

COVID-19 NEUROLOGY SCIENTIFIC ADVISORY BOARD UPDATE



Editorial board

Amer Aboukasem MD, Ashhar Ali DO, Hassan Aboul Nour MD, Muhammad Affan MD, Owais Alsrouji MD, Gregory Barkley MD, Andrew Biondo DO, Arun Chandok MD, Song Chen MS, Omar Danoun MD, Elissa Fory MD, Shailaja Gaddam MD, Kavita Grover MD, Mohammed Ismail MD, Holly Lorigan DO, Ghada Mahmoud Mohamed MD, Daniel Newman MD, Neepa Patel MD, Phillip Ross MD, Bin Rui PhD, Naganand Sripathi MD, Aarushi Suneja MD, Vibhangini Wasade MD, Iram Zaman DO

Chairs: Gamaleldin Osman MD, Ahmad Riad Ramadan MD

The SAB Newsletters can now be found at: <https://www.henryford.com/hcp/academic/neurology-newsletter>

COVID-19 PANDEMIC: THE NUMBERS (as of 5/27/20, 10 am EST)

- **World:**¹ 5,618,829 confirmed cases. Total deaths: 351,146. Total recovered: 2,311,404.
- **US:**¹ 1,699,073 confirmed cases. Total deaths: 100,393; Total recovered: 490,130.
- **Michigan:**² 55,608 confirmed cases. Total deaths: 5,334 New cases in the last 24h: 504. New deaths in the last 24h: 68. Total recovered: 33,168.
- **Peak resource use in the United States was on April 17, 2020**
- **Evolution of the pandemic:**⁴ The US is in the plateau phase of the pandemic. The number of deaths increased doubled in the past 34 days.

HENRY FORD HEALTH SYSTEM AND COVID-19

- The “Will Hydroxychloroquine Impede or Prevent COVID-19” or WHIP-COVID trial continues to enroll. Our home-based trial studies the benefit of hydroxychloroquine as prophylaxis for front-line workers. **So far, close to 600 front-line workers have enrolled.** Visit <https://www.henryford.com/whip-covid-19> for more information on how to enroll.
- **SARS-CoV-2 testing:** We now have the capacity to test 1000 samples per day with a turnaround time of less than 24 hours. All tests are run in-house, no tests are being sent out.

- Convalescent Plasma (courtesy of Dr. Ileana Lopez-Plaza): Henry Ford Health System (HFHS) was one of the first Michigan health systems to participate in a convalescent plasma program. As of this date, **81 COVID-19 patients have been treated with convalescent plasma.** Convalescent plasma is the name given to the plasma of an individual that has been infected with the SARS-CoV-2 and then developed protecting antibodies against that specific infection. The premise for the current investigational treatment is the hope that this plasma infusion will provide some level of protection against the virus in patients with COVID-19. Currently, the FDA considers the convalescent plasma as an investigational product. Convalescent plasma donors must meet regular volunteer blood donor criteria in addition to specific criteria related to the COVID-19 infection. The plasma collection takes place at a blood center collection site. Plasma distribution is provided by the blood center.

BEST EXPOSURE PREVENTION PRACTICES

- CoV-2 may be aerosolized through talking, toileting and exhaling. Recent data from the University of Nebraska Medical Center showed that viral PCR was detected in air samples inside and outside isolation rooms even in the absence of coughing and across

all degrees of severity of patients' respiratory illnesses.⁵ It is however still unclear what proportion of these viral particles are transmitted via aerosolization and whether this route is clinically significant and leads to infection. These findings were relayed in a letter written by the National Academies Standing Committee on Emerging Infectious Diseases and 21st Century Health Threats to the White House on April 1, 2020.⁶

- CoV-2 was detected in aerosols for up to 3 hours, 4 hours on copper, 24 hours on cardboard and 2-3 days on plastic and stainless steel.⁷
- Continue to perform basic hygiene and apply droplet precautions (cover cough, wash hands for at least 20 sec, do not touch face/eyes, disinfect the surroundings with 60-95% alcohol, social distancing of at least 6 feet).⁸
- Before entering in contact with suspected or known COVID-19 infected patients, familiarize yourself with the donning and doffing procedures. Proper PPE includes: respirator or facemask (N95, P100; or PAPR), gloves, gown, and eye protection (e.g., reusable goggles or disposable face shield).⁸
- The CDC now recommends cloth face masks be used in public settings where it is not feasible to exercise appropriate social distancing such as grocery stores.⁹ Some experts remain skeptical of this recommendation due to the following points: 1) scarcity of PPE, 2) false sense of protection and relaxation of social distancing measures, 3) lack of solid scientific data regarding efficacy.¹⁰
- A case of possible vertical mother-to-fetus transmission was reported in China. Infection was confirmed in the symptomatic mother by PCRs. 23 days later, she was delivered by C-section. Two hours post-delivery, the baby had positive IgM and IgG titers but negative PCRs. Importantly, IgM does not cross the placenta so this was not transmitted immunity.¹¹
- Temporal Dynamics of SARS-COV2: A group from China investigated temporal dynamics of viral shedding in 94 patients with laboratory confirmed COVID-19 infection, modeled patterns of transmission among 77 transmission pairs and demonstrated that the highest viral load was present at the time of symptom onset, suggesting that infectiousness peaks at or immediately before symptom onset. However, 44% of patients got infected during index cases' presymptomatic phase,

highlighting the importance of social distancing even among healthy individuals.¹²

- A simulation out of Haifa, Israel provides insight into the imperfect protection conferred by standard PPEs. Using adult and pediatric manikins experiencing respiratory distress and coughing spells and having to be endotracheally intubated, the group was able to show that despite full standard PPE application, all team members (nurses and physicians) had aerosolized particles detected by fluorescence on their uncovered skin, hair and shoes, making the point that "the current recommendations for personal protective equipment may not fully prevent exposures in emergency department settings".¹³
- Montpellier University Hospital in France performed video study in operating rooms using two types of intubation: direct laryngoscopy (DL) using Macintosh blade, and video laryngoscopy (VL). They concluded that VL-intubation reduced risk of exposure to airway secretion and patient-to-provider transmission, in part because the provider can distance themselves better with VL than DL. Data worldwide shows that 80% of intubations in COVID-19 patients are being performed using VL.¹⁴
- **New! A case series published in The Lancet demonstrates PCR detection of SARS-CoV-2 in the breastmilk of an infected and symptomatic mother. Mother had tested positive for CoV-2 on day 8 and her breast milk was found to be positive on days 10-13. On day 11, the newborn tested positive for the virus (as well as RSV) and was admitted for icterus and breathing problems. It is unclear however whether the SARS-CoV-2 transmission was through breastfeeding or other forms of contact.**¹⁵

DISCOVERIES IN SARS-COV-2 PATHOGENICITY

- Similarly to CoV (SARS epidemic), CoV-2 uses the ACE2 receptor for entry into cells via its spike protein. ACE2 is expressed in human airway epithelia, lung parenchyma, vascular endothelium, kidney cells, and small intestine cells. Also expressed in some neuronal populations - cardiorespiratory centers in the brainstem, raphe nucleus, hypothalamus and motor cortex.
- CoV-2, like CoV, may gain access to the CNS via the olfactory receptor neurons (may explain anosmia common in these infections), spreading to the olfactory bulbs and then to other parts of the brain via

trans-synaptic transfer (e.g., thalamus, hypothalamus, brainstem). The medullary cardiorespiratory centers appear to be highly infected, which may play a role in central respiratory failure in these patients.¹⁶ Coronaviruses infect both neurons and glia. Neuroinfection, along with the systemic inflammatory response, leads to a breakdown of the blood-brain barrier and contributes to the activation of microglia and astroglia.¹⁷

- Mild disease in 81% of cases, severe disease (respiratory failure, ARDS, requiring oxygen +/- ventilatory support) in 14% cases, and critical disease (shock, MODS, MOSF) in 5% cases.¹⁸
- Cytokine storm: A hallmark of severe CoV-2 disease is the development of a potent “cytokine storm”. This is not unique to COVID-19 and has been described in MERS and SARS, both of which are closely related coronaviruses. IL-6, TNF and IL-1 β , all proinflammatory cytokines, are central in this process. The inflammatory state seen in COVID-19 is closely associated with a procoagulant state, caused by consumption of anticoagulant factors, overproduction of prothrombotic factors and endothelial injury. This leads to microthrombosis, DIC and venothrombotic events frequently seen in COVID-19+ patients and associated with a worse prognosis. Thrombin and Factor Xa have pro-inflammatory properties via activation of proteinase-activated receptors (PARs) and therefore their antagonists such as Factor Xa inhibitors (e.g., apixaban, rivaroxaban) and LMWH (e.g., enoxaparin) could not only have anticoagulant properties but anti-inflammatory ones as well.¹⁹
- Is there a CNS control of the immune system? The answer is yes. The autonomic system is an important modulator of the immune system. Dysregulating the autonomic system stimulates the inflammatory response of both innate and adaptive immune systems. There is strong evidence to support the direct sympathetic innervation of immune organs such as the spleen. Sympathetic activation causes splenic cytokine production (IL-1 β , IL-2, IL-5, IL-16 and TGF β 1), whereas vagus nerve stimulation quiets the immune response.²⁰ One wonders whether blocking the sympathetic outflow may halt or prevent the development of this exuberant inflammatory response.
- Evidence is mounting around the role of CoV-2 poisoning heme porphyrin. Using bioinformatic analysis, a group from China showed that some viral

proteins bind the porphyrin, while others bind the heme (iron-porphyrin complex) component of the hemoglobin beta-1 chain. This binding leads to a dissociation of iron to porphyrin and the hemoglobin loses its oxygen-carrying capacity. This is analogous to carbon monoxide poisoning. This phenomenon can lead to 1) profound hypoxia seen in some COVID-19 patients, 2) heme and iron accumulation which may be toxic to tissues and produce an inflammatory cascade, 3) increased synthesis of ferritin to chelate the excess iron being deposited in tissues and not being utilized for oxygen carrying purposes.²¹

- Endothelial injury: Autopsy studies have demonstrated the presence of viral inclusions in endothelial cells and evidence of inflammation involving endothelial cells of the lungs, heart, kidney and liver suggesting an important role for endothelial dysfunction the pathogenesis of COVID-related organ failure.²²
- Important clinical features of the disease:
 - A minority of patients will develop hypoxia and deteriorate very quickly, going from oxygen supplementation by oxygen to high flow nasal cannula to intubation within a few hours.
 - Initial CT chest made the right diagnosis in 96.1% of cases in one series.²³ Most common findings were ground glass opacities, consolidations, vascular enlargement, interlobular septal thickening, and air bronchogram sign.
 - 2-10% of COVID-19 presented with GI symptoms, such as diarrhea, abdominal pain, and vomiting in 2% to 10% of cases.²⁴
 - Elevation of several serum inflammatory markers-IL-6, ferritin, LDH, CRP, D-dimer, and triglycerides, indicating the presence of a potent cytokine storm and secondary hemophagocytic lymphohistiocytosis.
 - Neutrophil-to-lymphocyte ratio (NLR) of ≥ 3.13 predicts disease progression
 - Lymphopenia and thrombocytopenia
 - Myocardial injury: in one study of 416 patients admitted with COVID-19, 20% had evidence of cardiac injury as defined as elevated troponin.²¹ Patients with underlying cardiovascular disease and elevated troponin were found to have the highest mortality.²⁵ Autopsies have revealed infiltration of myocardium by interstitial mononuclear inflammatory cells, evidencing a myocarditis.²⁶ ARDS, myocarditis, sympathetic

hyperactivity, hypercoagulable state, and the cytokine storm all contribute to direct myocardial injury, mismatch myocardial oxygen supply/demand and plaque rupture, leading to increase in the risk of myocardial infarction, arrhythmias and heart failure.²⁷

- **New! A small series of lung autopsies from 7 patients who died from COVID-19-related respiratory failure was recently published in NEJM by a group in Hannover, Germany and Leuven, Belgium. These autopsies were compared to those of 7 patients who died from influenza A H1N1-related respiratory failure and 10 non-infected donors. The histological findings confirm the presence of diffuse alveolar hemorrhage (DAH) and infiltrative perivascular T-lymphocytes, both of which are common to COVID-19 and H1N1. However, the most distinctive features of COVID-19 lungs were 1) severe endothelial injury with presence of intracellular viruses and breakdown of basement membrane, 2) “widespread thrombosis, with microangiopathy and occlusion of alveolar capillaries”, and 3) angiogenesis, especially of the intussusceptive (non-sprouting) type, which is not a main characteristic of H1N1 infection. While this sample is small and needs to be validated by larger scale studies, it gives the important insight that pulmonary capillary thrombosis, endotheliitis and angiogenesis may be central in the pathophysiology of COVID-19-related respiratory failure.²⁸**

UPDATES ON SARS-COV2 TESTING

- Per the CDC,²⁹ priority for testing goes to 1) hospitalized patients with signs/symptoms compatible with COVID-19, 2) vulnerable patient populations (older adults, immunocompromised state, chronic medical conditions (e.g., HTN, DM, CKD, lung, heart disease), 3) HCP who had close contact with a COVID-19 suspect or positive patient within 14 days of symptom onset (*close contact= being within 6 feet for a prolonged period of time or direct contact with secretions of COVID-19 case, while not using recommended PPE*).
- **Methods for sample collection:** nasopharyngeal (NP) swab, tracheal aspirate/BAL (intubated patients, but increases exposure risk), sputum (induction not

recommended).³⁰ HFH has expanded testing sites to NP and tracheal aspirates in intubated patients. BALs are not being done at HFH due to the risk of aerosolization. A recent study, still in print, shows that saliva sampling may be superior than NP sampling. SARS-CoV-2 titers were higher and collection was less variable and more consistent in saliva compared with NP specimens.³¹

- New: A study from China reported PCR results in semen specimens among 38 patients with COVID-19 infection including 23 patients achieving clinical recovery and demonstrated that 6 (15.8%) patients had positive semen PCR including 2/23 (8.7%) patients achieving clinical recovery. However, sexual transmission cannot be confirmed based on these results as viral particles can be detected in semen in patients with other viral illnesses not known to be sexually transmitted. Nevertheless, if sexual transmission is to be proven, abstinence or condom use might then be considered part of preventative measures to halt spread of infection.³²
- rRT-PCR: Almost all diagnostic testing for CoV-2 is done using rRT-PCR. In the US, testing is performed by the CDC, hospital and public health laboratories.
 - On March 21, the FDA approved a point-of-care (POC) test by Cepheid with a turnaround time of 45 minutes.³³ Abbott has been granted emergency use authorization (EUA) by the FDA for its POC test that will detect CoV-2 in “as little as 5 min” and “negative results in 13 min”, making it the fastest POC test for the virus at this stage. The company claims they will produce 5 million tests per month.³⁴
 - PCR specificity is thought to be 100% (i.e., false positive rate ~0%) due to the specificity of the SARS-CoV-2 genome primer utilized. Sensitivity, however, varies based on the source of the specimen: lowest in pharyngeal swab (32%), nasal swab (63%), sputum (72%), highest in BAL (93%), in one study of 205 patients.³⁵
 - The virus can usually be isolated from the respiratory tract starting 1 week before to about 1 week after symptom onset (i.e., time of maximal infectivity). Beyond 7-8 days from symptom onset, it is unlikely that a patient remains infectious, unless they get reinfected.³⁶
 - In some cases, PCR was positive for as long as 6 weeks despite recovery. It is unlikely that these patients were infectious for as long as 6 weeks.

The correct interpretation is that a positive PCR means viral RNA detection but not necessarily viral viability. PCR positivity may persist beyond 6 weeks in stool and BAL. In one study, PCR remained positive in stool 4-11 days beyond NP sample.³⁷

- **Serology:** tests that detect IgM and IgG antibodies and provide information about the immune response of the host to the virus antigens.
 - IgM and IgG antibodies appear as early as 4 days from symptom onset and peak at 2-3 weeks. IgM usually disappears by week 7 whereas IgG persists well beyond week 7.³⁸ While IgM positivity indicates a recent or current infection, IgG positivity indicates recent or previous infection (or vaccinated status). Negative IgM and IgG antibodies does not guarantee that the patient is not infected as they could still be in the early phase before seroconversion (PCR is usually + during this time). Therefore, serological testing should not be used alone to diagnose active infection.
 - Specificity of the available ELISA IgM/IgG tests is roughly 95%. In one study, sensitivity of a single PCR was 52% but improved to 98.6% when combined with an anti-nucleocapsid (NC) IgM ELISA test. The NC protein is the most abundant protein in the SARS-CoV-2. Therefore, tests that detect antibodies directed against it have higher sensitivities but are not as specific due to cross-reactivity with SARS-CoV.³⁹
 - On April 2nd, the FDA approved antibody testing by Cellex which can provide results in 15 min.⁴⁰ So far, the FDA has issued four EUAs for serological tests and continues to evaluate their performance. It is important to remember that we still do not know the length of immunity imparted by positive antibodies or whether reinfection is possible.⁴¹
 - While antibody testing is not full proof at this time, it may become an important tool to transition people out of lockdown and allow them to join the workforce again. Several European countries, such as Italy, Germany and the UK, are planning nationwide antibody testing to determine when to reopen their economies and loosen social distancing policies.⁴² In LA county, USC researchers and public health officials are conducting antibody testing, so far showing that

the estimate of infected cases is “28 to 55 times higher than the (number) of confirmed cases at the beginning of the study in early April”.⁴³

- **Immunoassays:** monoclonal antibody tests that detect viral antigens such as the nucleocapsid (N) protein, spike protein of the virus or multiple antigens. Faster results (20-60 min) but longer to develop and less accurate than PCR.⁴⁴
- The FDA continues to warn the public against the marketing of at-home COVID-19 test kits.⁴⁵
- A South Korea hospital launched a phone-booth-style CoV-2 testing- a row of 4 negative-pressure, single-occupancy plastic booths under a tent outside the hospital. The patient gets inside the booth and a consultation takes place with a HCP who, from outside of the booth, can obtain samples via arm-length rubber gloves built into the plastic panel. Process takes about 7 min to complete and the booth is easy to disinfect.⁴⁶
- *Kinsa Health* smart thermometers are able to track fever across the US via a web-based app. Although it cannot discriminate fever from different etiologies, it can identify new clusters of fever, track fever curve and gauge the response to implemented measures such as social distancing. It was first created to track the spread of the flu and a million thermometers have been sold since the inception of the company.⁴⁷

SARS-COV2 NEUROLOGICAL SYNDROMES

- **Symptomatology:**
 - **CNS symptoms:**
 - **Stroke:** A case series of 5 COVID-19+ patients younger than 50 years old presenting to Mount Sinai Hospital in NYC over a two-week period was published in NEJM. 4/5 were males, age range was 33-49 and admission NIHSS range was 13-23. All 5 had large vessel occlusions (MCA, ICA, PCA territories). 3/5 had cardiovascular comorbidities (DM, HTN, HLP and one had a prior mild stroke). 3/5 had symptoms consistent with COVID-19. Only one presented within the IV-tPA window and received the thrombolytic. 3/5 had clot retrieval and one of them also had a stent placed in the MCA. 2/5 were treated with aspirin, one of them went from craniectomy, the patient who received the stent was placed on dual antiplatelet and the remaining 2 were

anticoagulated with full-dose apixaban. one patient was discharged home, 2 to rehab and the remaining 2 are still hospitalized at this time.⁴⁸

- A retrospective study from New York that 32/3556 (0.9%) patients had imaging-proven ischemic strokes. Patients with strokes in the setting of COVID-19 were more likely to have higher NIHSS and elevated D-Dimer value at presentation compared to contemporary controls and were more likely to be of younger age and have elevated troponin and ESR compared to historical controls. Mortality was higher among patients with strokes in the setting of COVID-19 (63.6%) compared to contemporary (9.3%) and historical (6.3%) controls.⁴⁹
- In one study, 24.8% of cases (dizziness and headache).⁵⁰ In another study of 221 patients at a single center in China, 5% cases had AIS, 0.5% CVST and 0.5% ICH.⁵¹ Ischemic and hemorrhagic strokes, impaired consciousness and muscle injury were more prevalent in patients with more severe respiratory disease. A case series from Careggi Hospital in Florence, Italy, mentions that out of 19 cases with LVO acute ischemic strokes, 10 had suspicious respiratory symptoms and 4 (21%) were found to be positive for SARS-CoV2. Out of 6 cases of aneurysmal SAH, 1 (16%) was positive for SARS-CoV2.⁵² A group from China reported three cases of ischemic stroke involving various territories associated with positive antiphospholipid antibodies, raising the possibility of a role for COVID19-infection related antiphospholipid syndrome in the pathomechanism of COVID-19 related thrombotic episodes. However, the baseline status of these antibodies is unclear in these patients and a causal relationship remains to be determined.⁵³ Another series from Italy reported 4 cases with ischemic strokes and 2 cases with hemorrhagic strokes. 5/6 patients had severe COVID pneumonia, while 4/6 patients had disturbed coagulation tests. Poor outcome was noted in the majority of patients as 4/6 patients died, 1 patient was

still in coma and 1 patient had severe neurological disability (mRS 4).⁵⁴

- A case of a 36 year old male with no significant past medical history who presented to the ED with a 2-day history of fever, headache, myalgias, cough and GI symptoms, tested negative for SARS-CoV-2 by NP swab. He was discharged home and presented again 4 days later with the same symptoms in addition to encephalopathy and drowsiness. Repeat PCR via swab was positive.. CTH revealed ICH, SAH and a thin SDH. No trauma reported. LP was not performed due to the mass effect. Despite a stable exam (GCS 14), the patient was taken for evacuation of the now chronic SDH on day 14 of hospitalization. The fluid was tested and was found to be positive for SARS-CoV-2. Article does not mention treatments received or the patient's outcome.⁵⁵
- **Seizures:** There is a single case report from Italy of focal SE as the initial presentation of COVID-19 infection in a 78-year-old lady with remote history of HSV encephalitis.⁵⁶ In another case series from China involving 304 patients with COVID-19 infection, only two patients exhibited seizure like phenomena. The first patient had bilateral body spasms, attributed to acute anxiety disorder, while the 2nd patient had myoclonic movements involving all extremities that were attributed to underlying electrolyte abnormalities. These movements resolved upon correction of underlying metabolic abnormalities. None had acute symptomatic seizures or SE. However, EEG was not obtained in any of the studied patients.⁵⁷
- A series from New York reported EEG findings in 28 patients with suspected COVID including 22 with positive COVID PCR. Epileptiform discharges were seen in 40.9% of COVID+ve patients compared to 16.7% of COVID-ve patients. No electrographic seizures were detected.⁵⁸
- Multiple other case reports of new onset seizure and new onset SE as well as recurrent seizure in patients with Epilepsy have been published. A study reported two

cases of de novo status epilepticus (SE) in patients with COVID19 and convulsive SE was the initial presentation in one patient and in the second patient Myoclonic SE accompanied pneumonia and respiratory failure.⁵⁹ One pediatric series looking at Ultrasound findings reported one patient aged 15 out of 10 patients to have seizures.⁶⁰ One patient was reported to develop seizures and demyelinating lesions in the brain with a history of anterior communicating aneurysm surgically treated 20 years before.⁶¹ A case of a 41 year-old woman presented with new-onset seizures was found to have meningoencephalitis associated with COVID19.⁶² One case report described new onset seizures after COVID19 pneumonia and respiratory failure in a 71 year old man.⁶³

- **Encephalopathy/encephalitis:** Henry Ford Hospital's Radiology Department published the first reported case of hemorrhagic acute necrotizing encephalopathy (ANE) in a COVID-19 patient, a 58 year-old female who presented with altered mental status in addition to URI symptoms. Virology studies were negative for influenza and other viruses. CSF could not be tested for CoV-2. Non-contrast head CT revealed bithalamic hypoattenuating lesions while brain MRI revealed T2 FLAIR hyperintense signal with internal hemorrhage in the bilateral thalami and medial temporal lobes. Vessels were patent on CT angiogram and CT venogram.⁶⁴ The patient was discharged to rehab after 22 days of hospitalization in improved condition. **There is another report of hemorrhagic ANE in a 59 year-old female with past medical of transfusion-dependent aplastic anemia who presented with altered mental status and seizures 10 days after onset of headache, cough and fever. She tested positive for SARS-CoV-2. A head CT showed diffuse brainstem edema. Her mental status declined to the point that she had to be intubated for airway protection. Brain MRI revealed "symmetrical hemorrhagic lesions in the brain stem, amygdalae, putamina, and thalamic nuclei". Patient did not respond**

to a course of steroids and she eventually expired on day 8 of admission.⁶⁵ A group from Japan reported the first case of CSF-proven SARS-COV2 meningo-encephalitis in a 24-year-old gentleman presenting with new-onset seizure and altered consciousness preceded by an 8-day history of fever, malaise and sore throat. CSF PCR was positive for SARS-COV2 while nasopharyngeal swab PCR was negative. MRI showed evidence of restricted diffusion along the wall of the inferior horn of the right lateral ventricle as well as T2 FLAIR hyperintense signal involving right mesial temporal structures.⁶⁶

- A group from Italy reported a case of steroid-responsive encephalitis in a 60 year-old male presenting with mild respiratory symptoms and akinetic mutism. CSF demonstrated mild lymphocytic pleocytosis and hyperproteinorrhachia but CSF PCR for SARS-COV2 was negative, while MRI was normal and EEG demonstrated mild generalized slowing. Progressive clinical and CSF improvement was seen after completion of 5-day IV pulse steroid course.⁶⁷
- **Demyelinating lesions:** A report from Italy of a 54 year-old woman with a remote history of anterior communicating aneurysm rupture who underwent presumably clipping, was found unconscious at home and tested positive for COVID-19 on arrival. Of note, she reported anosmia and ageusia for a few days prior to presentation. Initial CT was normal but CXR showed "interstitial pneumonia". A few hours later, she went into hypoxic respiratory failure and was intubated. She later developed two seizures captured on EEG, emanating from the side of her craniotomy, for which she was treated with combination AEDs. MRI brain revealed periventricular and C/T spine T2/FLAIR hyperintense yet non-enhancing lesions, consistent with demyelination. CSF was essentially unremarkable and negative for neurotropic viruses (unspecified which ones were tested) and SARS-CoV-2. Paper does not mention OCB or IgG index. Patient received HCQ, antiviral (not specified) when

COVID was diagnosed and high dose dexamethasone after lesion discovery. She received a tracheostomy and was transferred to rehab without sensory or motor deficits on day 12. This case highlights the possible local neuroinflammatory response that results from the more systemic cytokine storm and sHLH. It is unclear from the report if the patient has a history of seizure (from her prior aneurysmal rupture). It remains questionable whether this is a viral encephalitis or a viral-triggered neuroinflammatory response.⁶⁸

- In a series of 58 consecutive COVID-19-confirmed patients with ARDS admitted to 2 ICUs in Strasbourg, France, neurological symptoms were found in 14% of cases on admission, and in 67% after sedation and paralytics were weaned. The most common symptom was encephalopathy (69%), closely followed by corticospinal signs (67%) and dysexecutiveness (36%). All 11 patients who were imaged with MRI had bifrontal hypoperfusion and 62% of them had leptomeningeal enhancement. 2/11 patients were found to have small acute strokes. CSF was obtained in 7 patients, none of them positive for CoV-2 PCR. No cells were present in any of the samples and 2 patients had elevated protein levels with only 1 having elevated IgG index.⁶⁹
- **Psychiatric symptoms:** A meta-analysis and systematic review published by Rogers and colleagues in *The Lancet* reviewed the psychiatric and neuropsychiatric manifestations of SARS, MERS and COVID-19. Much like in the previous pandemics, confusion (65%), agitation (69%), altered consciousness (21%) have been reported in the acute phase of COVID-19. Depression, anxiety, insomnia, fatigue and PTSD were commonly reported during the recovery of patients with SARS and MERS, yet not with any significant frequency in COVID-19 so far. Mania and psychosis were uncommon in post SARS and MERS and usually associated with the use of steroids. This study suggests that, similarly to the previous coronavirus pandemics, more neuropsychiatric disorders may be seen in the post-infectious COVID-19 state.⁷⁰
- **Peripheral symptoms:**
 - In one study, 8.9% of patients (hypogeusia, hyposmia, neuralgia).⁵⁰ Myalgias were found in 10.7% of cases.
 - Sudden olfactory dysfunction (OD) is recognized as a marker for COVID-19. Anosmia and dysgeusia often happen in mild or asymptomatic cases. In one report from Iran, 50 of 60 patients hospitalized with COVID-19 had OD.⁷¹ It is believed that this sensory disturbance is primarily an olfactory impairment rather than a gustatory one since detecting flavor depends on retronasal olfaction. A proposed approach for the assessment and management of COVID-19-related OD, published in JAMA, recommends a full otolaryngologic examination which includes a three-pass nasendoscopy when appropriate PPE is available. It also recommends CT to assess the paranasal sinuses, and MRI brain to examine brain and olfactory tracts.⁷² A psychophysical assessment using validated tests of odorants/tastants should complement the subjective assessment. Treatment may be needed in persistent (>2 weeks) OD. This includes olfactory training by sniffing specific odorants such as rose, lemon, cloves, and eucalyptus, at least twice daily for at least 3 months. Other promising therapies which work in post-infectious OD include intranasal vitamin A and systemic omega-3 but have not been tested in COVID-19 specifically. Corticosteroids, on the other hand, whether oral or intranasal, are not recommended due to lacking evidence of benefit and potential harm.
 - Generalized muscle aching, pain and fatigue are known to be a part of a viral symptom complex. However, rhabdomyolysis has not been commonly reported. Jin and Tong reported a case who developed rhabdomyolysis during the course of infection. The patient presented with fever and respiratory symptoms initially with normal CPK levels. Nine days into hospitalization, he developed lower extremity weakness and pain and was found to have markedly elevated CPK, myoglobin and LDH. Over the

next few days, with treatment, his muscle pain and fatigue improved.⁷³

- A case report of MRI-proven myositis associated with COVID-19 infection from France was published in *Annals of the Rheumatic diseases*. The patient initially presented with generalized muscle weakness with no fever, became febrile on day 4, required oxygen supplementation on day 7 of presentation and remained in critical condition at the time of publication.⁷⁴
- *Lancet Neurology* published the first known case of Guillain-Barre syndrome (GBS) in a COVID-19 patient. A 61 year-old female from Wuhan presented with ascending bilateral lower extremity weakness without initial fever, respiratory or GI symptoms. LP showed elevated protein and normal cells. EMG showed absent F-waves. All these findings are consistent with early findings of GBS. Patient received an IVIG course. 8 days later, she developed a fever and a dry cough, and tested positive for CoV-2. She was treated with arbidol, lopinavir, and ritonavir. She was discharged on day 30 with full strength and return of reflexes.⁷⁵
- In *Neurology*, a group in Spain reported two cases of Miller Fisher syndrome (MFS) and polyneuritis cranialis, respectively. The first patient, a 50 year-old man developed the cardinal features of MFS (ataxia, areflexia and ophthalmoparesis) 5 days after the onset of flu-like illness. He was found to have positive GD1b antibodies and albuminocytologic dissociation. He was treated with IVIG for 5 days on the fifth day of his neurological symptoms, resulting in complete recovery, save for residual anosmia and ageusia. The second patient, a 39 year-old man presented with bilateral abducens palsies, ageusia and areflexia, 3 days after diarrhea and fever. While albuminocytologic dissociation was present, anti-ganglioside antibodies testing was not performed. Patient was treated with acetaminophen and made a complete recovery.⁷⁶
- Three hospitals in Northern Italy reported a series of 5 COVID-19 cases who presented

with GBS symptoms 5-10 days after onset of respiratory symptoms. Four had paraparesis progressing to tetraparesis/plegia and 1 had facial diplegia. Antiganglioside antibodies were negative in all tested patients. Albuminocytological dissociation was demonstrated in 3/5 patients. CSF was negative for CoV-2 PCR in all patients. Three had an axonal variant whereas 2 had demyelinating features on EMG. All received IVIG, one had plasmapheresis in addition. At 4 weeks, 2 patients were still mechanically ventilated, 1 was discharged and 2 were undergoing physical rehabilitation.⁷⁷

- Arnaud et. al, report of a 64 y.o. man who presented to a hospital outside of Paris, France with a severe case of COVID-19. He was treated with Cefotaxime, Azithromycin and Hydroxychloroquine and discharged. He returned to the hospital with rapidly progressive lower extremity weakness. His exam showed flaccid paraparesis, areflexia, and a length dependent neuropathy in the lower extremities. CSF showed an albuminocytologic dissociation with no pleocytosis. Otherwise, an extensive laboratory workup was negative. EMG showed classic demyelinating features including conduction block meeting criteria for GBS. He received IVIG and responded well. This represents another case of GBS suggestive of an autoimmune cross-reactivity response to Covid-19, however, antibodies to SARS-CoV-2 are not currently available.⁷⁸
- **A case of isolated facial nerve palsy in a previously healthy 27 year-old male was reported in *Neurology*. Patient had recently come back from Spain. He was admitted to a hospital in Singapore with flu-like symptoms and unilateral throbbing headache for 4 days but no clinical evidence of meningitis. His NP swab PCR was positive for SARS-CoV-2. On day 6 from symptom onset, he developed a left peripheral facial weakness. CSF was non-inflammatory and PCRs for SARS-CoV-2 and other viruses were negative. MRI revealed contrast enhancement of the left facial nerve. He**

was treated with prednisone, valacyclovir and lopinavir/ritonavir. He became undetectable on repeat testing by end of week 2.⁷⁹

- **Movement disorders: New! This *Neurology* report is the first one on myoclonus in patients with SARS-CoV-2 infection. Three patients admitted to a Madrid hospital and diagnosed with SARS-CoV-2 developed generalized myoclonus in the setting of respiratory illness despite not having experienced prolonged hypoxia or respiratory arrest. The patients were two males, 63 and 76 year old, and one 88 year-old woman. They developed generalized myoclonus predominantly in nasopharyngeal, facial and upper limb areas. These myoclonic jerks had both positive and negative elements and were exquisitely stimulus-dependent with exaggerated startle response. All three patients had anosmia, fever and dyspnea. 2/3 had lab confirmation of SARS-CoV-2, whereas the last patient was not tested and was diagnosed on clinical and radiographic grounds. CSF was reported on one patient and found to be normal. EEG and brain imaging on all 3 patients were unremarkable. All 3 received methylprednisolone pulse treatment with variable clinical responses. One patient also received a course of plasmapheresis. The authors hypothesized that this manifestation is likely a post-inflammatory complication but could not rule out a direct neuroinvasive process.⁸⁰**
- **Laboratory findings:** Patients with CNS symptoms were more likely to have lower lymphocyte and platelet counts, and elevated BUN levels. There were no characteristic laboratory findings in patients with PNS symptoms. Patients with muscle injury had higher neutrophil counts, lower lymphocyte counts and higher CRP levels and D-dimer levels as well as evidence of multiorgan system failure.⁵⁰
- **Neuroimaging or neuroelectrophysiological characteristics:** nothing specific has been described in COVID-19 patients yet.
- **Pediatric population:**
 - Children are not completely immune to infection, but infection is usually less severe. One study from New York demonstrated the age-dependent nature of ACE2 gene representation in nasal epithelial cells with lower ACE2 gene expression among younger children.⁸¹ 5.9% of children with COVID confirmed or suspected infection had severe to critical presentation in one retrospective study from China including 731 children with confirmed and 1412 suspected COVID infections. Infants in particular were more likely to have severe symptoms than older children.⁸² A systematic review including 18 studies of 1065 pediatric cases demonstrated that the majority of children present with mild symptoms or no symptoms at all. Only 1 patient (a 13-month old infant) had severe infection. No deaths were reported.⁸³ An additional case report published in NEJM not included in the systematic review described severe COVID-19 infection in a 3-week old boy.⁸⁴
 - A series from France reported that 4/5 infants <3 months old with COVID-19 infections had neurological manifestations including axial hypotonia, drowsiness and moaning sounds or both upon presentation. CSF analysis was unremarkable and CSF SARS-COV2 PCR was negative. Prognosis was favorable as patients were discharged 1-3 days after admission.⁸⁵
 - A multi-center case series published in JAMA pediatrics reported 48 children with COVID-19 who were admitted to PICU. 83% of patients had pre-existing comorbidities. 11 (23%) patients had organ failure involving ≥ 2 organs. At the time of follow up, 2 (4%) patients died, and 15 (31%) were still hospitalized; 3 (6%) of those were ventilator dependent and 1 (2%) required ECMO.⁸⁶
 - Pediatric multi-system inflammatory syndrome: There has been 1 published case report from California of severe inflammatory syndrome resembling Kawasaki disease or toxic shock syndrome in association with COVID-19 improving with IVIG and high dose ASA.⁸⁷ Subsequently, NY Governor Andrew Cuomo reported that at least 100 cases in NY involving children aged 5-14 were being investigated for the same syndrome; three out of which have died so far.⁸⁸ One series from Italy reported 30-fold increase in the number of Kawasaki syndrome-like illness during the COVID-19

outbreak. Cardiac complications were more common among children developing the syndrome after COVID-19 infection compared to historical controls.⁸⁹ The UK pediatric intensive care society also released a statement reporting an increase in the number of reported cases in the UK with similar presentation.⁹⁰

- Despite the concern among many practitioners about the increased risk for severe COVID-19 infections among chronically immunosuppressed patients, a review of pediatric hepatic transplant patients from Bergamo, Italy did not show an increase in COVID-19 severe infections as would have been expected. 3/200 patients being followed there, tested positive for SARS-CoV2 infection, however, none developed pulmonary disease. The authors felt that it is likely that the children are asymptomatic carriers of the infection, despite their suppressed immune status.⁹¹

CARING FOR THE NEUROLOGICAL PATIENTS INFECTED WITH COVID-19

● Stroke:

- Cardiovascular comorbidities are prevalent in COVID-19 patients, similarly to SARS and MERS. These comorbidities increase the risk of mortality and morbidity from the infection.
- With ACE2 serving as the portal for infection, the role of ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB) requires further investigation. A small study from China demonstrated markedly elevated levels of serum angiotensin II in 12 patients with COVID-19 infection and its correlation with increased viral load as well as the severity of lung injury, suggesting a possible beneficial role of ACEIs and ARBs in patients with COVID-19 infection.⁹²
- Furthermore, a multi-center retrospective trial from China including 1128 patients with COVID-19 infection which included 188 patients taking ACEi/ARB demonstrated reduced COVID-19 mortality risk in patients receiving ACEi/ARB compared to non-ACEi/ARB group (3.7% vs 9.8%, P=0.01. Further subgroup analysis demonstrated that ACEi/ARB use was associated with reduced mortality risk compared to the use of other anti-HTN therapies in HTN patients.⁹³ Another multicenter observational

study from 169 hospitals led by Brigham and Women's hospital involving 8910 patients with COVID-19 infection demonstrated that ACEi use was associated with mortality reduction (OR 0.33; 95% CI 0.2-0.54).⁹⁴ Authors advised taking these results with extreme caution given the non-randomized nature of the trial. The American Heart Association recommends at this point continuing ACEi and ARB medications if clinically indicated.⁹⁵ In a study of 187 patients hospitalized with COVID-19, use of ACEi and ARB were not associated with increased mortality, even in the group of patients with higher cardiac injury.⁹⁶

- The extent to which a community outbreak of infection like COVID-19 stresses other parts of the healthcare system is largely unknown. The question is whether our time metrics for tPA and thrombectomy will be affected by the suspected or confirmed infectious status of the patient. A study comparing timeline in STEMI patients at a hospital in Hong Kong showed numerically longer median times in all components when compared with historical data from the prior year. The largest time difference was in the time from symptom onset to first medical contact.⁹⁷
- COVID-19 pandemic poses a unique challenge in achieving timely treatment of acute stroke patients with thrombolytics and thrombectomy. **One study from a large data platform from 280 hospitals in China reported 40% drop in stroke admissions and 25% drop in thrombolysis and thrombectomy cases during COVID outbreak. The most common reasons for reduced admissions and delays to presentation were lack of stroke knowledge among patients and caregivers, lack of proper transportation and fear of getting infected.⁹⁸ Similarly, a comprehensive stroke center in Barcelona reported 23% reduction in stroke admissions when compared with a similar timeline a year ago and 24% drop in thrombectomies, despite a more than 300% increase in all EMS activations during study defined COVID 19 period.⁹⁹ Another report from Hong Kong reported about 1 hour delay from onset to hospital presentation during pandemic and significantly lower number of patients presenting to hospital within 4.5 hours from onset.¹⁰⁰ These data highlight the**

importance of public awareness and education for time sensitive medical emergencies like stroke and also highlight the importance of faster and efficient screening process.

- Similarly, with the current strain imposed by the pandemic on staffing beds and other resources, it will be important to study the impact this will have on triaging and disposition of patients from the ED.
- The Society of Neuro-interventional Surgeons released a guideline statement recommending screening for fever and respiratory symptoms in all patients undergoing mechanical thrombectomy and having a low threshold for intubation prior to transport to the angiography suite.¹⁰¹
- AHA/ AHA stroke council leadership published temporary emergency guidance of stroke centers in the US. This document highlighted the challenges which included usage of PPE and availability of hospital beds, healthcare personnel. This guidance recommends treating stroke patients appropriately, encouraging conserving PPE and using telemedicine services (televideo or telephone). Most importantly, it highlighted the importance of teamwork for delivery of care.¹⁰²
- For acute management of stroke patients, a concept of “protected stroke code” PCS is suggested. A pre-code screening based on information from pre-notification (infection screen, close contact with infectious person and travel history) and patients’ history and examination (no or positive infection screen, patient unable to communicate or depressed level of consciousness) determines if a PCS is required or not. The cornerstone of PCS is appropriate use of PPE. All PCS are considered to be droplet and contact precautions. This requires a full-sleeved gown, surgical mask, eye protection (face shield and/or goggles), and gloves. Head covering is currently optional in some protocols. Precautions are upgraded to include airborne precautions, using N95 respirator when there is an aerosolizing procedure. A surgical mask should be placed on non-intubated patients all the time.¹⁰³
- Recently proposed recommendations for management of large vessel occlusion from

Cincinnati was published and highlighted the importance of maintaining safety for health personnel. To preserve hospital resources during this crisis, patients most likely to benefit from thrombectomy, should be prioritized based on AHA/ASA guidelines.¹⁰⁴

- Guidance statement from SVIN also highlighted several aspects of thrombectomy care. The statement suggested to obtain CT chest with initial stroke imaging for patients with positive pulmonary symptoms. An approach of direct transfer to angiography suite should be considered for patients with stroke symptoms onset within 24 h, who are transferred from other hospitals with time from last neuroimaging within 2 h and ASPECTS ≥ 7 . Clinical-core mismatch on ASPECT scores (6-10) on CT overlaps with clinical core mismatch by CT perfusion or MRI using DAWN criteria, this can be used as a substitute for patients in late window and mere absence of advance imaging should not preclude from patients getting thrombectomy.¹⁰⁵
- Stroke teams are posed with several challenges to ensure time-sensitive acute therapies. In Veneto (Italy) they implemented a protocol for evaluating COVID positive and suspected patients in a “hot spot” (a pre-triage unit outside ER) and utilized mobile CT units outside ER to perform CT, CTA and CT perfusion studies and triaged acute stroke patients accordingly to keep stroke unit COVID free.¹⁰⁶
- **Epilepsy:**
 - Animal and human studies have demonstrated the neuro-invasive potential of SARS-COV as well as coronavirus strains including HCoV-OC43 with preferential involvement of the thalamus and brainstem.¹⁰⁷⁻¹⁰⁹
 - So far, there is no evidence to suggest increased predisposition for acquiring COVID-19 among patients with epilepsy. However, COVID infection can possibly increase risk for breakthrough seizure in a similar fashion to other febrile illnesses. Therefore, the CDC lists epilepsy patients among high risk conditions for COVID.¹¹⁰ Patients with epilepsy syndromes known to be susceptible to febrile illnesses such as Dravet Syndrome and genetic epilepsy with febrile seizures plus (GEFS+) are likely to be particularly

at increased risk for breakthrough seizures or increased seizure frequency in the setting of COVID-19 infection.¹¹¹ Consensus recommendations emphasized administering care at home as much as possible instead of health care facilities to avoid exposure, minimizing seizure exacerbation through adherence, and ensuring a regular supply of medication and rescue therapies.¹¹²

- A survey in Spain assessing seizure or behavioral changes among patients with genetic epilepsies based on caregiver responses to provided questionnaires demonstrated that 39/277 (14%) patients had increase in seizure frequency, while 87/277 (30.3%) patients had behavioral changes. Multivariate logistic regression revealed association of seizure increase with age and difficulty finding anti-seizure medications (ASMs), while type of epilepsy, living in a home without a terrace or a yard and caregiver's anxiety were associated with changes in behavior.¹¹³
- The American Epilepsy Society released a statement recommending the prescriptions be refilled 1 week in advance for 30-day refills and 2 weeks in advance for 90-day refills.¹¹⁴ CMS has made healthcare plans more flexible which included removing prior authorization requirements, waiving prescription refill limits, allowing mail delivery of prescription medications and supporting tele visits.¹¹⁵
- Prescribers are advised to review drug interaction profiles of medications currently used for treatment of COVID-19 such as hydroxychloroquine with seizure medications and use caution when prescribing along with hepatically metabolized or hepatotoxic ASMs.¹¹⁶ A list of the known drug interactions between ASMs and drugs used for COVID-19 treatment is available on the ILAE website as a useful reference for prescribing clinicians and clinical pharmacists.¹¹⁷

- **Multiple sclerosis and demyelinating diseases:**

- It is important here to distinguish between immunosuppressive and immunomodulatory DMTs. While it is usually ok to continue immunomodulatory DMTs including IFNs, glatiramer acetate, teriflunomide and dimethyl

fumarate, patients on cell depleting therapies including alemtuzumab, ocrelizumab and cladribine are at increased risk for severe infections including COVID-19 infections. A series from Italy demonstrated that among 232 patients with MS who developed symptoms and signs suggestive of COVID including 57 patients with positive COVID PCR, the majority of patients (223 (96%)) had mild disease, while 4 (2%) patients had severe disease and 6 (3%) patients had critical disease. Among those patients with critical disease, 1 patient recovered while 5 patients died. These data suggest that it is likely safe to continue DMDs in the majority of patients with MS¹¹⁸. National MS Society recommends that the decision of continuing or discontinuing DMTs be taken on an individualized basis, taking into account the higher risk of infections associated with cell depleting agents and the higher risk of worsening disability among medications including natalizumab and fingolimod.¹¹⁹

- **Neuromuscular disorders**

- There is one small case series of 5 patients from Brigham and Women's hospital with COVID-19 and comorbid MG. Clinical course and outcome were variable as 2 patients were intubated for hypoxemic respiratory failure and 1 patient required supplemental oxygen therapy, while 1 patient with previously stable MG developed myasthenic exacerbation. One patient received tocilizumab for severe COVID-19 and was successfully extubated and two patients received IVIG for MG with no thrombotic complications.¹¹⁹
- A group of International MG experts formed MG/COVID-19 work group which recently released a guideline statement which recommends continuing existing medications for patients who are already on them.¹²⁰ They also stated that symptomatic therapies such as pyridostigmine and 3,4 diaminopyridine do not increase the risk for infection and thus should be continued as well. As for patients receiving infusion therapies requiring transport to hospitals or infusion centers, the decision on whether to continue the infusion therapy or not should be individualized based on the regional incidence of COVID-19 and the risk vs benefit of treatment for

the individual patient. They also state that there is no evidence of increased risk for COVID infection with eculizumab therapy. There is also no evidence of any increased risk of COVID infection from PLEX or IVIG therapy, but the risk derived from visits to healthcare facilities should be considered.

- The decision to switch patients to an alternative immunosuppressive therapy should take into account the presence of other comorbid conditions and the risk of viral infection should be balanced against the risk of developing MG crisis when discussing initiating Rituximab therapy. Blood draws should be done judiciously in order to avoid unnecessary hospital visits and patients on immunosuppressive therapies are advised to practice extra cautious social isolation.¹²⁰
- The AANEM has established guidance for triaging electrodiagnostic studies during COVID-19. Urgent electrodiagnostic testing is appropriate for those neuromuscular conditions presenting with acute, rapidly progressive neurological decline and would be necessary to determine treatment options. Possibly urgent are those that after carefully reviewing the case, an EMG is necessary to make a diagnosis and escalate treatment to prevent the development of a poor patient outcome. Non-urgent are those cases that are mild, chronic, or when electrodiagnostic testing is not necessary to make a diagnosis or determine treatment. These can be deferred to when conditions are safe for practice.¹²¹
- Guidon and Amato reviewed the potential COVID-19 has on neuromuscular disorders. An acquired inflammatory neuropathy and/or myopathy, exacerbating or revealing an unrecognized underlying neuromuscular disorder, as well as, developing a critical illness neuropathy or myopathy are possible. Those immunocompromised and/or on disease modifying drugs are at increased risk of contracting COVID-19, other infections, and more severe disease. However, this is not expected in patients treated with immunoglobulin therapy, complement inhibitors, plasma exchange, or Fc receptor antagonists. Most patients on immunotherapy should continue treatment. Risks vs. benefits of stopping treatment should be

discussed, and abrupt cessation of immunosuppressive medications is not advised.¹²²

- **Spinal muscular atrophy (SMA): Onasemnogene abeparvovec-xioi gene transfer is a one-time IV infusion after which the patient goes on corticosteroids. This treatment has shown better outcomes in patients with SMA and therefore the recommendation is that treatment should not be interrupted, that infants have urgent testing completed and that treatment is started without delay. It is also felt that the assessments that are required by insurance should be deferred and treatment continued.**¹²³
- **Duchenne, Becker, and other muscular dystrophies: It is suspected that those with Duchenne and Becker muscular dystrophy (DBMD) are at increased risk to have severe manifestations if infected by COVID-19. The expert recommendations are the following:**¹²⁴
 - **Corticosteroid treatment should continue in those who are taking it.**
 - **Exon-skipping agents can be continued but a discussion should be had with the specialist in regards to whether the risk outweighs the benefit.**
 - **Home infusion is encouraged and it is felt that delays in some monitoring may be warranted for safety/decrease exposure to patients.**
 - **If patients become symptomatic/ill then they should discuss with the specialist (caution with regards to precipitating adrenal crisis if steroids are abruptly discontinued).**
 - **Angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers for cardiomyopathy (prophylaxis or treatment) should be continued.**
 - **If patients become symptomatic and need to go to the ER, it is recommended that they bring their home ventilatory support.**
 - **Neuromuscular blockade is to be avoided if intubation is needed.**
 - **Hydroxychloroquine is not recommended.**

- **Movement disorders**

- **Parkinson's disease: New: One study from India involving 100 PD patients reported worsening or new motor or non-motor symptoms of PD which were reported by 10% of patients and 11% of caregivers during the COVID-19 epidemic.¹²⁵ Another study from Egypt involving 38 PD patients reported worsening of depression, anxiety and QOL scores in most PD patients compared to controls, highlighting the importance of the role of telemedicine in management of these changes.¹²⁶**

- Patients admitted to the hospital or ICU must continue with their outpatient regimen of medications. If intubated carbidopa/levodopa must be crushed and given via NG tube.

- **Huntington disease:** Patients admitted to the hospital or ICU must continue with their outpatient regimen of medications. If intubated contact movement disorders physician to determine if medication (or alternative) should be continued inpatient.
- **Essential tremor:** Those patients treated with primidone may potentially have a drug-interaction with Remdesivir (there are no known drug interactions for this medication reported) Primidone is a strong CYP3A4 inducer and a weak CYP1A2, CYP2A6, CYP2B6 inducer that is relatively contraindicated with several other antiviral therapies. If pharmacist raises concerns for drug-drug interaction it is reasonable to hold primidone for the duration of antiviral therapy
- **Other:** General recommendations are to continue all outpatient regimens as prescribed.

- **Headache**

- Large retrospective studies both in the Chinese and European population report an incidence of headache >70.3% in COVID-19 patients; higher percentages are reported in young & female patients with mild-to-moderate disease.¹²⁷
- Healthcare professionals also had a high-incidence (81%) of self-reported headache during the COVID-19 pandemic, thought to be related to the PPE and work-related stress.¹²⁸
- Headache management for chronic headache patients not affected by COVID-19 has been

significantly altered due to the development of exclusive telehealth measures implementing outpatient management plans and alternative plans for Botox administration¹²⁹. Bridging therapies and use of CGRP antagonists continues to be the upcoming trends to manage Headache patients in the COVID-19 pandemic era.¹³⁰

THERAPIES: YES, MAYBE, NO

- **Therapies targeting viral replication:**

- **Lopinavir/ritonavir (LPV/RTV):** not recommended; not effective when tested alone in COVID-19 pneumonia (did not change mortality, discharge, length of stay).¹³¹ No mention of severe neurologic sequelae in any of these patients. A multi-center study from six centers in Hong Kong involving 127 patients with COVID-19 demonstrated that triple therapy including LPV/RTV, ribavirin and SC IFNβ1B was superior to LPV/RTV and ribavirin alone in achieving viral clearance. Median time to negative nasopharyngeal PCR was 7 days (IQR 5-11) in the triple therapy arm compared to 12 days (IQR 8-15) in the control arm (HR 4.37;95% CI 1.86-10.24; P=0.001)¹³². Currently still being investigated along with other therapies in the French-led Discovery trial.^{133,34}
- **Remdesivir ("GS5734"):** prodrug of adenosine analog, promising in cell and animal models against CoV, crosses BBB in rhesus monkeys [tested in Ebola - also neuro-invasive]; in phase 2 and 3 human trials,¹³⁵⁻¹³⁸ A case series was published of 53 patients with COVID-19 and hypoxia who had received remdesivir via compassionate-use; overall mortality was 13%, and 68% had improvement in need for oxygen support.¹³⁹ A randomized placebo-controlled trial including 237 patients with severe COVID-19 infection from 10 centers in Wuhan, China failed to demonstrate clinical benefit for IV remdesivir therapy. However, there was a trend towards shorter duration to recovery among patients with symptom-duration ≤10 days, though this did not reach statistical significance.¹⁴⁰ A larger NIH-sponsored clinical trial involving 1063 patients released today demonstrated 31% faster time to recovery among patients receiving IV remdesivir compared to placebo (P<0.001). The median time to recovery was 11 days in

remdesivir arm compared to 15 days in placebo arm. Mortality was lower among patients receiving remdesivir (8%) compared to those receiving placebo (11.6%), though this was not statistically significant ($P=0.059$).¹⁴¹ FDA approved emergency use of remdesivir based on these results.¹⁴² **A more recent trial published in NEJM involving 397 patients with moderate to severe COVID-19 pneumonia randomized to 5 vs 10 days of IV remdesivir therapy showed similar outcomes among both groups.**¹⁴³

- **Ribavirin:** guanosine analogue, usually combined with recombinant interferon. Not effective in MERS.¹⁴⁴ Looks good in vitro with poor in vivo activity (hard to get high enough serum levels in humans/limited by toxicity). **Promising data in combination therapy (see above).**¹³²
- **Favipiravir:** A viral RNA polymerase inhibitor used to treat influenza in Japan.¹⁴⁴ A non-randomized open label trial evaluated its use in SARS-COV2 infection in addition to inhaled interferon- α compared to LPV/RTV therapy. 35 patients received favipiravir compared to 45 patients receiving LPV/RTV. Favipiravir therapy was associated with shorter viral clearance time (median 4 days (IQR 2.5-9) than LPV/RTV (median 11 days (IQR 8-13) ($P<0.001$). In addition, 91.4% of patients receiving favipiravir demonstrated chest CT improvement compared to 62.2% of patients receiving LPV/RTV ($P=0.004$).¹⁴⁵
- **Oseltamivir:** A drug commonly used to treat influenza infections; it works by blocking viral neuraminidase enzyme, therefore preventing shedding of viral particles in the respiratory tract. Oseltamivir is being studied in clinical trials among combination therapies involving chloroquine and famipiravir.¹⁴⁶⁻¹⁵⁰
- **Arbidol (also known as umifenovir) :** Approved in Russia and China for the treatment of influenza virus infections. Arbidol's antiviral mechanism against influenza A and B involves viral fusion inhibition with the targeted membrane, which blocks virus entry into the cell. A small retrospective cohort study of non-intubated patients in China with COVID-19 showed possible clearing of the virus (negative RT-PCR from NP swabs) more quickly in patients treated

with the combination of arbidol and LPV/RTV than with LPV/RTV alone, although the latter group was statistically more likely to have received steroids.¹⁵¹ The drug is currently being investigated in 4 clinical trials in China.¹⁵²⁻¹⁵⁵

- **Hydroxychloroquine (HCQ) +/- azithromycin (AZT):** In vitro data has demonstrated efficacy of chloroquine and hydroxychloroquine in suppressing SARS-CoV2.¹⁵⁶ Based on this data, Gautret et al. studied the antiviral activity in a non-randomized trial that included 20 patients receiving HCQ 200 mg q8h compared to 16 non-matched controls receiving standard of care.¹⁵⁷ Viral eradication was assessed via repeat PRC nasopharyngeal swab on day 6. Viral eradication was achieved in 14/20 (70%) of patients in the treatment arm compared to 2/16 (12.5%) control patients. 6/6 (100%) patients receiving AZT in addition to HCQ achieved viral eradication. However, this study was criticized by the lack of randomization and lack of blinding as well as the exclusion of three patients who were transferred to ICU and one patient who died which could have altered the outcome, in addition use of a different PCR cycle threshold for defining positive test than the one adapted by CDC.¹⁵⁸ The same group from Marseille reported updated results from a larger cohort including 80 patients admitted to the ID ward, who received daily HCQ+AZT regimen (HCQ= 200 mg t.i.d. for 10 days; AZT= 500 mg on day 1, followed by 250 mg qd for 4 days). 65/80 (81.3%) achieved a favorable outcome. Only 15% required oxygen supplementation. 3 patients required ICU transfer, 2 of which managed to be stepped down back to the ward. One patient who was not transferred to the ICU died. 83 % of PCR results turned negative on day 7 and 93% turned negative on day 8 of treatment. However, comparison with a control group was lacking in this trial. Surprisingly, only 15% of included patients had fever and 4 patients were asymptomatic carriers.¹⁵⁹ The inclusion of these patients in this trial, in addition to the lack of a control group, limit the validity of these results. A more recent pilot trial from another French group failed to demonstrate clinical benefit or evidence of viral suppression in 10 patients receiving HCQ+AZT therapy,¹⁶⁰ and a French trial was

halted due to emergence of serious cardiac adverse events.¹⁶¹ Another pilot trial from China randomized 30 patients to receiving HCQ therapy vs conventional treatment only. HCQ was not superior to standard therapy in achieving viral suppression.¹⁶² A larger clinical trial from China randomized 60 patients to receiving HCQ vs placebo and demonstrated significant shortening of body temperature recovery and cough remission times in HCQ arm. In addition, 80.6% of patients in the HCQ arm demonstrated radiologic improvement of pneumonia compared to 54.8% in the control arm.¹⁶³ Another multicenter open label randomized controlled trial failed to demonstrate significant association between hydroxychloroquine use and viral suppression, while a significant association with 28-day symptom alleviated was only demonstrated in post-hoc analysis after excluding confounding effect of antiviral agents.¹⁶⁴ Another preprint retrospective study involving 368 veterans with COVID-19 infection also failed to demonstrate a significant effect of hydroxychloroquine +/- azithromycin on the rates of ventilation. Surprisingly, all-cause mortality risk was higher in patients in HCQ arm compared to HCQ+AZT and placebo arms (adjusted hazards ratio 2.61; 95% CI 1.1 to 6.17; P=0.03).¹⁶⁵ Two large retrospective studies from New York first including 1446 and 2nd including 1438 hospitalized patients with COVID-19 demonstrated no statistically significant change in mortality risk in association with hydroxychloroquine use with or without azithromycin.^{166,167} A phase 2 trial investigating the use of high vs low dose chloroquine therapy was halted prematurely due to emergence of evidence of increased risk for QTc prolongation and increased mortality risk in high dose chloroquine arm upon interim analysis.¹⁶⁸ **A multinational registry analysis including data from 96,032 patients from 671 hospitals in 6 continents demonstrated that hydroxychloroquine or chloroquine use with or without a macrolide antibiotics was independently associated with increased risk for de-novo ventricular arrhythmias (4.3-8.1%) and in-hospital mortality (16.4-23.8%) compared to controls (0.3% and 9.3%, respectively).**¹⁶⁹ Based on these results, the

WHO decided to pause the enrollment hydroxychloroquine group in the multinational Solidarity trial.¹⁷⁰ Clinical trials assessing pre-exposure and post-exposure prophylaxis of healthcare workers including Henry-Ford based WHIP trial are still underway¹⁷¹⁻¹⁷⁴ Given the lack of strong evidence supporting its use in the light of potential cardiotoxicity, NIH COVID-19 treatment guidelines panel recommends against the use of HCQ+AZT outside the scope of clinical trials but does not recommend for or against HCQ monotherapy given limited data at this point.¹⁷⁶

- **Teicoplanin:** A glycopeptide antibiotic used to treat gram positive infections, active *in vitro* against SARS-CoV2 & other viruses, prevents release of genomic viral RNA and stops viral replication at doses lower than reached in human blood. No human trials yet.¹⁷⁶
- **Ivermectin:** Antiparasitic medication with reported in-vitro activity against multiple RNA viruses including Influenza¹⁷⁷ and West Nile¹⁷⁸ viruses. The mechanism likely involves blocking entry of viral proteins into the cellular nuclei.¹⁷⁸ A recent study demonstrated in-vitro viral suppression within 48 hours of administration.¹⁷⁹ No human trials yet.
- **Nitazoxanide:** Antiparasitic agent with reported in-vitro activity against MERS-COV and SARS-CoV-2.^{180,181} No human trials yet.
- **Camostat:** A medication used in Japan for treatment of pancreatitis; shown to have in-vitro activity against SARS-COV2 via inhibiting cellular protease TMPRSS2 which plays an essential role in facilitating viral entry into cells.¹⁸²
- **Baricitinib:** JAK1 and JAK2 inhibitor approved for treatment of rheumatoid arthritis. Artificial intelligence-based algorithms identified this medication as a potential treatment for COVID-19 infections via inhibition of clathrin-mediated endocytosis and subsequently viral entry into cells.¹⁸³ One clinical trial is currently underway in Italy investigating its use.¹⁸⁴
- **Soluble ACE2 molecules:** May play a role in competitively blocking membrane ACE2 viral bindings sites, and subsequently blocking viral entry and replication.¹⁸⁵ No clinical trials yet.

- **Immunosuppressive/modulatory therapies**

- **Methylprednisolone:** The use of corticosteroids in the management of ARDS of various etiologies has been evaluated in multiple studies with mixed results.¹⁸⁶⁻¹⁸⁹ Two studies demonstrated the association of corticosteroid administration with improvement in respiratory and cardiovascular function in patients with ARDS and one study demonstrated that early introduction of IV steroids was associated shortened ICU stay and reduced ICU mortality in patients with ARDS as well. In addition, the use of corticosteroids in patients with acute hypoxic respiratory failure related to COVID infection may ameliorate the development of cytokine storm which is thought to be the main driver of morbidity and mortality. A retrospective study from China involving 201 patients with COVID-19 related ARDS demonstrated statistically significant association between methylprednisolone use and reduced mortality risk (HR, 0.38; 95% CI, 0.20-0.72).¹⁹⁰ Current Henry Ford protocol recommends a 3-7-day course of IV Steroids in all patients with hypoxic respiratory failure related to COVID infection. A clinical trial is currently underway in Italy evaluating the role of IV methylprednisolone in management of ARDS in the setting of COVID-19 infection.¹⁹¹ A preprint study from Henry Ford involving 212 patients with moderate to severe COVID-19 infections demonstrated that the implementation of this protocol has been associated with reduction in mortality, ICU admissions and need for mechanical ventilation. Multivariate regression analysis demonstrated independent association with reduction in reaching primary composite endpoint including mortality, ICU admissions and mechanical ventilation in patients receiving steroids after controlling for other risk factors (OR 0.45; 95% CI: 0.25-0.81).¹⁹²
- **Tocilizumab:** humanized monoclonal antibody targeting IL6 receptors. A case series from China demonstrated clinical improvement in 20/20 and radiologic improvement in 19/20 (90.5%) patients with severe to critical COVID-19 infection.¹⁹³ Preliminary data from a French trial involving 129 patients with moderate to severe infection demonstrated significant benefit on mortality reduction and decreased need for life support

interventions.¹⁹⁴ Another study from Italy involving 85 patients with COVID-19 infection and respiratory failure not requiring mechanical ventilation demonstrated improved survival and recovery rates among patients receiving low dose tocilizumab compared to historical controls (HR for death 0.035; 95% CI 0.004-0.347; P value=0.004). 2/62 in the tocilizumab arm died compared to 11/23 in the historical control arm. Respiratory function improved in 64.8% of patients receiving tocilizumab, while 100% of controls had worsening or respiratory function requiring intubation.¹⁹⁵ There are two currently ongoing clinical trials in China further investigating this drug.¹⁹⁶

- **Sarilumab:** Another monoclonal antibody targeting IL6 receptors. A clinical trial evaluating its use is currently enrolling patients in New York (NCT04315298).¹⁹⁷ Preliminary analysis of a phase 2 trial involving 457 patients with severe to critical COVID-19 pneumonia showed no clinical benefit when both severe and critical groups were combined but positive trend towards clinical benefit was noted among the critical patient group. Based on these preliminary data, Sanofi announced amending phase 3 trial to include critical patients only.¹⁹⁸
- **Siltuximab:** Another monoclonal antibody targeting IL6. A case series from China including 21 patients with COVID pneumonia/ARDS demonstrated clinical improvement in 7/21 (33%) patients, clinical stabilization in 9/21 (43%) patients and clinical worsening in 5/21 (24%) patients.¹⁹⁹ A clinical trial is currently underway investigating its utility.²⁰⁰
- **Eculizumab:** Humanized monoclonal antibody targeting complement protein C5, thus preventing the formation of membrane attack complex (MAC). A clinical trial sponsored by Hudson Medical is currently underway investigating its use in COVID-19 infections of various severities.²⁰¹
- **Anakinra:** recombinant form of IL1 receptor antagonist. This drug is proposed to ameliorate the cytokine storm. A retrospective study from Italy involving 29 patients with moderate to severe COVID-related ARDS on NIV receiving high dose IV Anakinra and 16 controls demonstrated progressive improvement in

respiratory function in 72% of patients receiving Anakinra compared to 50% of controls. At 21 days, 90% of patients receiving Anakinra survived compared to 56% of controls ($P=0.009$)²⁰². Another clinical trial underway in Italy (sponsored by SOBI).²⁰³

- **Emapalumab:** monoclonal antibody targeting IFN- γ , a proinflammatory cytokine with a central role in various inflammatory processes. No clinical trials are currently underway evaluating this drug, but one trial is planned in Italy.²⁰³
- **IC14:** A recombinant chimeric monoclonal antibody targeting CD14 (which is thought to play an important role in cellular activation leading to development of ARDS). A compassionate open label trial is currently underway in Italy.²⁰⁴
- **Bevacizumab:** recombinant humanized monoclonal antibody blocking angiogenesis by targeting VEGF receptors. Based on promising data from ARDS trials, a clinical trial was initiated in China to assess its utility in management of severe or critical COVID-19 pneumonia.²⁰⁵
- **Convalescent plasma:** Convalescent plasma from recovering patients has been used in SARS-COV with reported success. One case series from China demonstrated clinical improvement and viral suppression in 5 patients with COVID-19 infection and ARDS. ARDS resolved in 4/5 patients and three patients were weaned from mechanical ventilation and were successfully discharged from the hospital.²⁰⁶ Another case series from China reported resolution of clinical symptoms and radiological improvement of varying degrees in 10 patients with severe COVID-19 infections and conversion of positive to negative RT-PCR in 7/10 patients receiving convalescent plasma.²⁰⁷ Based on these data and the state of the current public health crisis, the FDA allowed access to this treatment through single patient emergency IND.²⁰⁸ A multi-center safety analysis published as pre-print included 5000 patients with severe or critical COVID-19 infection demonstrating that convalescent plasma administration was well-tolerated with <1% incidence rate of serious adverse and 0.3 % mortality.²⁰⁹ One clinical trial evaluating its role in COVID-19 infection (NCT04292340) is currently underway in China as well.²¹⁰
- **Neutralizing antibodies:** Neutralizing antibodies can recognize a wide variety of glycoproteins (GPs) in virus surfaces or the protein shell of a non-enveloped virus. A trial utilizing human immunoglobulin in patients with pneumonia caused by 2019-nCoV who recovered is currently underway.²¹¹
- **IVIG:** Cao et al. reported improvement in 3 cases with severe COVID-19 infection from China.²¹² Trials are currently underway to further assess its utility.²¹³
- **Fingolimod:** A sphingosine-1-phosphate receptor regulator (FTY720) with an effective immunology modulator that is used in multiple sclerosis. Study NCT04280588 aims to determine the efficacy of fingolimod for COVID-19. Currently Phase 2.²¹⁴
- **Thalidomide:** has an anti-inflammatory action due to its ability to speed up the degradation of messenger RNA in blood cells and thus reduce tumor necrosis factor- α (TNF α). Furthermore, thalidomide can increase the secretion of interleukins, such as IL-12, and activate natural killer cells. Currently phase 2.^{215,216}
- **Vazegapant:** An intranasal CGRP antagonist currently under trial as abortive therapy for migraine. Postulated role in COVID-19 infection therapy involves blocking CGRP-mediated alveolar inflammation. A phase 2 trial is currently underway.²¹⁷
- **International Clinical Trials:** There are two large international clinical trials that are currently underway:
 - **Solidarity trial:** A WHO-funded trial evaluating various therapies including remdesivir, chloroquine/hydroxychloroquine, LPV/RTV, and IFN- β .¹³³ WHO has stopped enrolling patients into HCQ arm given negative data and concern for associated harm from other published retrospective studies.
 - **Discovery trial:** A European trial similar to Solidarity trial except for exclusion of chloroquine.^{133,134}
- **Vaccines**
 - COVID Vaccines Phase 1 clinical trials: To date, there are no vaccines for COVID-19. The projected time for the development of a commercially available vaccine is 12-18 months. We will mention the phase 1 clinical trials here.

- mRNA-1273:^{218,219} This investigational vaccine was developed by NIAID scientists and *Moderna* (biotechnological company) using a mRNA that undergoes translation into the synthesis of the viral spike protein. As a result, the immune system produces antibodies against the spike protein attacking the virus prior to it entering the host cells.
- Ad5-nCoV:^{218,220,221} Developed by CanSino Biologics (China), this vaccine is a genetically engineered CoV-2 virus that incorporates the adenovirus type 5 vector to express the viral spike protein, while having lost its virulence. **A phase 1 study involving 108 subjects was published in *Lancet*. ELISA and neutralizing antibodies increased significantly at day 14 post-vaccination, peaked at day 28 and so serious adverse events were noted.**²²¹
- ChAdOx1^{218,222} Similarly to the Ad5-nCoV vaccine, this vaccine instead incorporates the chimpanzee adenovirus vaccine vector ChAdOx1. It is being developed by the UK company, Vaccitech (University of Oxford)
- BCG vaccine: A live attenuated vaccine used in certain countries to protect against the development of pulmonary tuberculosis. BCG

vaccine administration may enhance the development of innate immune response which targets various infections, and multiple studies have demonstrated a lower risk for respiratory tract infections and lower infantile mortality among those receiving BCG vaccine.²²³⁻²²⁵ In addition, most countries with large number of fatalities including USA, Italy and Spain either do not routinely administer BCG vaccine or only had BCG vaccines introduced in 1980s which is the case with Iran, leaving many elderly unvaccinated patients susceptible to severe infections based on this theory.²²⁶ However, a retrospective study from Israel found no statistically significant difference in rates of COVID positivity between BCG-vaccinated and unvaccinated groups.²²⁷ An Australian clinical trial is currently underway investigating the role of BCG administration in prevention of COVID-19 infections among healthcare workers.²²⁸

For more information about ongoing clinical trials, visit <https://www.av.co/covid> for an updated list of currently active trials in diagnostics, therapeutics and vaccines.²²⁹

References

1. Dong et al, An Interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. Published February 19, 2020. doi:10.1016/S1473-3099(20)30120-1.
2. Coronavirus. *Michigan.gov*. Published online March 24, 2020. Available www.Michigan.gov/coronavirus
3. COVID-19 projections. *IHME*. Published online April 1, 2020. <http://covid19.healthdata.org/>
4. Coronavirus Disease (COVID-19) - statistics and research. *Our World in Data*. Published online March 24, 2020. ourworldindata.org/coronavirus
5. Santarpia J, et al. Transmission potential of SARS-CoV-2 in viral shedding observed at the University of Nebraska Medical Center. *Preprints*. Published online March 26, 2020. <https://doi.org/10.1101/2020.03.23.20039446>.
6. Fineberg H. Rapid expert consultation on the possibility of bioaerosol spread of SARS-CoV-2 for the COVID-19 pandemic. *The National Academies Press*. Published online April 1, 2020. <https://www.nap.edu/read/25769/chapter/>
7. N van Doremalen, et al. Aerosol and surface stability of HCoV-19 (SARS-CoV-2) compared to SARS-CoV-1. *NEJM*. Published online March 17, 2020. doi:10.1056/NEJMc2004973
8. Infection Control: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Centers for Disease Control and Prevention*, Published online March 19, 2020. www.cdc.gov/coronavirus/2019-ncov/infection-control/control-recommendations.html
9. Recommendation regarding the use of cloth face coverings, especially in areas of significant community-based transmission. *Centers for Disease Control and Prevention*, Published online April 3, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/cloth-face-cover.html>
10. Brosseau L, et al. Commentary: masks-for-all for COVID-19 not based on sound data. *Center for Infectious Disease Research and Policy*. Published online April 1, 2020. <https://www.cidrap.umn.edu/news-perspective/2020/04/commentary-masks-all-covid-19-not-based-sound-data>
11. Dong L, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *JAMA*. Published online March 26, 2020. doi:10.1001/jama.2020.4621.
12. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature Medicine*. 2020.

13. Feldman O, *et al.* Exposure to a surrogate measure of contamination from simulated patients by emergency department personnel wearing personal protective equipment. *JAMA*. Published online 2020 April 27. doi:10.1001/jama.2020.6633
14. De Jong A, *et al.* Airway management for COVID-19: a move towards universal videolaryngoscope? *Lancet Respir Med*. Published Online 2020 May 5. [https://doi.org/10.1016/S2213-2600\(20\)30221-6](https://doi.org/10.1016/S2213-2600(20)30221-6)
15. Groß R, *et al.* Detection of SARS-CoV-2 in human breastmilk. *The Lancet*. Published online 2020 May 21. DOI:[https://doi.org/10.1016/S0140-6736\(20\)31181-8](https://doi.org/10.1016/S0140-6736(20)31181-8)
16. Li, Y-C, Bai, W-Z, Hashikawa, T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol*. 2020;1-4.
17. Steardo L, *et al.* Neuroinfection may potentially contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol (Oxf)*. Published online Mar 29, 2020. <https://doi.org/10.1111/apha.13473>
18. Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. Published online February 24, 2020. doi:10.1001/jama.2020.2648.
19. Jose RJ, *et al.* COVID-19 cytokine storm: the interplay between inflammation and coagulation. *Lancet Respir Med*. Published online 2020 April 27. [https://doi.org/10.1016/S2213-2600\(20\)30216-2](https://doi.org/10.1016/S2213-2600(20)30216-2)
20. Abboud F, *et al.* Autonomic neural regulation of the immune system: implications for hypertension and cardiovascular disease. *Hypertension*. 2012 Apr;59(4):755-62.
21. Liu W, *et al.* COVID-19: attacks the 1-beta chain of hemoglobin and captures the porphyrin to inhibit human heme metabolism. *Preprints*. Published online March 30, 2020. https://chemrxiv.org/articles/COVID-19_Disease_ORF8_and_Surface_Glycoprotein_Inhibit_Heme_Metabolism_by_Binding_to_Porphyrin/11938173
22. Varga, Z., *et al.*, *Endothelial cell infection and endotheliitis in COVID-19*. *The Lancet*, 2020. 395(10234): p. 1417-1418.
23. Li Y, *et al.* Coronavirus disease 2019 (COVID-19): role of chest CT in diagnosis and management. *AJR Am J Roentgenol*. Published online Mar 4, 2020. <https://doi.org/10.2214/AJR.20.22954>.
24. Yeo C, *et al.* Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? *Lancet Gastroenterol Hepatol*. 2020;5(4):335-337.
25. Shi S, *et al.* Cardiac injury in patients with coronavirus disease 2019. *JAMA Cardiol*. Published online March 25, 2020. doi:10.1001/jamacardio.2020.0950
26. Guo T, *et al.* Association of cardiovascular disease and myocardial injury with outcomes of patients hospitalized with 2019-coronavirus disease (COVID-19). *JAMA Cardiol*. Published online March 27, 2020. doi:10.1001/jamacardio.2020.1017
27. Xu Z, *et al.* Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020:S2213-2600(20)30076-X.
28. Ackermann M, *et al.* Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med*. Published online 2020 May 21. doi: 10.1056/NEJMoa2015432.
29. Evaluating and testing persons for Coronavirus Disease 2019 (COVID-19). *Centers for Disease Control and Prevention*. Published online March 9, 2020 www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html
30. Interim guidelines for collecting, handling, and testing clinical specimens from persons for Coronavirus Disease 2019 (COVID-19). *Centers for Disease Control and Prevention*. Published online March 19, 2020. www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html
31. Wylie AL, *et al.* Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs. *Preprint*. Published online on April 22, 2020. doi: <https://doi.org/10.1101/2020.04.16.20067835>
32. Li, D., *et al.*, *Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019*. *JAMA Network Open*, 2020. 3(5): p. e208292-e208292.
33. FDA approves first rapid COVID-19 test. *NPR*. Published online March 21, 2020. www.npr.org/sections/coronavirus-live-updates/2020/03/21/819629909/fda-approves-first-rapid-covid-19-test
34. Detect COVID-19 in as little as 5 minutes. *Abbott*. Published online March 27, 2020. <https://www.abbott.com/corpnewsroom/product-and-innovation/detect-covid-19-in-as-little-as-5-minutes.html>
35. Wang W *et al.* Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA*. 2020. Published online March 11, 2020. doi:10.1001/jama.2020.3786
36. Sethuraman N, *et al.* Interpreting diagnostic tests for SARS-CoV-2. *JAMA*. Published online May 6, 2020. doi:10.1001/jama.2020.8259
37. Wölfel R, *et al.* Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020. Published online April 1, 2020. doi:10.1038/s41586-020-2196-x
38. Xiao AT, *et al.* Profile of specific antibodies to SARS-CoV-2: the first report. *J Infect*. 2020;S0163-4453(20)30138-9. Published online March 21, 2020. doi:10.1016/j.jinf.2020.03.012
39. Guo L, *et al.* Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clin Infect Dis*. 2020;ciaa310. Published online March 21, 2020. doi:10.1093/cid/ciaa310
40. Mandavilli A. FDA approves first coronavirus antibody test in U.S. *The New York Times*. Published online April 2, 2020. <https://www.nytimes.com/2020/04/02/health/coronavirus-antibody-test.html>
41. Hahn S. Coronavirus (COVID-19) update: serological test validation and education efforts. *FDA*. Published online on April 18, 2020. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-serological-test-validation-and-education-efforts>
42. Abbasi J. The Promise and peril of antibody testing for COVID-19. *JAMA*. Published online April 17, 2020. doi:10.1001/jama.2020.6170
43. Hopper L. Early antibody testing suggests COVID-19 infections in L.A. County greatly exceed documented cases. *USC News*. Published online on April 20, 2020. <https://news.usc.edu/168987/antibody-testing-results-covid-19-infections-los-angeles-county>
44. Sheridan C. Fast, portable tests come online to curb coronavirus pandemic. *Nat Biotechnol*. Published online March 23, 2020. <https://www.nature.com/articles/d41587-020-00010-2>
45. Coronavirus (COVID-19) update: FDA alerts consumers about unauthorized fraudulent COVID-19 test kits. Published online March 20, 2020.

- <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-alerts-consumers-about-unauthorized-fraudulent-covid-19-test-kits>
46. South Korea dials up coronavirus testing with hospital 'phone booths'. Published online March 17, 2020. <https://www.straitstimes.com/asia/east-asia/south-korea-dials-up-coronavirus-testing-with-hospital-phone-booths>.
 47. McNeil Jr, D. Can Smart Thermometers Track the Spread of the Coronavirus? *The New York Times*. Published online March 18, 2020. <https://www.nytimes.com/2020/03/18/health/coronavirus-fever-thermometers.html>
 48. Oxley T, et al. Large-vessel stroke as a presenting feature of Covid-19 in the young. *N Eng J Med*. Published online April 28, 2020. DOI: 10.1056/NEJMc2009787
 49. Yaghi, S., et al., *SARS2-CoV-2 and Stroke in a New York Healthcare System*. *Stroke*. 0(0): p. STROKEAHA.120.030335.
 50. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurology*. 2020.
 51. Li, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. *Lancet Neurol (Preprint)*. Published online March 13, 2020. [dx.doi.org/10.2139/ssrn.3550025](https://doi.org/10.2139/ssrn.3550025)
 52. Hong T, et al. SNIS Special Webinar: Neurointerventional Guidance for COVID-19. *Society of Neurointerventional Surgery*. Published online April 2, 2020. <https://www.snisonline.org/meetings/covid19webinar>.
 53. Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19. *New England Journal of Medicine*. 2020.
 54. Morassi M, et al. Cerebrovascular complications in patients with SARS-CoV-2 infection: case series. Preprint. Published online on April 20, 2020. DOI:10.21203/rs.3.rs-23137/v1
 55. Al Olama M, et al. COVID-19-associated meningoencephalitis complicated with intracranial hemorrhage: a case report. *Acta Neurochir (Wien)*. Published online 2020 May 20. doi: 10.1007/s00701-020-04402-w.
 56. Vollono C, Rollo E, Romozzi M, et al. Focal status epilepticus as unique clinical feature of COVID-19: A case report. *Seizure - European Journal of Epilepsy*. 2020;78:109-112.
 57. Lu L, Xiong W, Liu D, et al. New-onset acute symptomatic seizure and risk factors in Corona Virus Disease 2019: A Retrospective Multicenter Study. *Epilepsia*. 2020.
 58. Galanopoulou, A.S., et al., *EEG findings in acutely ill patients investigated for SARS-CoV2/COVID-19: a small case series preliminary report*. *Epilepsia Open*. Epub ahead of print. 2020.
 59. Sana Somani, Sandipan Pati, Tyler Gaston, Alissa Chitlangia, Shruti Agnihotri. *Ann Clin Transl Neurol*. 2020 May 14De Novo Status Epilepticus in Patients With COVID-19
 60. Anna Maria Musolino, Maria Chiara Supino, Danilo Buonsenso, et al. Lung Ultrasound in Children with COVID-19: Preliminary Findings. *Ultrasound Med Biol* 2020 May 3;S0301-5629(20)30198-8.
 61. Luca Zanin, Giorgio Saraceno, Pier Paolo Panciani et al. SARS-CoV-2 can induce brain and spine demyelinating lesions. *Acta Neurochir (Wien)*. 2020 May 4;1-4
 62. Lisa Duong, Prissilla Xu, Antonio Liu. Meningoencephalitis without respiratory failure in a young female patient with COVID-19 infection in Downtown Los Angeles, early April 2020. *Brain Behav Immun*. 2020 Apr 17;S0889-1591(20)30509-2.
 63. Sandeep Sohal, Mansur Mossammat. COVID-19 Presenting with Seizures. *IDCases*. 2020 May 1;20:e00782.
 64. Poyiadji N, et al. COVID-19-associated acute hemorrhagic necrotizing encephalopathy: CT and MRI Features. *RSNA*. Published online Mar 31, 2020. <https://doi.org/10.1148/radiol.2020201187>
 65. Dixon L, et al. COVID-19-related acute necrotizing encephalopathy with brain stem involvement in a patient with aplastic anemia. *Neurol Neuroimmunol Neuroinflamm*. 2020 May 26;7(5):e789. doi: 10.1212/NXI.0000000000000789.
 66. Moriguchi T, Harii N, Goto J, et al. A first Case of Meningitis/Encephalitis associated with SARS-Coronavirus-2. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases*. 2020.
 67. Pilotto, A., et al., *Steroid-responsive encephalitis in Covid-19 disease*. *Annals of Neurology*. Epub ahead of print. 2020
 68. Zanin L, et al. SARS-CoV-2 can induce brain and spine demyelinating lesions. *Acta Neurochir (Wien)*. 2020 May 4;1-4. doi: 10.1007/s00701-020-04374-x.
 69. Helms J, et al. Neurologic features in severe SARS-CoV-2 infection. *NEJM*. Published online on April 15, 2020. DOI: 10.1056/NEJMc2008597
 70. Rogers JP, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry*. Published online 2020 May 18. [https://doi.org/10.1016/S2215-0366\(20\)30203-01](https://doi.org/10.1016/S2215-0366(20)30203-01)
 71. Moein ST, et al. Smell dysfunction: a biomarker for COVID-19. *Int Forum Allergy Rhinol*. Published online 2020 April 17. doi:10.1002/alr.22587
 72. Whitcroft KL, et al. Olfactory dysfunction in COVID-19: diagnosis and management. *JAMA*. Published online 2020 May 20. doi:10.1001/jama.2020.8391
 73. Jin M and Tong Q. Rhabdomyolysis as potential late complication associated with COVID-19. *Emerg Infect Dis*. 2020 Jul <https://doi.org/10.3201/eid2607.200445>
 74. Beydon, M., et al., *Myositis as a manifestation of SARS-CoV-2*. *Annals of the Rheumatic Diseases*, 2020: p. annrheumdis-2020-217573
 75. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol*. Published online April 01, 2020. [https://doi.org/10.1016/S1474-4422\(20\)30109-5](https://doi.org/10.1016/S1474-4422(20)30109-5)
 76. Gutiérrez-Ortiz C, et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19. *Neurology*. Published online on April 17, 2020, DOI: <https://doi.org/10.1212/WNL.0000000000009619>
 77. Toscano G, et al. Guillain-Barré Syndrome Associated with SARS-CoV-2. *NEJM*. Published online on April 17, 2020. DOI: 10.1056/NEJMc2009191
 78. Arnaud S, et al. Post SARS-CoV-2 Guillain-Barré Syndrome. *Clin Neurophysiol*. 2020 May 11;131(7):1652-1654. doi: 10.1016/j.clinph.2020.05.003.
 79. Goh Y, et al. Pearls & oysters: facial nerve palsy as a neurological manifestation of Covid-19 infection. *Neurology*. Published online 2020 May 21. doi: 10.1212/WNL.0000000000009863.

80. Rabano-Suárez P, et al. Generalized myoclonus in COVID-19. *Neurology*. Published online 2020 May 21. doi: 10.1212/WNL.0000000000009829.
81. Bunyavanich, S., A. Do, and A. Vicencio. *Nasal Gene Expression of Angiotensin-Converting Enzyme 2 in Children and Adults*. JAMA, 2020
82. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *The Lancet Infectious Diseases*. Published online March 25, 2020. DOI:https://doi.org/10.1016/S1473-3099(20)30198-5
83. Castagnoli R, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr*. Published online April 22, 2020. doi:10.1001/jamapediatrics.2020.1467
84. Coronado Munoz A, et al. Late-Onset Neonatal Sepsis in a Patient with Covid-19. *NEJM*. Published online April 22, 2020. DOI: 10.1056/NEJMc2010614
85. Nathan N, Prevost B, Corvol H. Atypical presentation of COVID-19 in young infants. *The Lancet*. Epub ahead of print. 2020
86. Shekerdeman, L.S., et al., *Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units*. JAMA Pediatrics, 2020.
87. Jones, V.G., et al., *COVID-19 and Kawasaki Disease: Novel Virus and Novel Case*. Hospital Pediatrics, 2020: p. hpeds.2020-0123.
88. NY Times report. *About 100 N.Y. Children Treated for Illness Tied to Virus*. 2020 [cited 2020 May 13]; Available from: <https://www.nytimes.com/2020/05/12/nyregion/coronavirus-new-york-update.html>.
89. Verdoni, L., et al., *An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study*. The Lancet. Epub ahead of print. 2020.
90. PICS. *PICS Statement: Increased number of reported cases of novel presentation of multisystem inflammatory disease*. 2020 [cited 2020 May 14]; Available from: <https://picsociety.uk/wp-content/uploads/2020/04/PICS-statement-re-novel-KD-C19-presentation-v2-27042020.pdf>.
91. D'Antiga L. Coronaviruses and Immunosuppressed patients. The facts during the third epidemic. doi: 10.1002/LT.25756
92. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Science China Life sciences*. 2020;63(3):364-374.
93. Zhang P, Zhu L, Cai J, et al. Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19. *Circulation Research*. 2020. Epub ahead of print.
94. Mehra, M.R., et al., *Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19*. New England Journal of Medicine, 2020.
95. HFSA/ACC/AHA statement addresses concerns Re: Using RAAS Antagonists in COVID-19. Published online Mar 17, 2020. <https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19>.
96. Madjid M, et al. Potential Effects of Coronaviruses on the Cardiovascular System. *JAMA Cardiol*. Published online Mar 27, 2020. <https://doi.org/10.1001/jamacardio.2020.1286>.
97. Tam Chor-Cheung F, et al. Impact of Coronavirus Disease 2019 (COVID-19) outbreak on ST-segment-elevation myocardial infarction care in Hong Kong, China. *Circulation: Cardiovascular Quality and Outcomes*.0(0):CIRCOUTCOMES.120.006631.
98. Zhao, J., et al., *Impact of the COVID-19 Epidemic on Stroke Care and Potential Solutions*. Stroke, 2020: p. STROKEAHA120030225.
99. Rudilosso, S., et al., *Acute Stroke Care Is at Risk in the Era of COVID-19: Experience at a Comprehensive Stroke Center in Barcelona*. Stroke, 2020: p. STROKEAHA120030329.
100. Teo, K.C., et al., *Delays in Stroke Onset to Hospital Arrival Time During COVID-19*. Stroke, 2020: p. STROKEAHA120030105.
101. Fraser J, et al. Society of NeuroInterventional Surgery recommendations for the care of emergent neurointerventional patients in the setting of COVID-19. 2020; <https://www.snisonline.org/wp-content/uploads/2020/03/SNIS-COVID-Stroke-Protocol.pdf>. Accessed March 31, 2020.
102. Lyden P, et al. Temporary emergency guidance to US stroke centers during the COVID-19 pandemic. *Stroke*. Published online April 1, 2020. <https://doi.org/10.1161/STROKEAHA.120.030023>
103. Khosravani H, et al. Protected code stroke: hyperacute stroke management during the coronavirus disease 2019 (COVID-19) pandemic. *Stroke*. Published online Apr 2020. <https://doi.org/10.1161/STROKEAHA.120.029838>
104. Smith, M.S., et al., *Endovascular Therapy for Patients With Acute Ischemic Stroke During the COVID-19 Pandemic: A Proposed Algorithm*. Stroke, 2020: p. STROKEAHA120029863.
105. Nguyen, T.N., et al., *Mechanical Thrombectomy in the Era of the COVID-19 Pandemic: Emergency Preparedness for Neuroscience Teams: A Guidance Statement From the Society of Vascular and Interventional Neurology*. Stroke, 2020: p. STROKEAHA120030100.
106. Baracchini C, Pieroni A, Viaro F, et al. Acute stroke management pathway during Coronavirus-19 pandemic. *Neurol Sci*. 2020:1-3
107. Morfopoulou S, et al. Human Coronavirus OC43 Associated with Fatal Encephalitis. *New England Journal of Medicine*. 2016;375(5):497-498.
108. Li Y, et al. Coronavirus Infections in the Central Nervous System and Respiratory Tract Show Distinct Features in Hospitalized Children. *Intervirology*. 2016;59(3):163-169.
109. Netland J, et al. Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. *J Virol*. 2008;82(15):7264-7275.
110. <https://www.cdc.gov/coronavirus/2019-ncov/downloads/community-mitigation-strategy.pdf>. Accessed 03/24/2020.
111. <https://www.dravetfoundation.org/covid19-dsf-conference-update-3-18-20/>. Accessed 03/24/2020.
112. Aledo-Serrano, Á., et al., *Genetic epilepsies and COVID-19 pandemic: Lessons from the caregiver perspective*. Epilepsia. Epub ahead of print. 2020.
113. French JA, Brodie MJ, Caraballo R, Devinsky O, Ding D, Jehi L, Jette N, Kanner A, Modi AC, Newton CR, Patel AA, Pennell PB, Perucca E, Sander JW, Scheffer IE, Singh G, Williams E, Wilmshurst J, Cross JH. Keeping people with epilepsy safe during the Covid-19 pandemic. *Neurology*. 2020 Apr 23. PMID: 32327490
114. https://www.aesnet.org/about_aes/position_statements/covid-19. Accessed 03/24/2020.
115. <https://www.cms.gov/newsroom/press-releases/cms-issues-guidance-help-medicare-advantage-and-part-d-plans-respond-covid-19>, archived 3/23/20. Accessed 03/24/2020.
116. Plaquenil (hydroxychloroquine) package insert. St. Michael, Barbados: Concordia Pharmaceuticals, Inc.; 2017 Jan.
117. Italian League against Epilepsy. Clinically relevant Drug-Drug interaction between AEDs and medications used in the treatment of COVID-19 patients. https://www.ilae.org/files/dmfile/Antiepileptic-drugs-interactions_in_COVID-19.pdf. Accessed March 27th, 2020.
118. Sormani, M.P., *An Italian programme for COVID-19 infection in multiple sclerosis*. The Lancet Neurology. Epub ahead of print. 2020.

119. [https://www.nationalmssociety.org/What-you-need-to-know-about-Coronavirus-\(COVID-19\)/DMT-Guidelines-for-Coronavirus-\(COVID-19\)-and-](https://www.nationalmssociety.org/What-you-need-to-know-about-Coronavirus-(COVID-19)/DMT-Guidelines-for-Coronavirus-(COVID-19)-and-) Accessed 03/24/2020.
120. Anand, P., et al., *COVID-19 in patients with myasthenia gravis*. Muscle Nerve, 2020.
121. https://myasthenia.org/Portals/0/MG%20COVID19%20guidelines%20FINAL%203_23_20_1.pdf. Accessed 03/24/2020.
122. Guidance for managing NCS/EMG testing requests during COVID-19. Published online 2020 March 31. *American Association of Neuromuscular and Electrodiagnostic Medicine*. <https://www.aanem.org/getmedia/88faf677-8043-4ad3-ad0d-42c0cdd1dabe/Guidance-for-EMG-studies-during-COVID.pdf> J Intern Med. 2020 Apr 30. doi: 10.1111/joim.13089
123. Veerapandian, A., et al., *Spinal muscular atrophy care in the COVID-19 pandemic era*. Muscle & Nerve. Epub ahead of print . 2020.
124. Veerapandian, A., et al., *The care of patients with Duchenne, Becker, and other muscular dystrophies in the COVID-19 pandemic*. Muscle & Nerve. Epub ahead of print . 2020
125. Prasad, S., et al., *Parkinson's Disease and COVID-19: Perceptions and Implications in Patients and Caregivers*. Movement Disorders. Epub ahead of print. 2020..
126. Shalash, A., et al., *Mental health, physical activity and quality of life in Parkinson's disease during COVID-19 pandemic*. Movement Disorders. Epub ahead of print. 2020.
127. Lechien, J.R., et al., *Clinical and Epidemiological Characteristics of 1,420 European Patients with mild-to-moderate Coronavirus Disease 2019*. J Intern Med, 2020.
128. Ong, J.J.Y., et al., *Headaches Associated With Personal Protective Equipment – A Cross-Sectional Study Among Frontline Healthcare Workers During COVID-19*. Headache: The Journal of Head and Face Pain, 2020. **60**(5): p. 864-877.
129. Ali, A. (2020), Delay in OnabotulinumtoxinA Treatment During the COVID-19 Pandemic-Perspectives from a Virus Hotspot. Headache: The Journal of Head and Face Pain. doi:10.1111/head.13830
130. Silvestro, M., Tessitore, A., Tedeschi, G. and Russo, A. (2020), Migraine in the Time of COVID-19. Headache: The Journal of Head and Face Pain, 60: 988-989. doi:10.1111/head.13803
131. Cao, B *et al.* A trial of lopinavir-ritonavir in adults hospitalized with severe COVID-19. NEJM. 2020.
132. Sayburn A. Covid-19: trials of four potential treatments to generate "robust data" of what works. *BMJ*. 2020;368:m1206
133. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 April 8 – Identifier NCT04315948. Trial of Treatments for COVID-19 in Hospitalized Adults (DisCoVeRy). Available from <https://clinicaltrials.gov/ct2/show/NCT04315948>
134. <https://clinicaltrials.gov/ct2/show/NCT04280705> - Phase 2 trial - double-blind, placebo-controlled trial of remdesivir in SARS-CoV-2 with pulmonary disease in hospitalized patients; 200 mg IV once on day 1, followed by 100 mg IV daily up to 10 days
135. <https://clinicaltrials.gov/ct2/show/NCT04292899> - Phase 3 trial of remdesivir in severe pulmonary SARS-CoV-2 – 5 day versus 10 day treatment
136. <https://www.gilead.com/news-and-press/company-statements/gilead-sciences-statement-on-access-to-remdesivir-outside-of-clinical-trials>. Accessed 3/24/2020.
137. Chong YP, *et al.* Rapid Response T. Antiviral Treatment Guidelines for Middle East Respiratory Syndrome. *Infect Chemother*. 2015;47(3):212-222.
138. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 April 8 – Identifier NCT04323761. Expanded Access Treatment Protocol: Remdesivir (RDV; GS-5734) for the Treatment of SARS-CoV2 (CoV) Infection. Available from <https://clinicaltrials.gov/ct2/show/NCT04323761>
139. Grein J, Ohmagari N, Shin D, *et al.* Compassionate Use of Remdesivir for Patients with Severe Covid-19. *New England Journal of Medicine*. 2020.
140. Wang Y, Zhang D, Du G, *et al.* Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *The Lancet*. Epub ahead of print. 2020.
141. Beigel, J.H., *et al.*, *Remdesivir for the Treatment of Covid-19 — Preliminary Report*. New England Journal of Medicine, 2020.
142. Walker J. U.S. Explores Emergency-Use Approval for Gilead Drug After Study Found It Helped Recovery From Covid-19. 2020; <https://www.wsj.com/articles/gilead-says-remdesivir-as-effective-treating-severe-covid-19-in-shorter-period-11588166509>. Accessed April 29, 2020.
143. Goldman, J.D., *et al.*, *Remdesivir for 5 or 10 Days in Patients with Severe Covid-19*. New England Journal of Medicine, 2020.
144. Martinez, MA. Compounds with therapeutic potential against novel respiratory 2019 coronavirus. *Antimicrobial Agents and Chemotherapy*. Epub 9 March 2020.
145. Furuta Y, *et al.* Favipiravir (T-705), a broad spectrum inhibitor of viral RNA polymerase. *Proc Jpn Acad Ser B Phys Biol Sci*. 2017;93(7):449-463.
146. Cai Q, *et al.* Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study. *Engineering*. 2020
147. Rosa SGV, *et al.* Clinical trials on drug repositioning for COVID-19 treatment. *Rev Panam Salud Publica*. 2020;44:e40. <https://doi.org/10.26633/RPSP.2020.40>
148. Uyeki TM. Oseltamivir Treatment of Influenza in Children. *Clin Infect Dis*. 2018;66(10):1501–3.
149. Wang D, *et al.* Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020;Feb7:1–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32031570>
150. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 Mar 12 – Identifier NCT04303299, Various combination of Protease Inhibitors, Oseltamivir, Favipiravir, and Chloroquine for Treatment of COVID-19: A Randomized Control Trial (THDMS-COVID19)
151. Deng L, Chunna L, Zeng Q, *et al.* Arbidol combined with LPV/r versus LPV/r alone against CoronaVirus Disease 2019: a retrospective cohort study. *Jinfect*. 2020. Epub ahead of print.
152. Blaising J, *et al.* Arbidol as a broad-spectrum antiviral: an update. *Antiviral Res*. 2014;107(1):84–94. Available from: <http://dx.doi.org/10.1016/j.antiviral.2014.04.006>
153. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 Mar 12 – Identifier NCT04260594, Clinical Study of Arbidol Hydrochloride Tablets in the Treatment of Pneumonia Caused by Novel Coronavirus. Available from: <https://clinicaltrials.gov/ct2/show/NCT04260594>.
154. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 Mar 12 – Identifier NCT04255017, A prospective, randomized controlled clinical study of antiviral therapy in the 2019-nCoV pneumonia. Available from <https://www.clinicaltrials.gov/ct2/show/NCT04255017>.
155. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 Mar 12 – Identifier NCT04252885, The efficacy of lopinavir plus ritonavir and arbidol against novel coronavirus infection (ELACOI). Available from: <https://clinicaltrials.gov/ct2/show/study/NCT04252885>.
156. Liu J, *et al.* Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. *Cell Discovery*. 2020;6(1):16.
157. Gautret P, *et al.* Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *International Journal of Antimicrobial Agents*. 2020:105949.
158. CDC. Real-Time RT-PCR Panel for Detection of 2019-Novel Coronavirus 2020;

- <https://www.cdc.gov/coronavirus/2019-ncov/downloads/rt-pcr-panel-for-detection-instructions.pdf>
159. Gautret J-CL, *et al.* Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study. 2020.
 160. Molina JM, Delaugerre C, Goff JL, *et al.* No Evidence of Rapid Antiviral Clearance or Clinical Benefit with the Combination of Hydroxychloroquine and Azithromycin in Patients with Severe COVID-19 Infection. *Médecine et Maladies Infectieuses*. 2020
 161. Coronavirus: "nous avons déjà dû interrompre le traitement" de hydroxychloroquine-azithromycine au CHU de Nice. 2020; <https://www.nicematin.com/sante/coronavirus-nous-avons-deja-du-interrompre-le-traitement-de-hydroxychloroquine-azithromycine-au-chu-de-nice-489118#Echobox=1586243253>. Accessed April 8, 2020.
 162. Dandan, *et al.* A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19). *J Zhejiang Univ (Med Sci)*. 2020;49(1):0-0.
 163. Chen Z, *et al.* Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. *medRxiv*. 2020:2020.2003.2022.20040758.
 164. Tang, W., *et al.*, *Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial*. *BMJ*, 2020. **369**: p. m1849.
 165. Magagnoli J, Narendran S, Pereira F, *et al.* Outcomes of hydroxychloroquine usage in United States veterans hospitalized with Covid-19. *medRxiv*. 2020:2020.2004.2016.20065920.
 166. Geleris, J., *et al.*, *Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19*. *New England Journal of Medicine*, 2020.
 167. Rosenberg, E.S., *et al.*, *Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State*. *JAMA*, 2020.
 168. Borba MGS, Val FFA, Sampaio VS, *et al.* Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Clinical Trial. *JAMA Network Open*. 2020;3(4):e208857-e208857.
 169. Mehra, M.R., *et al.*, *Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis*. *The Lancet*. Epub ahead of print. 2020.
 170. BEAUBIEN, J. *WHO Halts Hydroxychloroquine Trial Over Safety Concerns*. 2020 [cited 2020 May 27]; Available from: <https://www.npr.org/sections/coronavirus-live-updates/2020/05/25/861913688/who-halts-hydroxychloroquine-trial-over-safety-concerns>
 171. Proactive Prophylaxis With Azithromycin and Chloroquine in Hospitalized Patients With COVID-19 (ProPAC-COVID) *ClinicalTrials.gov Identifier: NCT04322396*. 2020; <https://clinicaltrials.gov/ct2/show/NCT04322396?term=SARS+COV2&cond=covid&intr=Hydroxychloroquine&draw=3&rank=11>. Accessed March 27th, 2020.
 172. Hydroxychloroquine Chemoprophylaxis in Healthcare Personnel in Contact With COVID-19 Patients (PHYDRA Trial) (PHYDRA) *ClinicalTrials.gov Identifier: NCT04318015*. 2020; <https://clinicaltrials.gov/ct2/show/NCT04318015?term=SARS+COV2&cond=covid&intr=Hydroxychloroquine&draw=2&rank=2>. Accessed March 27, 2020.
 173. Chloroquine/ Hydroxychloroquine Prevention of Coronavirus Disease (COVID-19) in the Healthcare Setting (COPCOV) *ClinicalTrials.gov Identifier: NCT04303507*. 2020; <https://clinicaltrials.gov/ct2/show/NCT04303507?term=SARS+COV2&cond=covid&intr=Hydroxychloroquine&draw=2&rank=6>. Accessed March 27, 2020.
 174. NIH. *Will Hydroxychloroquine Impede or Prevent COVID-19 (WHIP COVID-19)* *ClinicalTrials.gov Identifier: NCT04341441*. 2020 [cited 2020 May 27]; Available from: <https://clinicaltrials.gov/ct2/show/NCT04341441>.
 175. NIH Panel NC-TG. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. 2020; <https://covid19treatmentguidelines.nih.gov/>. Accessed April 22, 2020
 176. Baron SA, *et al.* Teicoplanin: an alternative drug for the treatment of COVID-19? *International Journal of Antimicrobial Agents* 2020;18:epub ahead of print.
 177. Yip T-F, Selim ASM, Lian I, Lee SM-Y. Advancements in Host-Based Interventions for Influenza Treatment. *Front Immunol*. 2018;9:1547-1547.
 178. Mastrangelo E, Pezzullo M, De Burghgraeve T, *et al.* Ivermectin is a potent inhibitor of flavivirus replication specifically targeting NS3 helicase activity: new prospects for an old drug. *J Antimicrob Chemother*. 2012;67(8):1884-1894.
 179. Cally L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antiviral Research*. 2020:104787.
 180. Rossignol JF. Nitazoxanide, a new drug candidate for the treatment of Middle East respiratory syndrome coronavirus. *Journal of infection and public health*. 2016;9(3):227-230.
 181. Wang M, Cao R, Zhang L, *et al.* Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Research*. 2020;30(3):269-271.
 182. Hoffmann M, Kleine-Weber H, Schroeder S, *et al.* SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*. 2020
 183. Richardson P, *et al.* Baricitinib as potential treatment for 2019-nCoV acute respiratory disease. *The Lancet*. 2020;395(10223):e30-e31.
 184. Baricitinib in symptomatic patients Infected by COVID-19: an open-label, pilot study. (BARI-COVID) *ClinicalTrials.gov Identifier: NCT04320277*. 2020; <https://www.clinicaltrials.gov/ct2/show/NCT04320277>. Accessed March 31, 2020.
 185. Battle D, *et al.* Soluble angiotensin-converting enzyme 2: a potential approach for coronavirus infection therapy? *Clinical Science*. 2020;134(5):543-545.
 186. Meduri GU, Golden E, Freire AX, *et al.* Methylprednisolone infusion in early severe ARDS: results of a randomized controlled trial. *Chest*. 2007;131(4):954-963.
 187. Steinberg KP, Hudson LD, Goodman RB, *et al.* Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. *N Engl J Med*. 2006;354(16):1671-1684. Rosenberg, E.S., *et al.*, *Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State*. *JAMA*, 2020.
 188. Sessler CN, Gay PC. Are corticosteroids useful in late-stage acute respiratory distress syndrome? *Respiratory care*. 2010;55(1):43-55.
 189. Deal EN, Hollands JM, Schramm GE, Micek ST. Role of corticosteroids in the management of acute respiratory distress syndrome. *Clinical therapeutics*. 2008;30(5):787-799
 190. Wu C, Chen X, Cai Y, *et al.* Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Internal Medicine*. 2020.
 191. Efficacy of Methylprednisolone for Patients With COVID-19 Severe Acute Respiratory Syndrome (MP-C19) *ClinicalTrials.gov Identifier: NCT04323592*. 2020; <https://www.clinicaltrials.gov/ct2/show/NCT04323592>. Accessed April 4, 2020.
 192. Fadel R, *et al.*, *Early Short Course Corticosteroids in Hospitalized Patients with COVID-19*. *medRxiv*, 2020: p. 2020.05.04.20074609.
 193. Xu, X., *et al.*, *Effective treatment of severe COVID-19 patients with tocilizumab*. *Proceedings of the National Academy of Sciences*, 2020. **117**(20): p. 10970-10975.
 194. Martinetti I. Arthritis drug shows 'significant promise' in severe Covid-19 cases. 2020; <http://www.rfi.fr/en/science-and-technology/20200428-arthritis-drug>

- tocilizumab-shows-significant-promise-in-severe-covid-19-cases. Accessed April 29, 2020.
195. Capra, R., et al., *Impact of low dose tocilizumab on mortality rate in patients with COVID-19 related pneumonia*. European journal of internal medicine, 2020: p. 10.1016/j.ejim.2020.05.009.
 196. Tocilizumab in COVID-19 Pneumonia (TOCOVID-19) (TOCOVID-19). <https://clinicaltrials.gov/ct2/show/NCT04317092>. Accessed 03/24/2020.
 197. Evaluation of the efficacy and safety of sarilumab in hospitalized patients with COVID-19.
 198. Sanofi. Sanofi and Regeneron provide update on U.S. Phase 2/3 adaptive-designed trial in hospitalized COVID-19 patients. 2020; <http://www.news.sanofi.us/April-27-2020-Sanofi-and-Regeneron-pr-ovide-update-on-U-S-Phase-2-3-adaptive-designed-trial-in-hospitalized-COVID-19-patients?sf233246088=1>. Accessed April 29, 2020.
 199. Gritti G, Raimondi F, Ripamonti D, et al. Use of siltuximab in patients with COVID-19 pneumonia requiring ventilatory support. *medRxiv*. 2020:2020.2004.2001.20048561 <https://www.clinicaltrials.gov/ct2/show/NCT04315298>. Accessed 03/24/2020.
 200. Medicine UNLo. Treatment of COVID-19 Patients With Anti-interleukin Drugs (COV-AID) ClinicalTrials.gov Identifier: NCT04330638. 2020; <https://clinicaltrials.gov/ct2/show/NCT04330638>. Accessed April 8, 2020.
 201. Eculizumab (Soliris) in Covid-19 infected patients (SOLID-C19). <https://clinicaltrials.gov/ct2/show/NCT04288713>
 202. Cavalli, G., et al., *Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study*. The Lancet Rheumatology. Epub ahead of print. 2020.
 203. Efficacy and safety of emapalumab and Anakinra in reducing hyperinflammation and respiratory distress in patients with COVID-19 infection. ClinicalTrials.gov Identifier: NCT04324021. 2020; <https://www.clinicaltrials.gov/ct2/show/NCT04324021?term=intravenous+immunoglobulin&cond=covid&draw=2&rank=1>. Accessed March 27, 2020.
 204. Medicine UNLo. Compassionate Use Open-Label Anti-CD14 Treatment in Patients With SARS-CoV-2 (COVID-19) ClinicalTrials.gov Identifier: NCT04346277. 2020; <https://www.clinicaltrials.gov/ct2/show/NCT04346277?term=antibody&cond=covid+19&draw=2&rank=8>. Accessed April 15, 2020.
 205. Bevacizumab in severe or critical patients with COVID-19 pneumonia (BEST-CP). <https://clinicaltrials.gov/ct2/show/NCT04275414>. Accessed 03/24/2020.
 206. Shen C, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. *JAMA*. 2020.
 207. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proceedings of the National Academy of Sciences*. 2020:202004168.
 208. Anti-SARS-CoV-2 Inactivated Convalescent Plasma in the Treatment of COVID-19. <https://clinicaltrials.gov/ct2/show/NCT04292340>. Accessed 03/24/2020.
 209. FDA. Investigational COVID-19 Convalescent Plasma - Emergency INDs. 2020; <https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/investigational-covid-19-convalescent-plasma-emergency-inds>. Accessed March 27, 2020
 210. Joyner, M., et al., *Early Safety Indicators of COVID-19 Convalescent Plasma in 5,000 Patients*. medRxiv, 2020: p. 2020.05.12.20099879.
 211. Varadarajan R, et al. Broadly neutralizing antibodies for therapy of viral infections. *Antib Technol J*. 2016;1.
 212. Cao W, et al. High-dose intravenous immunoglobulin as a therapeutic option for deteriorating patients with Coronavirus Disease 2019. *Open Forum Infectious Diseases*. 2020.
 213. The Efficacy of Intravenous Immunoglobulin Therapy for Severe 2019-nCoV Infected Pneumonia ClinicalTrials.gov Identifier: NCT04261426. 2020; <https://www.clinicaltrials.gov/ct2/show/NCT04261426?term=immunoglobulin&cond=sars+cov2&draw=2&rank=1>. Accessed March 27, 2020.
 214. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 Mar 12 – Identifier NCT04280588, Fingolimod in COVID-19. Available from: <https://clinicaltrials.gov/ct2/show/NCT04280588?term=NCT04280588&draw=2&rank=1>
 215. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 Mar 12 – Identifier NCT04273529, The efficacy and safety of thalidomide in the adjuvant treatment of moderate new coronavirus (Covid-19) pneumonia. Available from: <https://clinicaltrials.gov/ct2/show/NCT04273529?term=NCT04273529&draw=2&rank=1>
 216. Newfield C. New Medical Indications for Thalidomide and its Derivatives New Medical Indications for Thalidomide and its Derivatives. *The Science Journal of the Lander College of Arts and Sciences*. 2018;12(1).
 217. Biohaven pharmaceuticals. Biohaven receives FDA may proceed letter to begin phase 2 trial of intranasal vazegepant to treat lung inflammation after covid-19 infection. 2020; <https://www.biohavenpharma.com/investors/news-events/press-rel-eases/04-09-2020>. Accessed April 22, 2020.
 218. <https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker>. Accessed March 30, 2020
 219. <https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins>. Accessed March 30, 2020
 220. <https://statnano.com/news/67536/China%E2%80%99s-First-Coronavirus-Vaccine-Delivered-for-Human-Trials>. Accessed March 30, 2020.
 221. Zhu, F.-C., et al., *Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial*. The Lancet. Epub ahead of print. 2020.
 222. <https://www.clinicaltrialsarena.com/news/oxford-university-covid-19-vaccine-trial/> Accessed March 30, 2020
 223. Moorlag SJCFM, Arts RJW, van Crevel R, Netea MG. Non-specific effects of BCG vaccine on viral infections. *Clinical Microbiology and Infection*. 2019;25(12):1473-1478.
 224. Hollm-Delgado M-G, Stuart EA, Black RE. Acute Lower Respiratory Infection Among Bacille Calmette-Guérin (BCG)-Vaccinated Children. *Pediatrics*. 2014;133(1):e73.
 225. Covián C, Fernández-Fierro A, Retamal-Díaz A, et al. BCG-Induced Cross-Protection and Development of Trained Immunity: Implication for Vaccine Design. *Front Immunol*. 2019;10:2806-2806.
 226. Miller A, Reandelar MJ, Fasciglione K, Roumenova V, Li Y, Otazu GH. Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: an epidemiological study. *medRxiv*. 2020:2020.2003.2024.20042937.
 227. Hamiel, U., E. Kozler, and I. Youngster, *SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adults*. *JAMA*, 2020.
 228. BCG Vaccination to Protect Healthcare Workers Against COVID-19 (BRACE). 2020; <https://clinicaltrials.gov/ct2/show/NCT04327206>. Accessed April 4, 2020.
 229. Ventures A. Healthcare innovations to combat Coronavirus. 2020; <https://www.av.co/covid>. Accessed April 8, 2020

This HFH COVID-19 Update is intended for the members of the Department of Neurology Henry Ford Hospital. Information concerning COVID-19 is rapidly evolving and the present text represents the authors' current interpretation, understanding, and evaluation of data at the time of writing. This update does not represent the official position of Henry Ford Hospital regarding COVID-19. For current updates concerning COVID-19, readers should consult the CDC website.