Covid-19 Panel Discussion (Covid-19 & Stroke)

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Learning Objectives

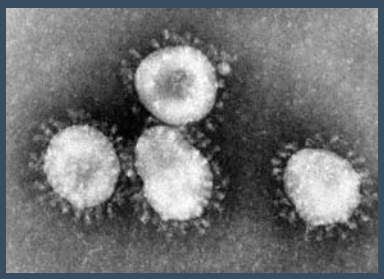
- Identify some basics concepts of the coronavirus
- Identify why the coronavirus may attack the central nervous system
- Identify the cerebrovascular complications of COVID-19
- Live Panel Discussion

Coronavirus Basics

Coronavirus Basics

- The coronavirus is normally found in avian and mammalian species
- Was originally grouped into the family *Coronaviridae* on the basis of the “crown” or “halo-like” appearance given by the glycoprotein-studded envelope on electron microscopy

BSIP/Universal Images Group via Getty

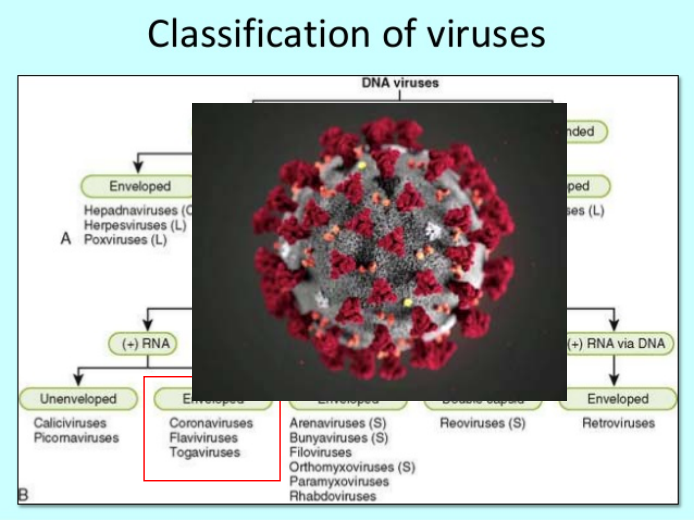


https://en.wikipedia.org/wiki/File:Coronaviruses_004_lores.jpg

Medical Microbiology. 4th edition. Chapter 60 - Coronaviruses
Baron S, editor. Galveston (TX): University of Texas Medical Branch at Galveston ; 1996.

Coronavirus Basics

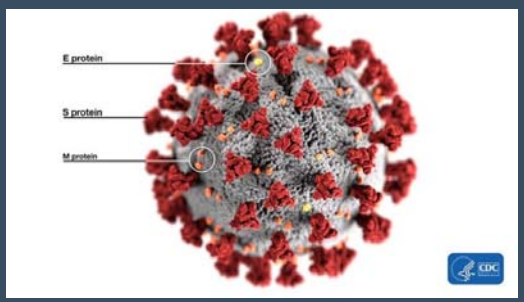
- Coronavirus is a positive-sense, single-stranded, enveloped, RNA virus
- The **envelope** is studded with projecting glycoproteins
  - Responsible for attachment to host cells
  - Also carries the main antigenic epitopes (recognized by neutralizing antibodies)
- The **core** consists of the single-strand RNA associated with nucleoprotein



https://www.slideshare.net/rakshithjnvd/viral-classification-and-types-of-replication-in-virus

Coronavirus Basics

- Although mucus and cilia generally clear the airways of particles, coronaviruses actually **infect the superficial cells of the ciliated epithelium**.
- Coronavirus membrane surface has 3 proteins:
  - **'S' (spike) Protein** – Allows for recognition of target receptor to bind on mucosal epithelium and invade
  - 'E' (envelope) protein
  - 'M' (membrane) protein

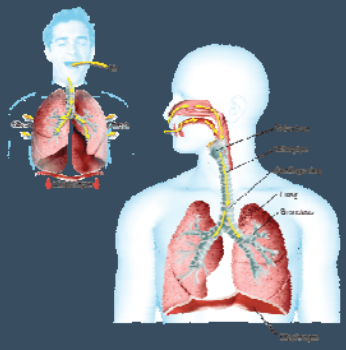


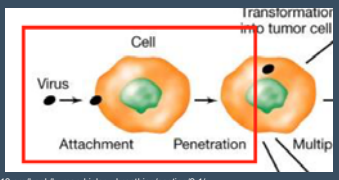
Medical Microbiology. 4th edition. Chapter 60 – Coronaviruses. Baron S, editor. Galveston (TX): University of Texas Medical Branch at Galveston; 1996.

Jin H, Hong C, Chen S, et al. Consensus for prevention and management of coronavirus disease 2019 (COVID-19) for neurologists. Stroke & Vascular Neurology 2020;

Coronavirus Basics

- Coronaviruses invade the respiratory tract via the nose
- After an incubation period of *about 3 days*, they cause the symptoms of a common cold, including nasal obstruction, sneezing, runny nose, and occasionally cough
- The disease *usually* resolves in a few days, during which virus is shed in nasal and droplet secretions.





https://www.ck12.org/book/human-biology-breathing/section/2.1/

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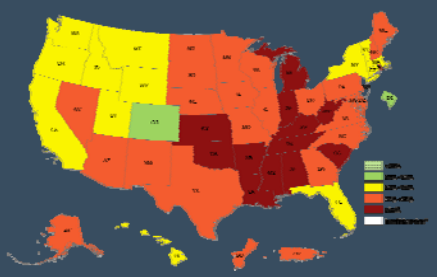
Baron S, editor. Galveston (TX): University of Texas Medical Branch at Galveston; 1996.

Coronavirus Basics

- SARS-CoV-2 seems to have a heightened immunogenic capability unlike other coronaviruses in some individuals – especially for:
  - Obese
  - Pregnant
  - Elderly
- In days 7-10 for these individuals, instead of just a viral syndrome, go on to have a much more robust immune response
  - Hypercoaguable
  - SIRS/Sepsis
  - Cytokine Release Storm

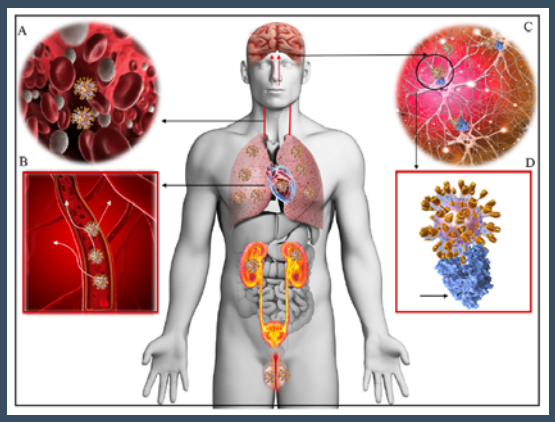


https://www.cdc.gov/obesity/data/obesity-and-covid-19.html

Ko JY, Danielson ML, Town M, Derado G, Greenlund KJ, Daily Kirley P, Alden NB, Yousey-Hindes K, Anderson EJ, Ryan PA, Kim S, Lynfield R, Torres SM, Barney GR, Bennett NM, Sutton M, Talbot HK, Hill M, Hall AJ, Fry AM, Garg S, Kim L; COVID-NET Surveillance Team. Risk Factors for COVID-19-associated hospitalization: COVID-19-Associated Hospitalization Surveillance Network and Behavioral Risk Factor Surveillance Systemexternal icon. Clin Infect Dis. 2020 Sep 18

SARS-CoV-2

- Spike glycoproteins are essential for viral entry via the ACE-2 receptor
- Expression of ACE-2 receptors are seen in may cell types, including the neurons and glial cells of the brainstem lending to potential neurotropism of SARS-CoV-2
- Possibility for neurological complications through both direct and indirect neurotropism

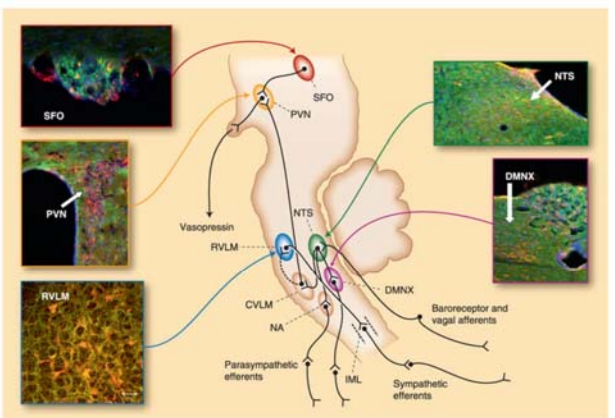


Coutard B, Valle C, de Lamballerie X, Canard B, Seidah NG, Decroly E. The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. Antiviral Res 2020; 176:104742. doi:10.1016/j.antiviral.2020.104742
Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B beta- coronaviruses. Nat Microbiol 2020; 5(4):562–569. doi:10.1038/ s41564-020-0688-y

SARS-CoV-2

ACE2 expression in the brain of mouse

- key regions that regulate blood pressure and fluid homeostasis
  - subfornical organ
  - neurons of the paraventricular nucleus (PVN),
  - nucleus of tractus solitarii (NTS),
  - dorsal motor nucleus of the vagus (DMNX),
  - rostral ventrolateral medulla (RVLM).
  - Caudal ventrolateral medulla
  - Intermediolateral cell column;
  - Nucleus ambiguous



Angiotensin-converting enzyme 2 (ACE2) expression in the mouse brain. ACE2 is widely expressed throughout the mouse brain, including in key brain regions involved in the regulation of blood pressure and body fluid homeostasis. This shows examples of ACE2 expression (red) in the subfornical organ (SFO), the neurons of the paraventricular nucleus (PVN), the nucleus of tractus solitarii (NTS), the dorsal motor nucleus of the vagus (DMNX), and the rostral ventrolateral medulla (RVLM). Green: MAP2 (neuronal marker); blue: DAPI (nuclei marker). CVLM—caudal ventrolateral medulla; IML—intermediolateral cell column; NA—nucleus ambiguus.

Cell Transplant. 2010; 12(3): 170–175.

Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol.

ACE-2 and SARS-CoV-2 Theories

- ACE2 is also expressed in some neuronal populations – especially in cardiorespiratory centers in brainstem, raphe nucleus, hypothalamus and motor cortex
  - May play a role in central respiratory failure
  - This may allow the virus to have other neurotropic effects
- SARS-CoV-2 may gain access to the CNS via the olfactory receptor neurons (some patients experience anosmia)
  - Medullary cardiorespiratory may play role in central respiratory failure as a direct result of this
- SARS-CoV-2 infects both neurons and glia – this can cause an inflammatory response leading to a breakdown of the BBB

ACS Chem. Neurosci. 2020, 11, 995−998
Jin H, Hong C, Chen S, et al. Consensus for prevention and management of coronavirus disease 2019 (COVID-19) for neurologists. Stroke & Vascular Neurology 2020;0

Acute necrotizing encephalopathy (ANE) was reported:

- Generally a rare complication of influenza and other viral infections and has been related to intracranial cytokine storms
- Results in blood-brain-barrier breakdown, but without direct viral invasion or parainfectious demyelination
- Proposed neurotropic mechanisms have been published and involve viral access to the CNS through systemic circulation or across the cribriform plate of the ethmoid bone leading to symptoms of hyposmia and hypogeusia

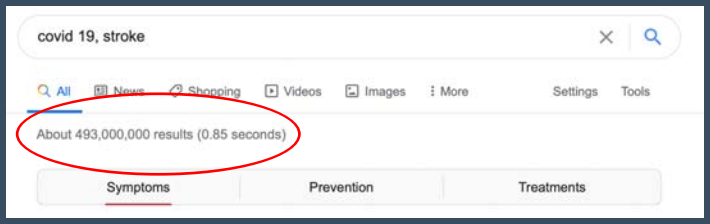
Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated Acute Hemorrhagic Necrotizing Encephalopathy: CT and MRI Features [published online ahead of print, 2020 Mar

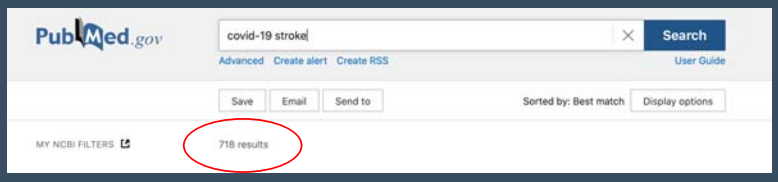
First retrospective study of COVID-19 neurological manifestations

- 221 patients at a single center in China
  - 5% cases had ischemic stroke
  - 0.5% CVST
  - 0.5% ICH.
  - Ischemic and hemorrhagic strokes, impaired consciousness and muscle injury were more prevalent in patients with more severe respiratory disease

Mao, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. Lancet Neurol (Preprint). Published online February 25, 2020.
Li, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Lancet Neurol (Preprint). Published online March 13, 2020.

COVID-19 Related Stroke





Acute Cerebrovascular Events

- With previous coronavirus outbreaks (SARS-CoV-1, MERS, etc), ischemic stroke was reported.
- Several case series published COVID-19 related stroke
  - Case series from NYC population reported LVO in 5 patients younger than 50. All had lymphopenia and elevated inflammatory markers on admission, 2 had no symptoms on admission
  - Systematic review of 39 patients from 6 studies showed mean age of 61.4, almost all had underlying risk factors (DM, HPL, HTN, CVA), and half died.

Oxley TJ, Mocco J, Majidi S, et al. Large vessel stroke as a presenting feature of COVID-19 in the young. N Engl J Med 2020; 382(20):e60. doi:10.1056/NEJMc2009787
Potential neurological symptoms of COVID-19.Wang HY, Li XL, Yan ZR, Sun XP, Han J, Zhang BW. Ther Adv Neurol Disord. 2020; 13

Acute Cerebrovascular Events

- How much higher of a ischemic stroke risk?
  - It was noted in a recent JAMA article that there is a 7.6-fold increase in the odds of stroke with COVID-19 compared with influenza
  - Reported incidence of cerebrovascular disease in patients testing positive for SARS-CoV-2 ranges from 1% to 6%

https://www.forbes.com/sites/robertglatter/2020/04/27/why-is-covid-19-coronavirus-causing-strokes-in-young-and-middle-aged-people/#835ec8134df4

Merkler AE, Parikh NS, Mir S, et al. Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) vs patients with influenza. JAMA Neurol. 2020
Ellul MA, Benjamin L, Singh B, et al. Neurological associations of COVID-19.Lancet Neurol. 2020; 19: 767-783

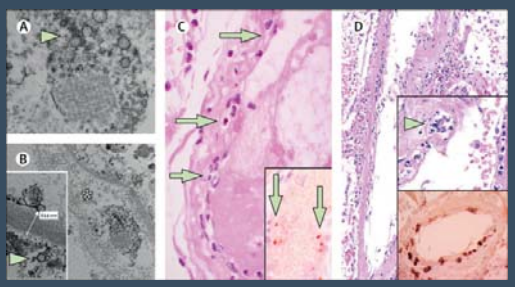
Acute Cerebrovascular Events

- Several Hypotheses of increased stroke risk:
  - Hypercoagulable state due to “sepsis-induced coagulopathy”
    - Elevated levels of d-dimer, fibrinogen, CRP and prothrombin time
    - Some improvement seen in studies with heparin/LMWH
    - Antiphospholipid antibodies were reported in patient with multiple territory stroke
  - SARS-CoV-2 also binds to and depletes ACE-2 through receptor endocytosis upon viral entry on brain endothelial and smooth muscle cells
    - ACE2 directly cleaves angiotensin II and angiotensin and has a direct anti-inflammatory effect.
    - ACE1 is left unopposed with generation of angiotensin II
    - May lead to pro-inflammatory state with further worsening of hypertensive state, lung injury and autonomic dysregulation

Hess, D.C., Eldahshan, W. & Rutkowski, E. COVID-19-Related Stroke. Transl. Stroke Res. 11, 322–325 (2020).

Acute Cerebrovascular Events

- Other proposed mechanisms for these cerebrovascular events include:
  - Post-infectious immune-mediated response
  - Direct viral-induced endotheliitis or endotheliopathy, potentially leading to angiopathic thrombosis, with viral particles having been isolated from the endothelium of various tissue, including brain tissue



Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19.Lancet. 2020; 395: 1417-1418
Paniz-Mondolfi A, Bryce C, Grimes Z, et al. Central nervous system involvement by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).J Med Virol. 2020; 92: 699-702
Fifi, JT Mocco, J. COVID-19 related stroke in young individuals. Lancet 2020; (19) 9: 713-715

Acute Ischemic Stroke

- There are several reports of COVID-19 presenting with thrombotic events, which has led to starting anticoagulation therapy early in the COVID-19 disease course before any thrombotic event.
- There are also reports in the literature specifically addressing macrothrombosis in the internal carotid artery in patients with mild respiratory symptoms of COVID-19 and stroke as a presenting symptom of the disease.

33yo female
no pMhx
Recent cough, no fevers

55yo male
pMhx: DM
Sx: Low grade fever
minimal oxygen req

Fifi, JT Mocco, J. COVID-19 related stroke in young individuals. Lancet 2020; (19) 9: 713-715
Fara MG, Stein LK, Skliut M, Morgello S, Fifi JT, Dhamoon MS Macrothrombosis and stroke in patients with mild Covid-19 infection. J Thromb Haemost. 2020
Mohamud AY, Griffith B, Rehman M, et al.Intraluminal carotid artery thrombus in COVID-19: another danger of cytokine storm?. AJNR Am J Neuroradiol. 2020

Acute Ischemic Stroke In The Young

- There has been an increase in the incidence of stroke in the young with COVID-19
  - As mentioned before - 5 patients younger than 50 years who tested positive for SARS-CoV-2, some with no vascular risk factors, were admitted with large vessel stroke during a 2-week period (March 23 to April 7, 2020) at the height of the pandemic in NYC
  - The mean patient age in several thrombectomy case series of COVID-19 patients showed:
    - mean age of 52.8 years in a series from NYC
    - mean age of 59.5 years in a series from Paris
    - mean age of 59.5 years in a combined series from NYC and Philadelphia
  - Data from the Mount Sinai Health System in New York City confirm that patients who tested positive for SARS-CoV-2 were significantly younger, with a mean age of 59 years than patients who tested negative for SARS-CoV-2, who had a mean age of 74 years

Oxley TJ, Mocco J, Majidi S, et al. Large vessel stroke as a presenting feature of COVID-19 in the young. N Engl J Med 2020; 382(20):e60. doi:10.1056/NEJMc2009787
Majidi SFJ, Fifi JT, Ladner TR, et al. Emergent large vessel occlusion stroke during New York City's COVID-19 outbreak: clinical characteristics and paraclinical findings. Stroke. 2020
Fifi, JT Mocco, J. COVID-19 related stroke in young individuals. Lancet 2020; (19) 9: 713-715
Wang A, Mandigo GK, Yim PD, Meyers PM , Lavine SD. Stroke and mechanical thrombectomy in patients with COVID-19: technical observations and patient characteristics. J Neurointerv Surg. 2020; 12: 648-653
Escalard S, Maïer B, Redjem H, et al. Treatment of acute ischemic stroke due to large vessel occlusion with COVID-19: experience from Paris. Stroke. 2020; 51: 2540-2543
Sweid A, Hammoud B, Bekelis K, et al. Cerebral ischemic and hemorrhagic complications of coronavirus disease 2019.Int J Stroke. 2020

COVID & Acute Ischemic Stroke

- Severe COVID-19 shares common risk factors with cerebrovascular diseases, and it is currently unclear whether the infection represents an independent stroke risk factor.
- A case-control analysis of acute stroke protocol imaging from late March to early April, 2020, across a large New York City health system showed that, after adjusting for age, sex, and vascular risk factors, SARS-CoV-2 positivity was independently associated with stroke
- The majority of stroke services worldwide have been negatively influenced in terms of care delivery and fear to access healthcare services
  - Stroke and ICH volumes have dropped in both COVID-19 and non-COVID-19 populations
  - NSGY volumes have dropped as well
  - Neurologists had a drop in their normal clinical outpatient volumes

Fifi, JT Mocco, J. COVID-19 related stroke in young individuals. Lancet 2020; (19) 9: 713-715

Tsivgoulis G, Palaiodimou L, Katsanos AH, et al. Neurological manifestations and implications of COVID-19 pandemic. Ther Adv Neurol Disord. 2020;13:1756286420932036.

Acute Ischemic Stroke Workup during the COVID Pandemic

- In otherwise healthy, young patients who present with stroke during the pandemic, the diagnosis of COVID-19 should be thoroughly investigated
- In patients with mild COVID-19 respiratory symptoms, a low threshold for investigation for stroke should be maintained if they present with new neurological symptoms

Fifi, JT Mocco, J. COVID-19 related stroke in young individuals. Lancet 2020; (19) 9: 713-715

Other Acute Ischemic Stroke Care Considerations during COVID 19 Pandemic

- The stroke community should be prepared for a shortage of physicians if numbers of COVID-19 patients begin to spike again (illness, redeployment)
- Neurointerventionalist quarantine could be devastating to a healthcare institution as they are a scarce resource
- Priority of scarce hospital beds to those patients eligible for indispensable interventions per local protocols, such as revascularization with thrombolytics or mechanical thrombectomy, surgical interventions such as hemicraniectomy or posterior fossa decompression, or severe strokes that benefit from a specialized stroke unit or neurologic intensive care management

Enrique C. Leira, Andrew N. Russman, José Biller, Devin L. Brown, Cheryl D. Bushnell, Valeria Caso, Angel Chamorro, Claire J.Creutzfeldt, Salvador Cruz-Flores, Mitchell S.V. Elkind, Pierre Fayad, Michael T. Froehler, Larry B. Goldstein, Nicole R. Gonzales, BrianKaskie, Pooja Khatri, Sarah Livesay, David S. Liebeskind, Jennifer J.Majersik, Asma M. Moheet, Jose G. Romano, Nerses Sanossian, Lauren H. Sansing, Brian Silver, Alexis N. Simpkins, Wade Smith, David L. Tirschwell, David Z. Wang, Dileep R. Yavagal, Bradford B.Worrall. Preserving stroke care during the COVID-19 pandemic. Potential issues and solutions. Neurology Jul 2020, 95 (3) 124-133

Other Acute Ischemic Stroke Care Considerations during COVID 19 Pandemic

- Hospitals that normally admit all patients post-IV thrombolysis and ICH to an ICU could develop a protocol with the critical care/neurocritical care team to place less acute patients in a step-down unit
- For patients admitted with suspected or confirmed COVID-19, telemedicine may allow the required and appropriate neurologic monitoring while limiting exposure of staff or consumption of PPE
- A low threshold to start with GETA for agitated patients may be advisable for endovascular procedures. Also, consideration can be given to eventually extubate these patients in a different location than the angiography suite preferably to minimize aerosolization and contamination

Enrique C. Leira, Andrew N. Russman, José Biller, Devin L. Brown, Cheryl D. Bushnell, Valeria Caso, Angel Chamorro, Claire J.Creutzfeldt, Salvador Cruz-Flores, Mitchell S.V. Elkind, Pierre Fayad, Michael T. Froehler, Larry B. Goldstein, Nicole R. Gonzales, BrianKaskie, Pooja Khatri, Sarah Livesay, David S. Liebeskind, Jennifer J.Majersik, Asma M. Moheet, Jose G. Romano, Nerses Sanossian, Lauren H. Sansing, Brian Silver, Alexis N. Simpkins, Wade Smith, David L. Tirschwell, David Z. Wang, Dileep R. Yavagal, Bradford B.Worrall. Preserving stroke care during the COVID-19 pandemic. Potential issues and solutions. Neurology Jul 2020, 95 (3) 124-133

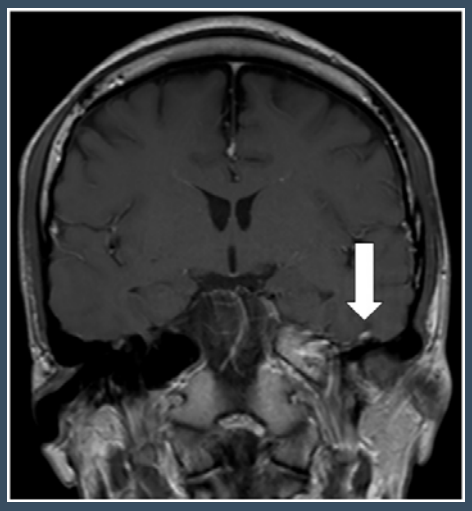
COVID 19 Neuromuscular disease

- Peripheral Nervous System also is affected.
- Severe deficits, axonal involvement and respiratory failure with subsequent need for mechanical ventilation were reported among a cohort of patients. Guillain-Barré syndrome was diagnosed 5 to 10 days after the onset of COVID-19 symptoms
- PNS involvement has also been documented in two patients who were diagnosed with Miller-Fisher syndrome and polyneuritis cranialis at 3 to 5 days after exhibiting COVID-19-related symptoms

Zhao H, Shen D, Zhou H, et al. Guillain-Barre syndrome associated with SARS-CoV-2 infection: causality or coincidence Lancet Neurol.1April 2020
Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain–Barré Syndrome Associated with SARS-CoV-2]. N Engl J Med. 2020.
Gutiérrez-Ortiz C, Méndez A, Rodrigo-Rey S, San Pedro-Murillo E, Bermejo-Guerrero L, Gordo-Mañas R, et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19. 2020 Apr 17. Neurology. 2020.

Cranial Nerve Palsies

- CSF PCR was negative for herpes simplex virus, varicella zoster virus and SARS-CoV-2.
- His magnetic resonance imaging of the brain showed contrast enhancement of the left facial nerve (Figure)



Anosmia and Gustatory Dysfunction

- Anosmia (inability to smell) and dysgeusia (dysfunction of taste) are common symptoms associated with COVID-19, likely secondary to the direct olfactory bulb access.
- A study of 417 patients with mild to moderate COVID-19 symptoms in 12 European hospitals reported sudden onset olfactory and gustatory dysfunction with a prevalence of 86% and 88%, respectively.
- There was a 25% recovery from both symptoms within 2 weeks.

Lechien JR, Chiesa-Estomba CM, De Siati DR, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-mod- erate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol 2020; 277(8):2251–2261.

Desforges M, Le Coupanec A, Dubeau P, et al. Human coronavi- ruses and other respiratory viruses: underestimated opportunistic pathogens of the central nervous system? Viruses 2019; 12(1):14.

Neuropathological findings

- Neuropathologic specimens were not originally obtained in COVID-19 patients due to the risk of potential aerosolization of viral particulate matter
- Delay in obtaining samples for review
- CSF samples:
  - False negative (improper analysis of samples)
  - False positive (contamination of CSF with virus particles due to bleed, sampling)

Neuropathological Findings

- One study of 10 patients (post-mortem CSF analysis) showed no evidence of viral invasion and no signs of encephalitis and nervous system vasculitis by CSF PCR testing
- Another post-mortem tissue study of 6 patients showed localized perivascular and interstitial encephalitis with neuronal cell loss and axon degeneration in the dorsal motor nuclei of the vagus nerve, CN V, nucleus tractus solitarii, dorsal raphe nuclei, and fasciculus longitudinalis medialis, but no territorial infarctions

JAMA. 2020 Jun 23; 323(24): 2518–2520.
Lancet. 2020 20-26 June; 395(10241): e109.

Neuropathological Findings

Table 1: **Clinical characteristics and pathological findings of six COVID-19 fatal outcomes**

Age (years) /Sex	58/ Male	59/ Male	64/Male	74/ Female	79/ Female	82/ Male
Time between onset of symptoms and admission to hospital/ ICU	10 Days / 10 Days	7 Days / 9 Days	14 Days / 14 Days	7 Days / 9 Days	2 Days / 23 Days	10 Days / 11 Days
Duration of ventilation	6 Days, 13 Hours	14 Days, 22 Hours	3 Days, 21 Hours	13 Days, 23 Hours	8 Days, 5 Hours	2 Days, 18 Hours
Neurological symptoms upon admission to ICU	GCS = 12 Somnolent	GCS = 10 Somnolent	GCS = 12 Somnolent	GCS = 15 NNS	GCS = 15 NNS	GCS = 15 NNS
Medical history	AA	HT	HT	HT, COPD, CRF	HT, PHT, CRF, PAD, CAD	HT, AF
Laboratory parameters upon admission to ICU:						
C-reactive protein (mg/L) Procalcitonin (µg/L) Interleukin-6 (ng/L)	67,5 0,76 333,0	138,7 0,30 237,2	304,4 0,43 1226,0	75,1 0,21 431,7	113,7 0,60 255,2	261,1 3,38 180,4
Leucocytes (/nl) Platelets (/nl) LDH (U/L) CK (U/L) FDP (mg/L)	6,1 189 1144 317 1,29	12,2 163 522 829 0,38	14,4 289 862 155 5,65	5,6 123 391 894 4,16	12,2 400 369 53 4,38	19,7 663 445 82 2,61
Lungs*	-DAD -OPP (spotty) -PP -PC-TYP II -Invasive Aspergillosis -Lung Infarction -Spotty Areas of sec. BP	-Pan-OPP -Interstitial T-Cell Reaction -Capillaritis -PP -SQ Metaplasia -PC-Typ II	-DAD -OPP -Edema -Small Areas of Acute Pneumonia	-DAD -OPP -Edema -PHT -PC-TYP II -SQ Metaplasia	-DAD -OPP -PC-Typ II -SQ metaplasia -Edema	-DAD -OP Pattern -PHT -Acute Pneumonia -Acute Pleuritis -interstitial T-Cell Reaction
Brain and Brainstem § *	-Encephalitis -Lymphocytic Meningitis -Petechial Bleedings ‡	-Petechial Bleedings -Lymphocytic Meningitis ‡	-Encephalitis -Lymphocytic Meningitis -Petechial Bleedings -NCL -AD	-Encephalitis -Lymphocytic Meningitis -Alzheimers Disease -NCL -AD	-Encephalitis -Lymphocytic Meningitis -Petechial Bleedings -NCL	-Encephalitis -Lymphocytic Meningitis -NCL -AD
Liver*	Cirrhosis	Periportal and Lobular T-Cell Reaction	Centro-Acinar Necrosis	Fatty Changes	Centro-Acinar Necrosis	Periportal and Lobular T-Cell Reaction
Heart*	Biventricular Hypertrophy	No Pathological Findings	Biventricular Excentic Hypertrophy	-Biventricular Excentic Hypertrophy -CAD with Sclerosis	-CAD with Stenosis, -ACVR, -Myocardial Scaring	-Left Ventricular Hypertrophy -Left Atrial Dilatation
Cause of Death	Herniation due to Massive Cerebral Hemorrhage	Herniation due to Massive Cerebral Hemorrhage	Pulmonary Artery Embolism	Cardio-Respiratory Failure	Cardio-Respiratory Failure	Cardio-Respiratory Failure

*Morphological Findings are listed in the order of their frequency in the respective organ

Neuropathological Findings

- Another study of 18 patients (only 6 with neuro symptoms – myalgia[3], headache[2], decreased taste[1])
  - showed no evidence of stroke, herniation or olfactory bulb damage.
  - Microscopic Examination showed acute hypoxic injury in the cerebrum and cerebellum in all of the patients with loss of neurons in the cerebral cortex, hippocampus, cerebellar purkinje cell layer but no thrombi or vasculitis.
- Testing of brain tissue was performed with quantitative RT-PCR (qRT-PCR) for the SARS-CoV-2 nucleocapsid protein
- "In conclusion, histopathological examination of brain specimens obtained from 18 patients who died 0 to 32 days after the onset of symptoms of Covid-19 showed only hypoxic changes and did not show encephalitis or other specific brain changes referable to the virus"

IH Solomon et al. N Engl J Med 2020;383:989-992.

Neuropathological Findings

Table 1. Gross Findings and Results of Histologic Analysis to Detect SARS-CoV-2.*

Patient No.	Days from Symptom Onset to Death	Hours from Death to Autopsy	Gross Inspection		Histologic Analysis
			Brain Volume	Observations	
			grams		
1	20	52	1290	No gross abnormalities	Acute hypoxic ischemic damage, mild arteriolosclerosis
2	6	32	1460	Moderate atherosclerosis	Acute hypoxic ischemic damage
3	12	21	1210	Moderate atherosclerosis, chronic infarcts	Acute hypoxic ischemic damage, chronic infarcts, mild arteriolosclerosis
4	6	36	1150	Moderate-to-severe atherosclerosis, pale substantia nigra and locus coeruleus	Acute hypoxic ischemic damage, moderate arteriolosclerosis, pathological features of Lewy body disease and Alzheimer's disease
5	9	40	1460	No gross abnormalities	Acute hypoxic ischemic damage
6	0	77	1330	Mild atherosclerosis	Acute hypoxic ischemic damage, moderate arteriolosclerosis, focal leptomeningeal chronic inflammation
7	2	54	1300	Moderate atherosclerosis, cortical atrophy	Acute hypoxic ischemic damage, mild arteriolosclerosis, pathological features of Alzheimer's disease
8	2	32	1350	Moderate atherosclerosis, chronic infarcts	Acute hypoxic ischemic damage, chronic infarcts, moderate arteriolosclerosis
9	21	21	1330	Mild atherosclerosis	Acute hypoxic ischemic damage, mild arteriolosclerosis
10	7	21	1120	Moderate atherosclerosis, anaplastic astrocytoma tumor resection cavity	Acute hypoxic ischemic damage, recurrent or residual anaplastic astrocytoma
11	26	41	1090	No gross abnormalities	Acute hypoxic ischemic damage, Alzheimer's type II astrocytosis
12	6	45	1130	Mild atherosclerosis, pale substantia nigra	Acute hypoxic ischemic damage, mild arteriolosclerosis, pathological features of Lewy body disease and Alzheimer's disease
13	12	61	1300	No gross abnormalities	Acute hypoxic ischemic damage, mild arteriolosclerosis, focal perivascular chronic inflammation, Alzheimer's type II astrocytosis
14	0	102	1650	Moderate atherosclerosis	Acute hypoxic ischemic damage, moderate arteriolosclerosis
15	8	20	1530	Moderate atherosclerosis	Acute hypoxic ischemic damage, mild arteriolosclerosis, Alzheimer's type II astrocytosis
16	32	31	1150	Moderate atherosclerosis, chronic infarcts	Acute hypoxic ischemic damage, chronic infarcts, mild arteriolosclerosis
17	7	25	1300	Moderate atherosclerosis	Acute hypoxic ischemic damage, moderate arteriolosclerosis, focal perivascular chronic inflammation, pathological features of Alzheimer's disease
18	9	26	1350	Mild atherosclerosis	Acute hypoxic ischemic damage, single microglial nodule, Alzheimer's type II astrocytosis

* The results of immunohistochemical analysis to detect SARS-CoV-2 were negative in all the patients.

IH Solomon et al. N Engl J Med 2020;383:989-992.

Summary

- There is an increased incidence of hypercoagulability with severe COVID-19 Disease
- There is an increased risk of stroke with COVID-19 disease secondary which is multifactorial
- There is suggestion in the literature that COVID-19 may affect brain cells through direct neurotropism

Summary

- Staffing and bed prioritization may become imperative if COVID patient population spikes
- For patients admitted with suspected or confirmed COVID-19, telemedicine may allow the required and appropriate neurologic monitoring while limiting exposure of staff or consumption of PPE
- A low threshold to start with endotracheal intubation for agitated patients and select patients with COVID may be advisable for endovascular procedures.
- In otherwise healthy, young patients who present with stroke during the pandemic, the diagnosis of COVID-19 should be thoroughly investigated.
- In patients with mild COVID-19 respiratory symptoms, a low threshold for investigation for stroke should be maintained if they present with new neurological symptoms

COVID-19:
NYC Amidst the Surge

Pravin George, DO & Danielle Fait, RN
Neurointensive Care

Valerie Lopez, MD
Emergency Medicine

Cleveland Clinic

Author: **WKYC Staff**
Published: **4:21 PM EDT April 9, 2020**
Updated: **4:25 PM EDT April 9, 2020**

CLEVELAND — With the continued spread of the coronavirus pandemic, Cleveland Clinic has announced that it will be providing caregivers to some of the nation's hardest hit areas.

The Clinic says it has connected with hospitals in New York and Michigan who need critical care nurses, nurse practitioners, board-certified critical care and emergency medicine physicians, physician assistants and CT and X-ray technicians.

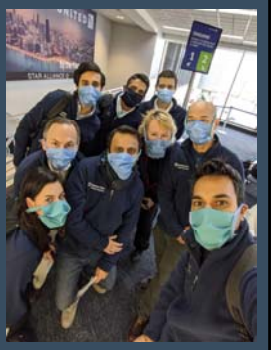
Who Went from CCF?

10 Physicians

15 Nurses

Expected for at least a 1-4 week deployment

- Could come back if sick
- Could come back if pandemic affected NE Ohio



What was the initial experience?

- Media

Queens - By The Numbers

Borough population: 2.3 million (27% of NYC)

50% White

28% Hispanic

24% Asian

21% Black

3% Mixed

48% Foreign born

56% Language other than English at home

Top Confirmed Cases by County

53,243 Queens
45,637 Kings
45,223 Cook
39,239 Bronx
37,152 Nassau
35,275 Suffolk

https://coronavirus.jhu.edu/

Top Counties by Number of Deaths

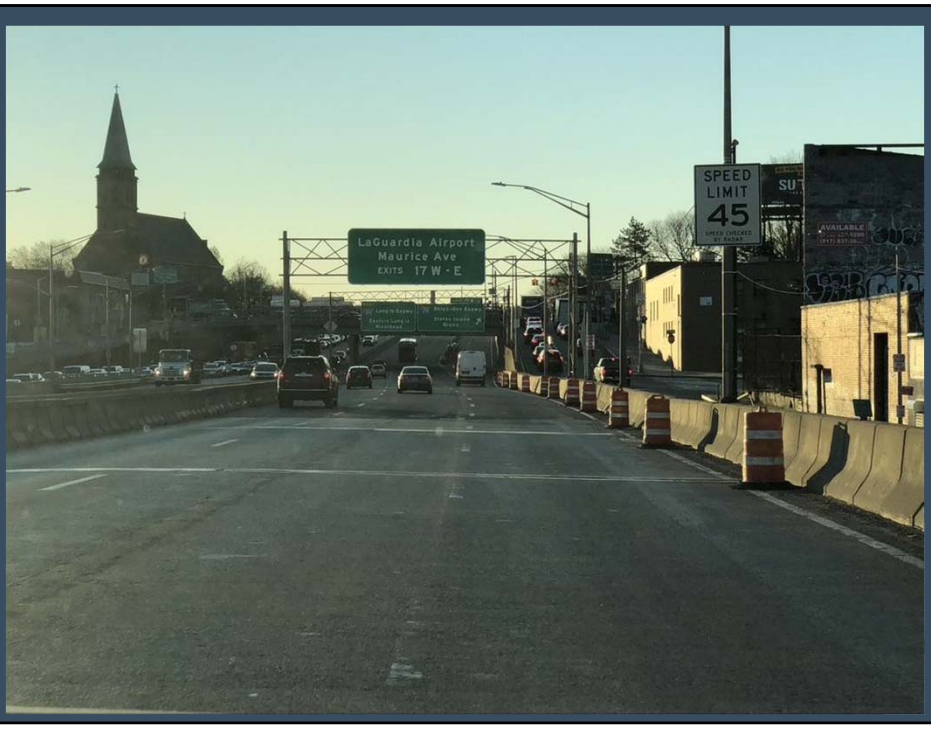
4,149 Queens
4,127 Kings
2,997 Bronx
1,945 Wayne
1,922 Cook
1,109 Nassau

https://coronavirus.jhu.edu/


SIX
THE MUSICAL
WINNER!
HADES
We are
in this
together.
We are
stronger
together.
AMERICAN EAGLE OUTFITTERS
CBAO


6:16 AM
NEW YORK CITY


CHASE
CHASE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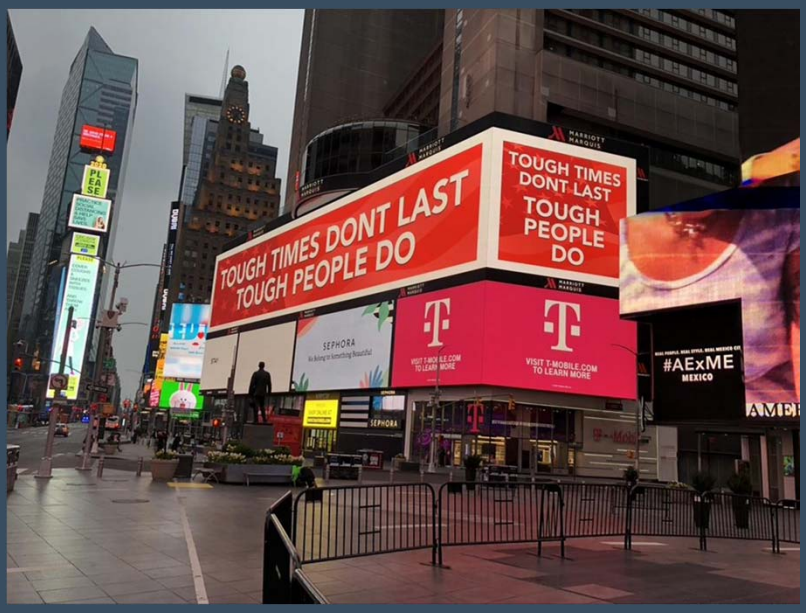
TOUGH TIMES DONT LAST
TOUGH PEOPLE DO
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VISIT T-MOBILE.COM
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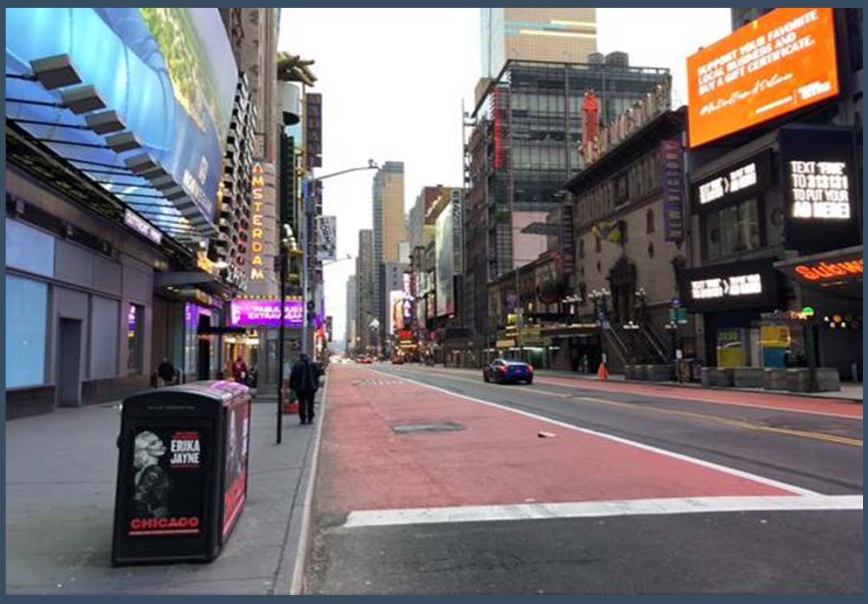
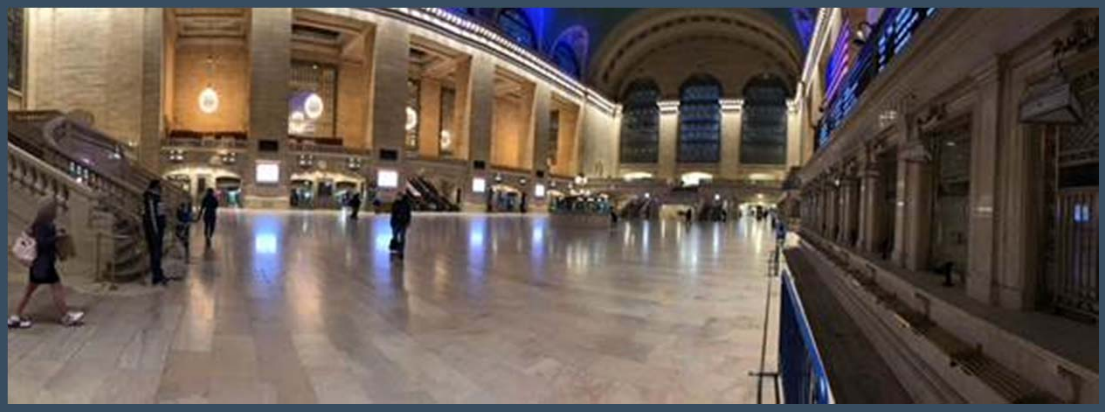


Broadway



NewYork-Presbyterian
Queens

- 535-bed tertiary care hospital
- Level I Trauma Center
- 15,000 Surgeries
- 162,000 Ambulatory care visits
- 124,000 ER visits

NewYork-Presbyterian
Queens

162K Patient care days*

CCF: 371k

Hillcrest: 116k

FV: 114k

AGMC: 103k

*American Hospital Directory

NewYork-Presbyterian
Queens

- ACGME Residency (115)
  - Internal Medicine (60), Surgery (31), Emergency Medicine (24)
- Fellowship (28)
  - CV (8), GI (6), ID (4)
  - Nephrology (5)
  - P/CCM (5)

Challenges

- Bed Capacity
- Equipment
- PPE
- Staff

Approach

- Negative pressure – Private – Cohort
- ICU's – PACU/Cath lab recovery – RNF overflow - Cafeteria
- 6 on/1 off, 7 on / 7 off, 3 on / 3 off
- Supervisory to Direct management
- All hands on deck

Effective Strategies

- Special teams
- Twice a day de-briefing
- Recharge Areas
- Volunteer integration

Live Panel Discussion