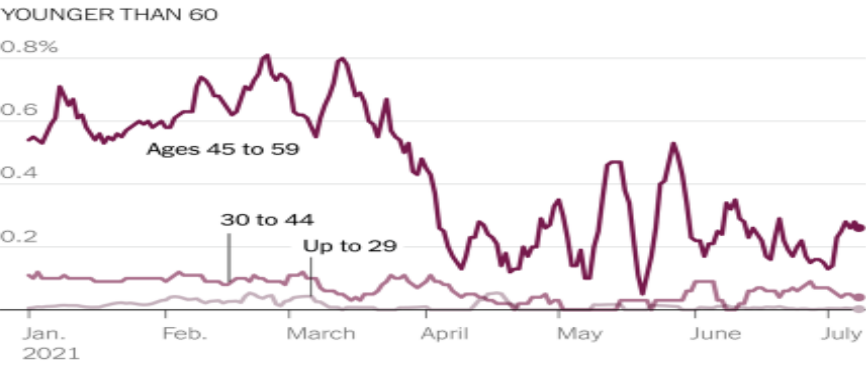
So next let us discuss current evidence. The Delta variant does not appear to be more severe, based on the data available so far. A good way to understand Delta is to look to the UK, where the variant has been circulating widely since May, much longer than in the US. If Delta were more severe than earlier versions of the virus, the percentage of cases leading to hospitalization or death should be rising. The charts below give us a clue. These are from Public Health England.

U.K. Coronavirus Cases ›



These are days with a reporting anomaly.

Share of U.K. Covid Cases That Are Fatal, By Age



If Delta were more severe than earlier versions of the virus, the percentage of cases leading to hospitalization or death should be rising and they are not. If the UK experience is a harbinger of what is to come, the overall number of infections may rise as the Delta variant spreads through the US. But hospitalizations and deaths are likely to be much lower than they were following the arrival of previous

variants, because first the average age of those infected has shifted downward and young people tend to have mild symptoms and second vaccinations. Vaccines are effective against the Delta variant especially against severe disease and death. A study from Public Health England last month demonstrated the Pfizer vaccine was 96% and AZ vaccine was 92% effective against hospitalization. The J&J vaccine produces strong neutralizing antibodies and cellular responses against the Delta variant, still present eight months after administration. [Both studies have been reviewed in the Briefing in the last month]. Hospitalizations are going up in the US in states with low vaccination rates, however, nationwide the numbers remain at some of the lowest levels since the beginning of the pandemic but are once again slowly trending upward. In the United States nearly 60 percent of adults are fully vaccinated. US hospitalization data to date show not only that higher Delta prevalence does not drive higher hospitalization rates but in fact in places that had higher percentages of the Delta variant they had lower ratios of hospitalized people to Covid-19 cases. 99% of hospitalizations for Covid-19 are among unvaccinated people. Another indicator of how far we have come, nationwide, Covid-19 has dropped from being the leading cause of death in January to now the seventh, averaging 330 deaths per day. In previous surges, there was a linear relationship between the number of infections, hospitalizations, and deaths in the US. Fortunately, this pattern does not seem to hold for the Delta variant to date, because a large proportion of people at the highest risk now have been vaccinated. [Over 85% of elderly have been fully vaccinated] Finally, fully vaccinated people should remain protected against severe disease. For children too young to be vaccinated, serious Covid symptoms would still be rare and still concentrated among children with underlying health problems. There have been vaccine breakthrough infections, but they tend to have mild symptoms and rarely have required hospitalization. So, a lot of noise, but no need to panic. What we need is to get FDA to fully approve the vaccines and “nudge” individuals who have been vaccine hesitant to get vaccinated.

Nurses Ask CDC to Reinstate Universal Masking Rule

National Nurses United, the largest union of registered nurses, is urging the CDC to reestablish its recommendation for everyone to wear masks in public, regardless of vaccination status, to prevent COVID-19 infections and variants from spreading.

"It should come as no surprise that cases are rising following the rapid reopening of many states and the removal of public health measures, including the CDC's May 13 guidance update that told vaccinated individuals they no longer needed to wear masks, observe physical distancing, avoid crowds, or get tested or isolate after an exposure, within only a few exceptions," the letter said. "The CDC's guidance failed to account for the possibility — which preliminary data from the United Kingdom and Israel now indicates is likely — of infection and transmission of the virus, especially variants of concern, by fully vaccinated individuals."

The union also urged the CDC to:

- Update guidance to fully recognize aerosol transmission.
- Track all COVID-19 infections among healthcare workers and other essential workers.
- Track all breakthrough infections, or cases that occur among fully vaccinated people, including mild and asymptomatic infections. Currently, the CDC only monitors breakthrough cases that lead to hospitalization or death.

Journal Review

Multisociety Statement on COVID-19 Vaccination as a Condition of Employment for Healthcare Personnel

Infect Control Hosp Epidemiol published online July 13, 2021

[DOI: 10.1017/ice.2021.322](https://doi.org/10.1017/ice.2021.322)

This consensus statement by the Society for Healthcare Epidemiology of America (SHEA) and The Society for Post-Acute and Long-Term Care Medicine (AMDA), The Association for Professionals in Epidemiology and Infection Control (APIC), the HIV Medicine Association (HIVMA), the Infectious Diseases Society of America (IDSA), the Pediatric Infectious Diseases Society (PIDS), and the Society of Infectious Diseases Pharmacists (SIDP), recommends that COVID-19 vaccination should be a condition of employment for all healthcare personnel.

Exemptions from this policy apply to those with medical contraindications to all COVID-19 vaccines available in the United States and other exemptions as specified by federal or state law. The consensus statement also supports COVID-19 vaccination of non-employees functioning at a healthcare facility (for example, students, contract workers, volunteers, etc.)

Rationale:

- The COVID-19 vaccines available in the US under the FDA EUA have high efficacy to prevent symptomatic COVID-19, even higher efficacy to prevent serious COVID-19 (i.e., hospitalizations and deaths), and high effectiveness against symptomatic and asymptomatic COVID-19 infection.
- The COVID-19 vaccines under FDA EUA have similar safety profiles to vaccines that are currently fully FDA-approved, shown by efficacy trials and effectiveness studies.
- Full vaccination against COVID-19 offers several advantages to patient and HCP safety: individual protection against COVID-19 infection; further protection for patients and HCP who are unable to receive COVID-19 vaccination or are not able to mount an adequate immune response; reduced risk of asymptomatic or pre-symptomatic transmission of SARS-CoV-2 between HCP, and from HCP to patients or patients to HCP; reduced risk of transmitting infection to household members and community contacts; increased protection for the healthcare workforce in the community setting.
- The COVID-19 vaccines appear to retain good effectiveness against currently circulating SARS-CoV-2 variants [including delta] against symptomatic illness and even higher effectiveness against severe disease.

The societies acknowledge that some information is not yet known. For example, additional data are needed on the duration of protection provided COVID-19 vaccines, and on the vaccines' effectiveness in immunocompromised persons. Data from randomized clinical trials in pregnancy are not available as of writing, although no maternal or fetal harm has yet been reported with over 120,000 pregnant people having received a COVID-19 vaccine. See next article.

The Case for Mandating COVID-19 Vaccines for Health Care Workers

Ann Intern Med published online July 13, 2021

[doi:10.7326/M21-2366](https://doi.org/10.7326/M21-2366)

The authors make the following points:

- The mortality rate for influenza is estimated to be 1 in 1000, whereas that for SARS-CoV-2 is closer to 1 in 100 to 250. Patients with COVID-19 are more likely to require hospital admission, have respiratory failure, and require prolonged intensive care than those with influenza.

- Vaccines save lives. Health care workers and other essential workers have higher rates of infection than people in other fields.
- Up to two thirds of cases of SARS-CoV-2 infection are attributable to asymptomatic and presymptomatic transmissions. Hospitals have undertaken considerable efforts to stop staff from working while sick, but these policies do not prevent staff with silent infections from coming to work and potentially infecting patients and colleagues. In some cases, staff-to-patient and staff-to-staff transmissions have led to large clusters. Universal masking diminishes this risk, but perfect adherence is not realistic and surgical masks are not perfectly protective. Vaccines, by contrast, provide constant protection without requiring reminders, persuasion, mask-fitting aids, or behavioral changes.
- The estimated effectiveness of influenza vaccines varies by season but generally ranges from 30% to 50%. The 2 messenger RNA vaccines for SARS-CoV-2, by contrast, are more than 90% effective.
- Vaccinating health care workers will help preserve workforce continuity. Workers with influenza are typically allowed to return to work 24 hours after their fever subsides. Staff with SARS-CoV-2 infection, however, are required to isolate for at least 10 days, even if their symptoms resolve well before then. Staff shortages have pushed some hospitals to cancel procedures, close units, and reduce elective admissions, thereby putting patients at risk due to deferred care.
- SARS-CoV-2 vaccines are safe and effective. Despite the enormous number of people who have now received SARS-CoV-2 vaccines, serious side effects have been exceedingly rare. The authors acknowledge that some life-threatening adverse effects and deaths have occurred, but the incidence of these complications is exceedingly small, is substantially lower than the risk for complications of COVID-19 and is far outweighed in their opinion by the likelihood of benefit to both health care workers and their patients.

Table. The Case for Mandating COVID-19 Vaccines for Health Care Workers: Comparison of Influenza Versus COVID-19

Effect	Influenza	COVID-19
Mortality	~1 in 1000	~4-10 in 1000
Number of people infected	Infects ~10% of the U.S. population each year	Infected ~30% of the U.S. population in 2020
Threat to patients	Nosocomial spread well documented but understudied	Nosocomial spread well documented but understudied
Impact on operations	Absorbed by routine operations	Unprecedented disruption of routine operations (e.g., masking, distancing, virtual meetings, visitor restrictions, testing requirements, attestations)
Time lost to work	Employees return to work 1 d after fever resolves	Mandatory absence of at least 10 d
Vaccine effectiveness	30%-50%	70% for adenovirus vector; 90%-95% for mRNA
Vaccine experience	~50% of adults get influenza vaccine each year	>65% of U.S. adults vaccinated thus far

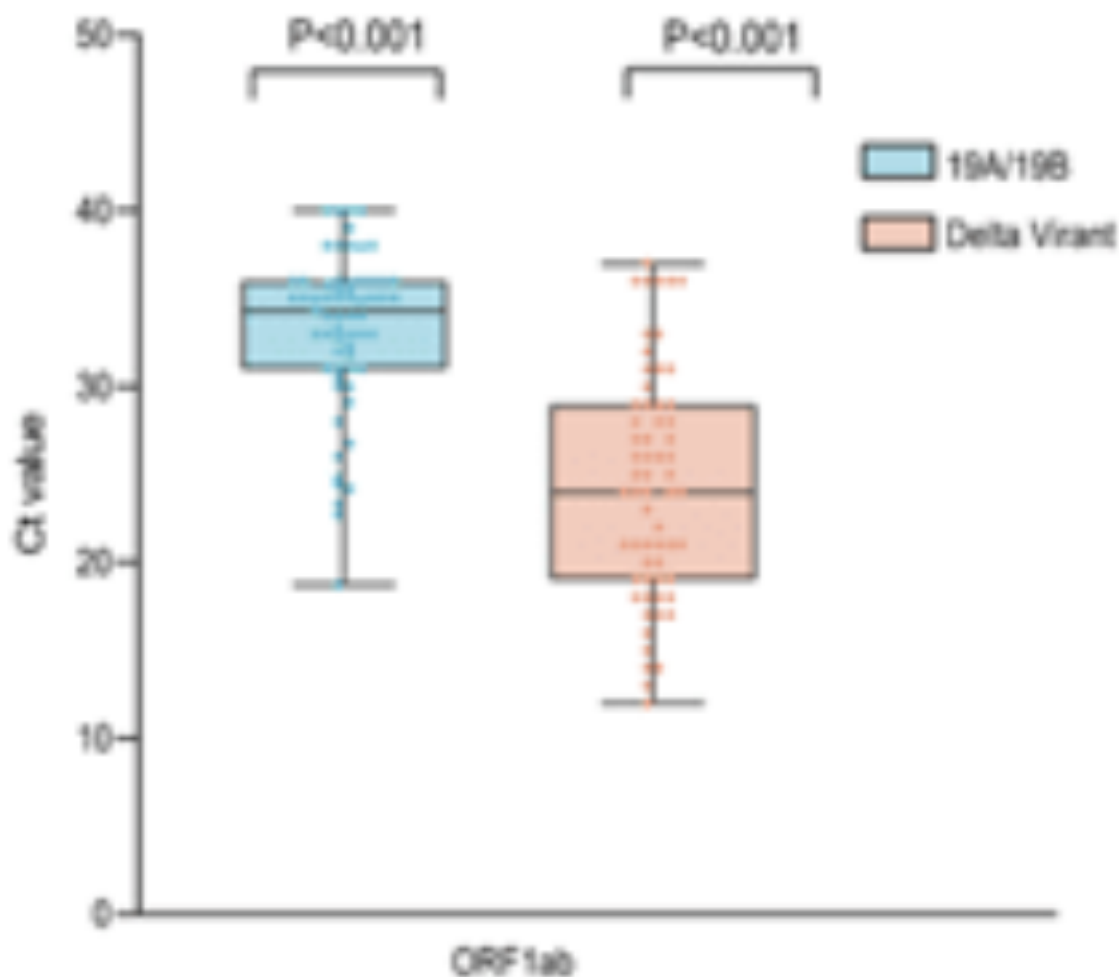
Comment: I think both publications make a compelling argument for vaccination of HCP. Many organizations contemplating mandating SARS-CoV-2 vaccines are reluctant to move forward while vaccines remain under emergency use authorization. As more safety data on the vaccines rapidly accumulate, however, there is every expectation of full approval from the FDA later this summer.

Viral Infection and Transmission in a Large Well-Traced Outbreak Caused by the Delta SARS-CoV-2 Variant

Genomic Epidemiol Virol published online July 2021 – suggested by Marion Kainer

The investigators report the first local transmission of the Delta SARS-CoV-2 variant in mainland China. All 167 infections could be traced back to the first index case. The investigation on daily sequential PCR testing of the quarantined subjects indicated the viral load of the first positive test of Delta infections was ~1000 times higher than that of the 19A/19B strains [wild type] infections back in the initial epidemic wave of 2020, suggesting the potential for faster viral replication rate and the potential for

higher transmissibility of the Delta variant at the early stage of the infection. The 126 high-quality sequencing data and reliable epidemiological data indicated some minor intra-host single nucleotide variants (iSNVs) could be transmitted between hosts and finally fixed in the virus population during the outbreak. Their results showed the time interval from the exposure to first PCR positive in the quarantined population (n=29) was 6.00 (IQR 5.00-8.00) days in the 2020 epidemic (peak at 5.61 days) and was 4.00 (IQR 3.00- 5.00) days in the 2021 (n=34) epidemic (peak at 3.71 days). They next evaluate the relative viral loads when SARS-CoV-2 viruses were firstly detected in hosts. Compared to the 19A/19B strains, the relative viral loads in the Delta variant infections (62 cases, Ct value 24.00 (IQR 19.00~29.00) for ORF1ab gene) were 1260 times higher than the 19A/19B strains infections (63 cases, Ct value 34.31 (IQR 31.00~36.00) for ORF1ab gene) on the day when viruses were first detected.

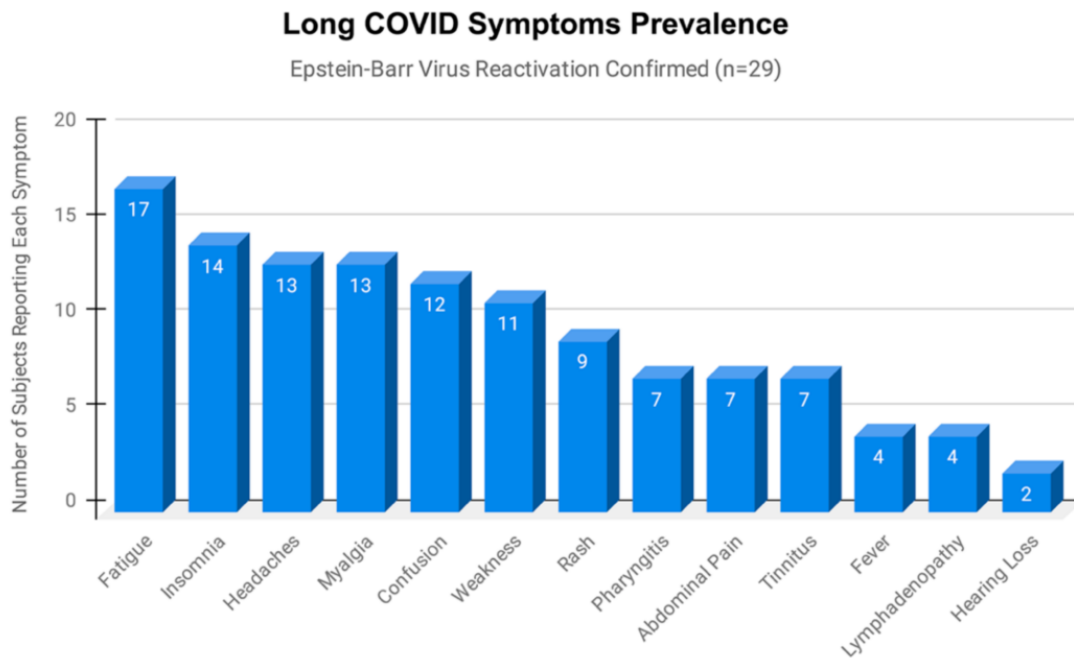


Comments: This study is very timely and supports the claim that the delta variant is more transmissible than the wild strain as well as the alpha variant. This also may explain some reports of limited exposures and transmission (< 15 minutes).

Investigation of Long COVID Prevalence and Its Relationship to Epstein-Barr Virus Reactivation

Their aim was to first determine long COVID prevalence in 185 randomly surveyed COVID-19 patients and, subsequently, to determine if there was an association between occurrence of long COVID symptoms and reactivation of Epstein-Barr virus (EBV) in 68 COVID-19 patients recruited from those surveyed.

They found the prevalence of long COVID symptoms to be 30.3% (56/185), which included 4 initially asymptomatic COVID-19 patients who later developed long COVID symptoms. Next, we found that 66.7% (20/30) of long COVID subjects versus 10% (2/20) of control subjects in our primary study group were positive for EBV reactivation based on positive titers for EBV early antigen-diffuse (EA-D) IgG or EBV viral capsid antigen (VCA) IgM. The difference was significant ($p < 0.001$, Fisher's exact test). A similar ratio was observed in a secondary group of 18 subjects 21-90 days after testing positive for COVID-19, indicating reactivation may occur soon after or concurrently with COVID-19 infection.



Comment: These findings suggest that many long COVID symptoms may not be a direct result of the SARS-CoV-2 virus but may be the result of COVID-19 inflammation-induced EBV reactivation. I am unclear if this is a true cause and effect, but worth exploring. An estimated 10% to 30% of all Covid-19 patients suffer from symptoms weeks and months after first getting the illness, including many young, previously healthy people whose initial Covid-19 cases were mild. Symptoms can include brain fog, fatigue, shortness of breath, racing heartbeat, and an inability to tolerate physical or mental exertion. Most adults—whether they have had Covid-19 or not—have latent viruses in their body they contracted years earlier. Among the most common are the herpes family of viruses. That includes EBV, HHV-6, HSV 1 & 2, and VZV. Such viruses can be reactivated at times by stress, including infections. In another review article, the investigators studied 200 long Covid-19 patients and did test for reactivated viruses, but often used additional tests to confirm a diagnosis. About 80% have evidence of reactivated EBV, with a smaller percentage also testing positive for a reactivated case of HHV-6. (Front. Microbiol.

| <https://doi.org/10.3389/fmicb.2021.698169>) Persistent viruses that activate under conditions of SARS-

CoV-2-driven immunosuppression or immune dysregulation might also infect new body sites and cell types, allowing them to drive new symptoms. Both herpesviruses and enteroviruses are neurotrophic pathogens, with the herpesvirus active life cycle relying on moving through nerves. In addition, the microbiome/virome dysbiosis can disrupt the homeostasis of host signaling pathways in a manner that might impact chronic disease development. The article in *Front Microbiol* concludes potential contributors to PASC (Post-acute sequelae of COVID-19) symptoms include consequences from acute SARS-CoV-2 injury to one or multiple organs, persistent reservoirs of SARS-CoV-2 in certain tissues, re-activation of neurotrophic pathogens such as herpesviruses under conditions of COVID-19 immune dysregulation, SARS-CoV-2 interactions with host microbiome/virome communities, clotting/coagulation issues, dysfunctional brainstem/vagus nerve signaling, ongoing activity of primed immune cells, and autoimmunity due to molecular mimicry between pathogen and host proteins. The individualized nature of PASC symptoms suggests that different therapeutic approaches may be required to best manage care for specific patients with the diagnosis. Currently, there are no pharmaceuticals licensed to specifically treat EBV reactivation. A more robust case-controlled study needs to be done since herpesviruses frequently reactivate with severe infection.