

Central Nervous System Effects of COVID-19: An Evolving Science

Cynthia Turner-Graham, M.D., DLFAPA
For Sound Mind Enterprises, Inc.

May 13, 2021



Central East (HHS Region 3)

MHTTC

Mental Health Technology Transfer Center Network

Funded by Substance Abuse and Mental Health Services Administration

MHTTC Network

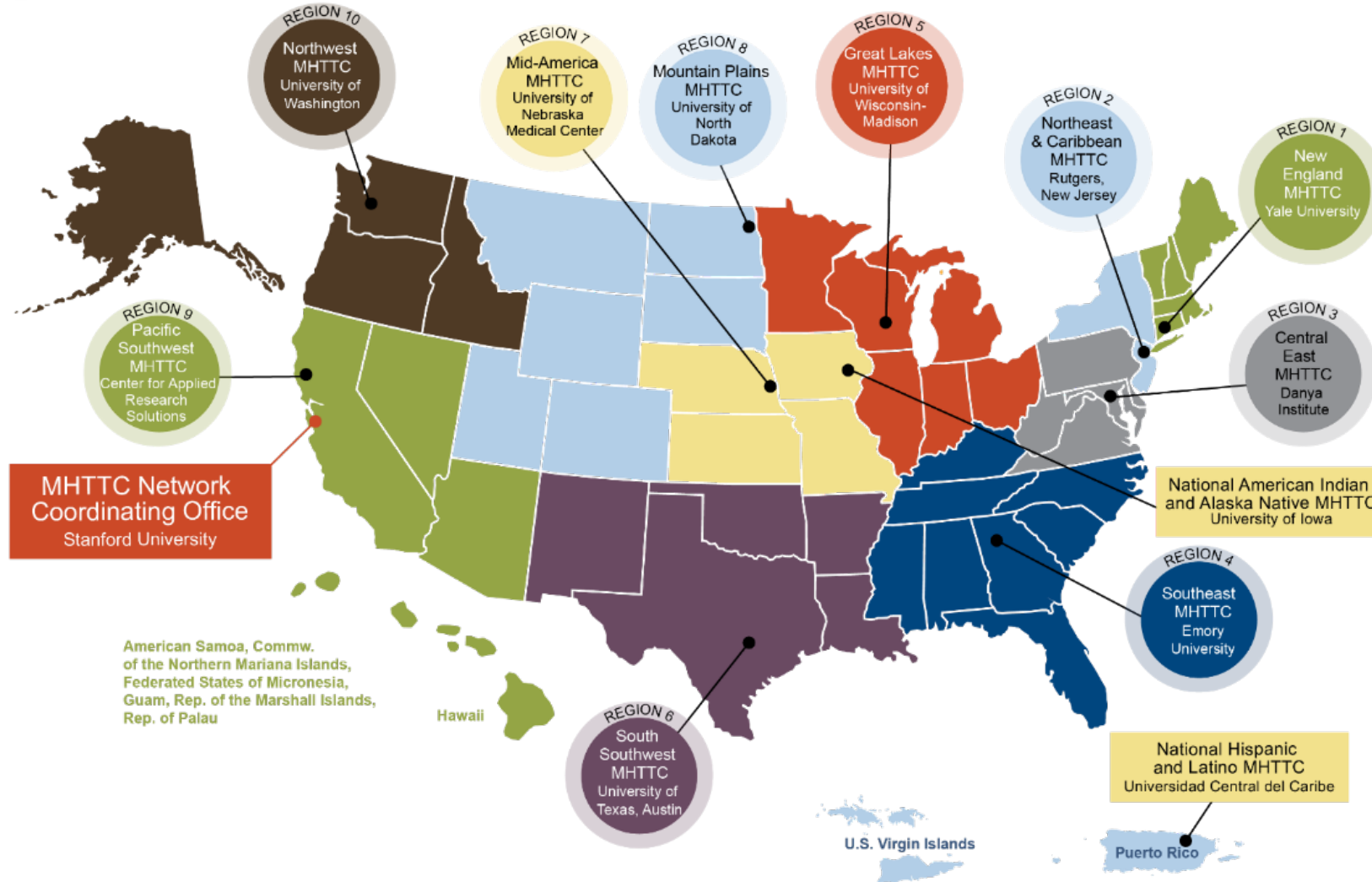


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MHTTC Purpose

The MHTTC Network vision is to unify science, education and service to transform lives through evidence-based and promising treatment and recovery practices in a recovery-oriented system of care.

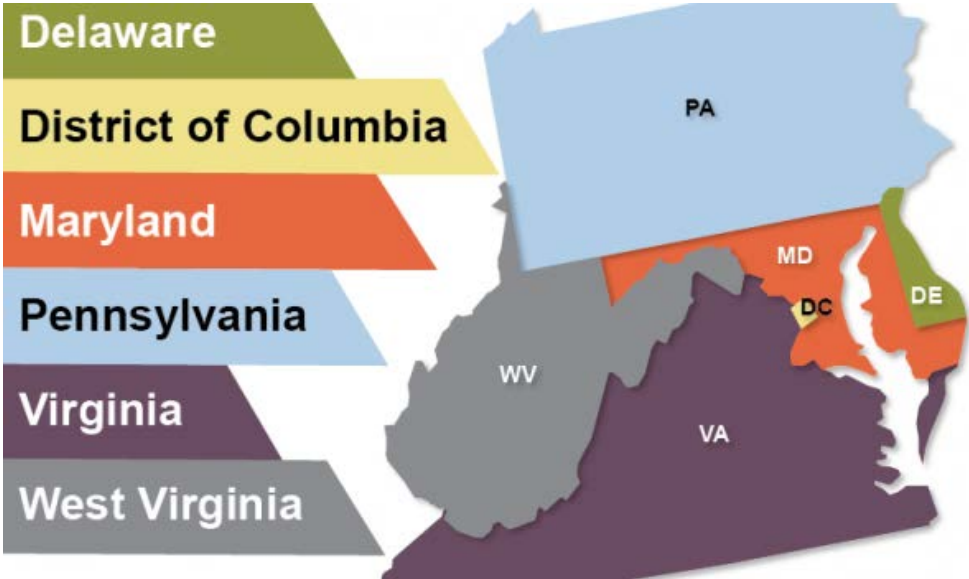


Central East MHTTC Goals

Funded by SAMHSA to:

- **Accelerate** the adoption and implementation of mental health related evidence-based practices
- **Heighten** the awareness, knowledge, and skills of the behavioral health workforce
- **Foster** alliances among culturally diverse practitioners, researchers, policy makers, family members, and consumers
- **Ensure** the availability and delivery of publicly available, free of charge, training and technical assistance

Central East Region 3



THE DANYA INSTITUTE



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At the time of this presentation, Tom Coderre served as Acting Assistant Secretary for Mental Health and Substance Use at SAMHSA. The opinions expressed herein are the views of the speakers, and do not reflect the official position of the Department of Health and Human Services (DHHS), or SAMHSA. No official support or endorsement of DHHS, SAMHSA, for the opinions described in this presentation is intended or should be inferred.

Evaluation Information

As part of receiving funding through SAMHSA to provide this training, the Central East MHTTC is required to submit data related to the quality of this event. At the end of today's presentation, please take a moment to complete a brief survey about today's training.

Central Nervous System Effects of COVID-19

An Evolving Science

Cynthia Turner-Graham, M.D., DFAPA
President-Elect, Black Psychiatrists of America

Health Equity Webinar Series
A collaboration of the Central MHTTC and the Black Psychiatrists of America
May 13, 2021

Moderator:
Annelle B. Primm, MD, MPH
Black Psychiatrists of America, Council of Elders

COVID-19: Unprecedented Disaster

- Disproportionate impact on Black and other marginalized communities with excess illness, death, and unemployment on top of multi-layered inequities in the social determinants of health
- COVID-19 infection can also affect the brain, mental health, and pre-existing mental illness adding to racial health disparities

Today's Program

- Special thanks to Central East MHTTC for its support of this eighth webinar in the Black Psychiatrists of America Health Equity Series
- Today's program features Cynthia Turner-Graham, MD, DFAPA, President-Elect of the Black Psychiatrists of America



Central Nervous System Effects of COVID-19: An Evolving Science

May 13, 2021

**Health Equity Webinar Series
Central East Mental Health Technology Transfer Center**

Cynthia Turner-Graham, MD, DLFAPA



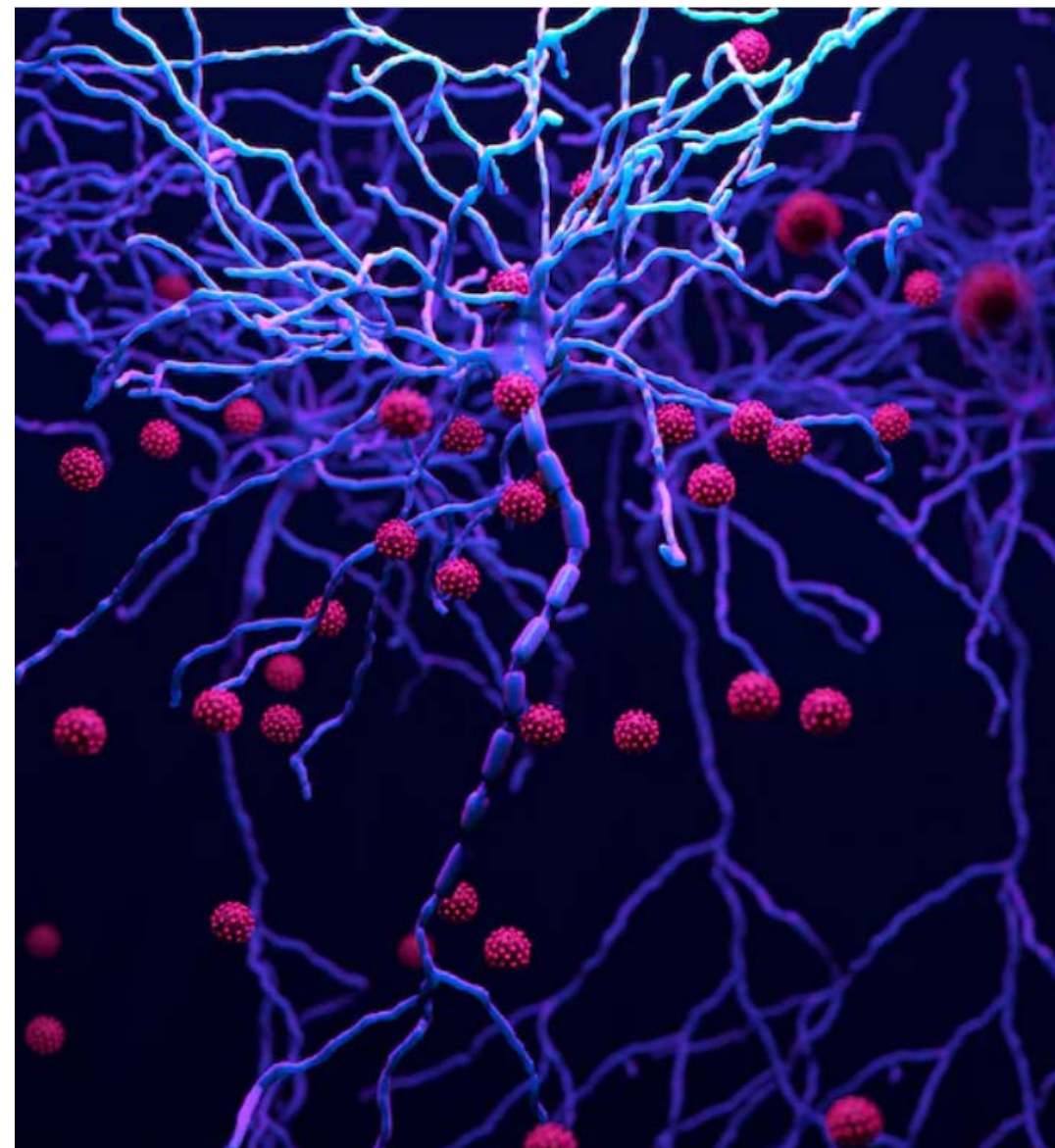
DocBLaw
@DocBLaw

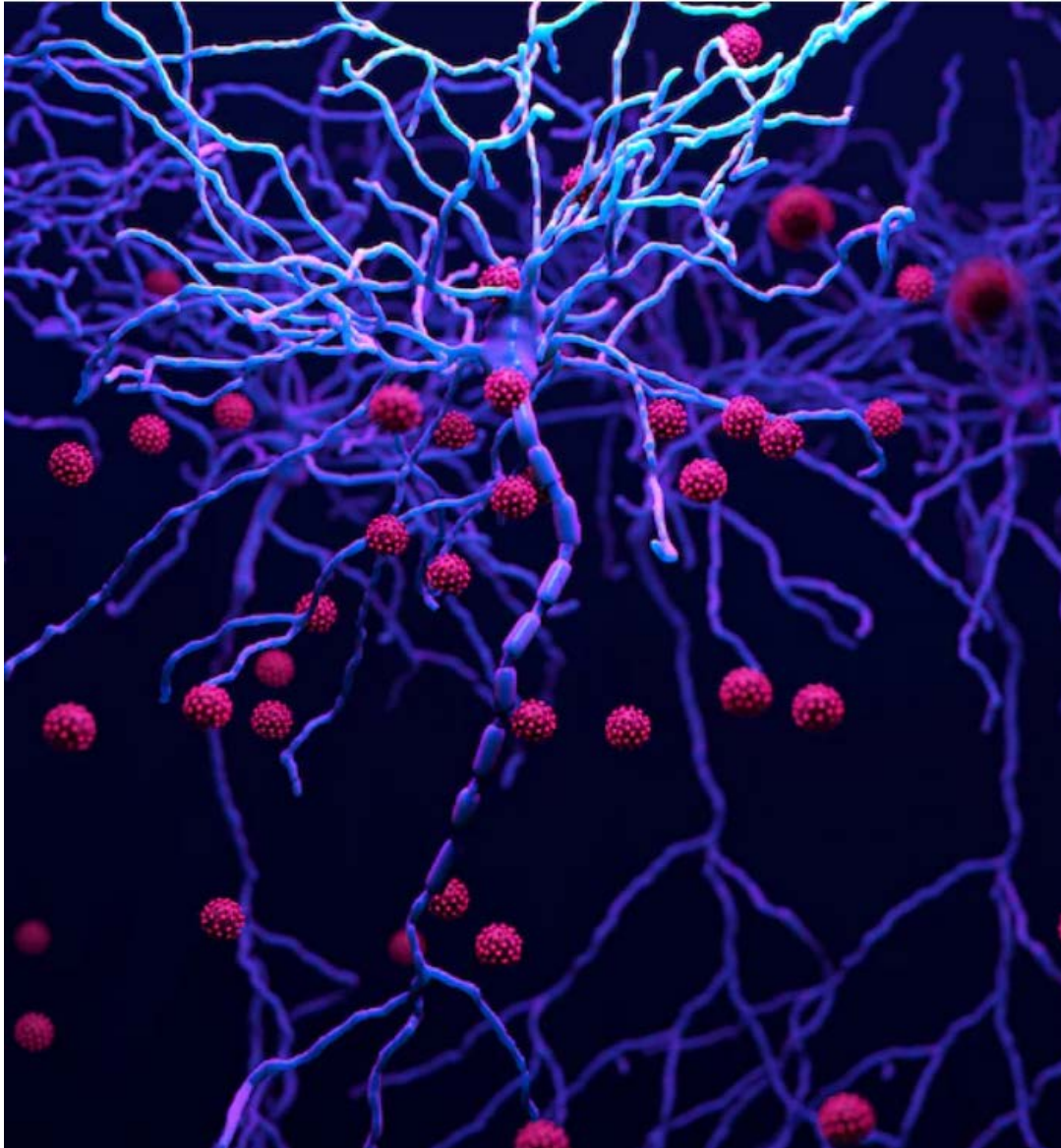


Yesterday I saw a perfectly healthy 37 yo pre covid. He contracted the illness in January. He's still on 3L of oxygen at all times and not improving. But, you know, keep quoting death and survival rates only.

4:52 PM · 4/26/21 · [Twitter for Android](#)

3,607 Retweets **135** Quote Tweets **15.8K** Likes





Replying to @DocBLaw

I'm 26. Contracted COVID in January. Due to lingering neurological problems, I've basically been forced to resign from my job, I've been unable to find one that I can actually physically/mentally do now, and I'm relying on my mom to stay afloat.

Yeah, I "survived."

13 36 267

This pales in comparison to the person you described. But it's just more proof that the "survived" doesn't mean "recovered."

I'm in two Facebook support groups for long-haulers — both with tens of thousands of people in them. Many of them unable to work as a result.

3 10 166

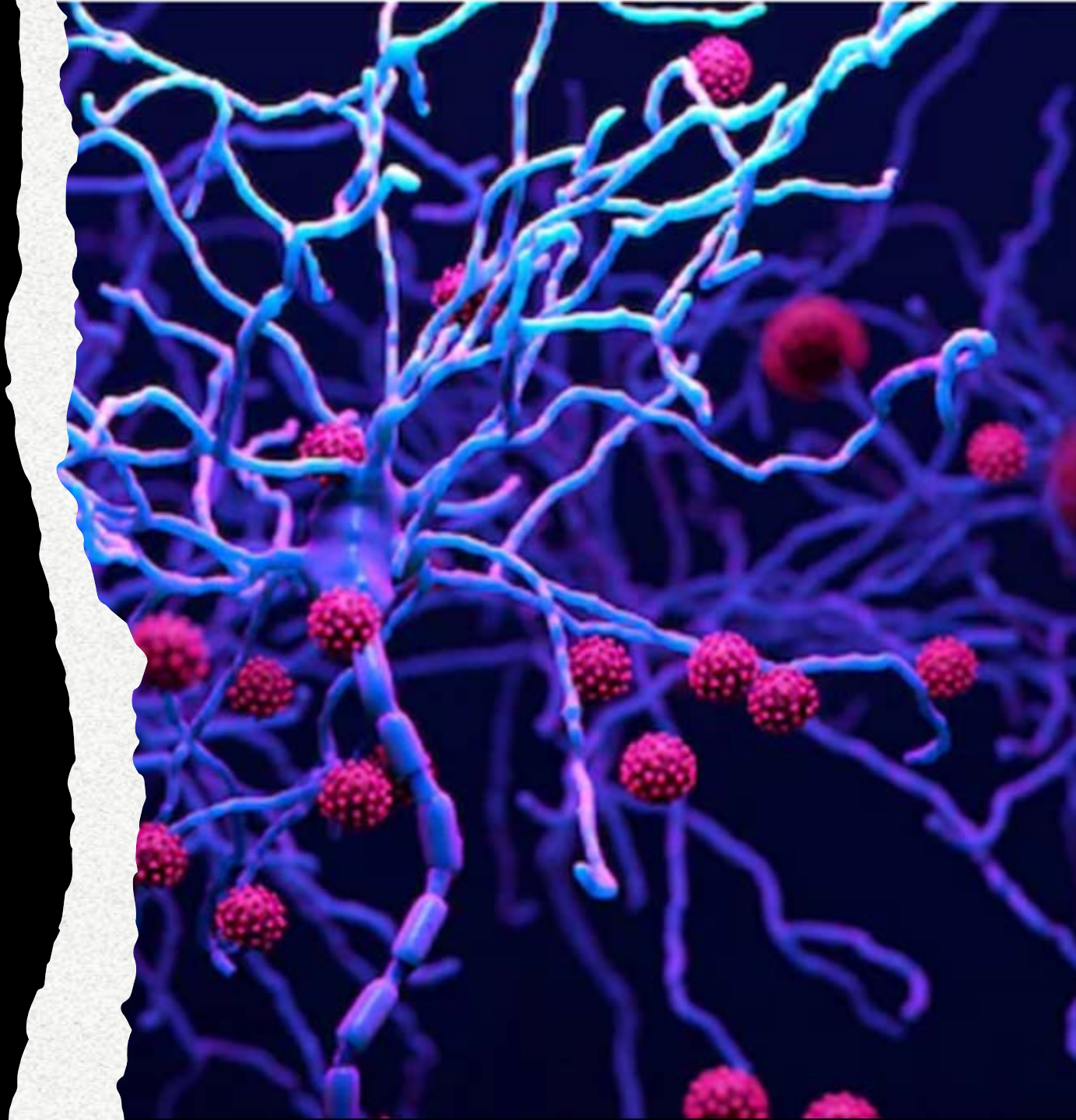


Central Nervous System Effects of CoVID-19

- **Why this is important**
- **Pathophysiology of CoVID-19**
- **Range of clinical presentations**
- **Neurological signs and symptoms**
- **What we can expect going forward**
- **Treatment Considerations**

Why this is important

- Medical and mental health providers deliver well-informed, compassionate care and treatment to those affected
- Address neurologic symptoms within larger syndrome of CoVID-19
- Effectively advocate for our patients' complex needs



PATHOPHYSIOLOGY

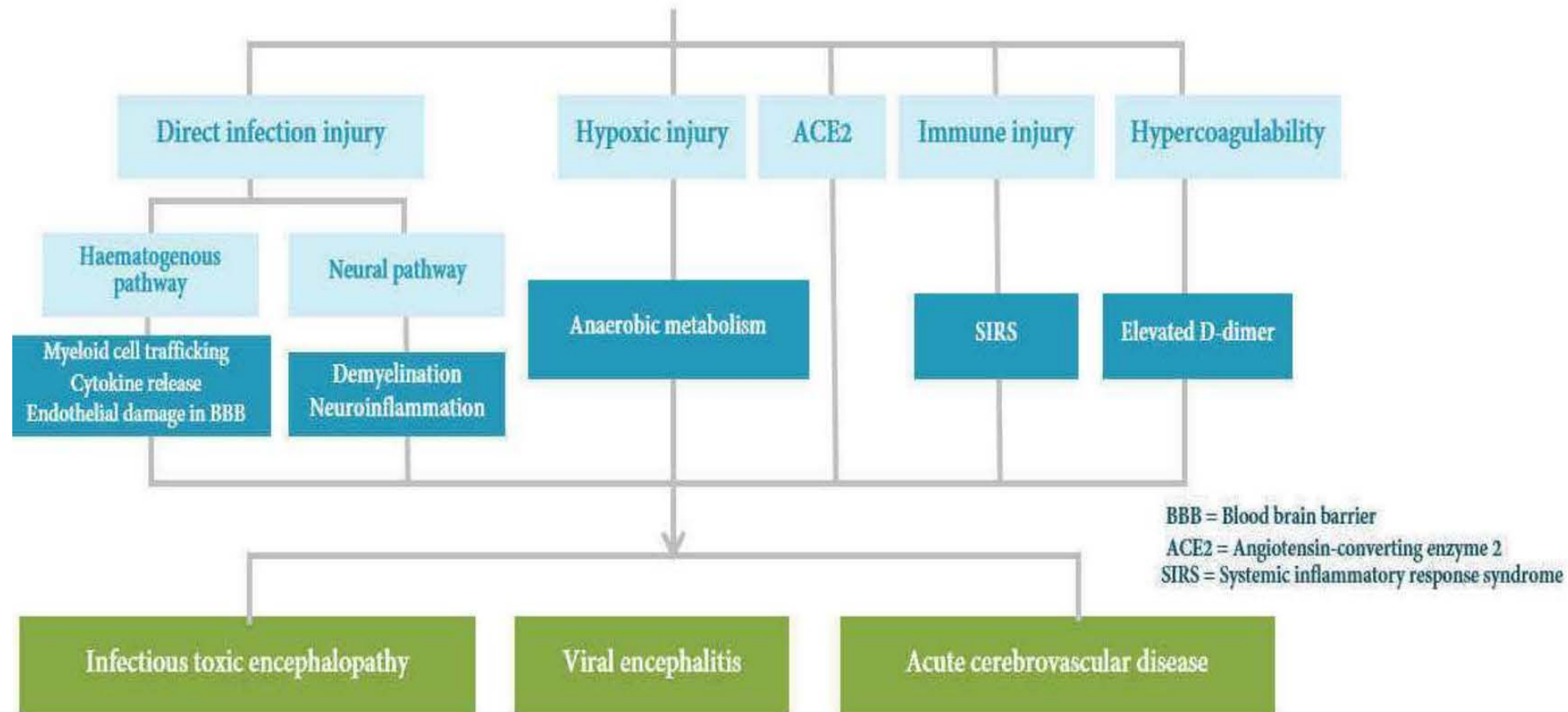


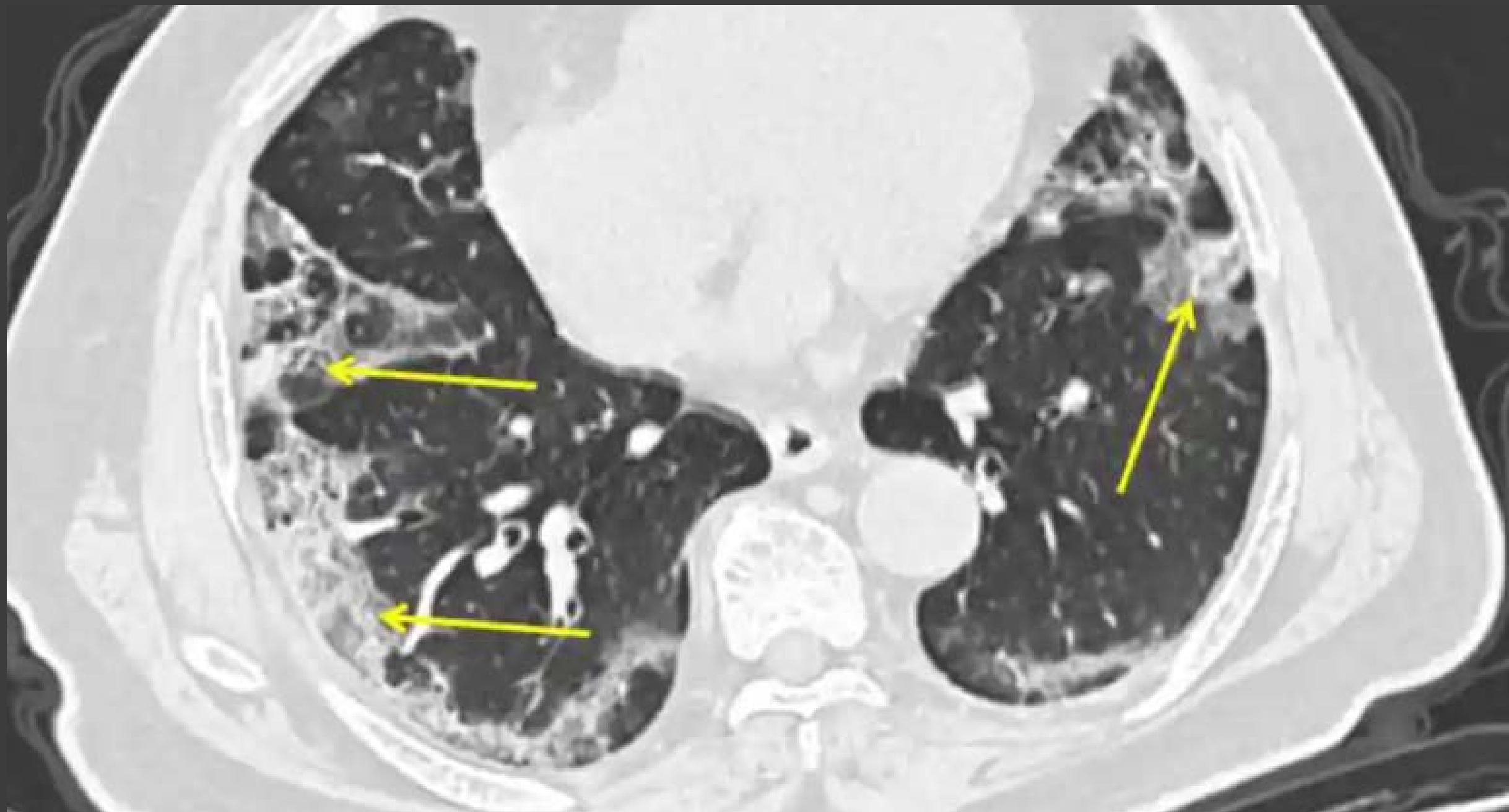
PATHOPHYSIOLOGY OF CNS INVOLVEMENT



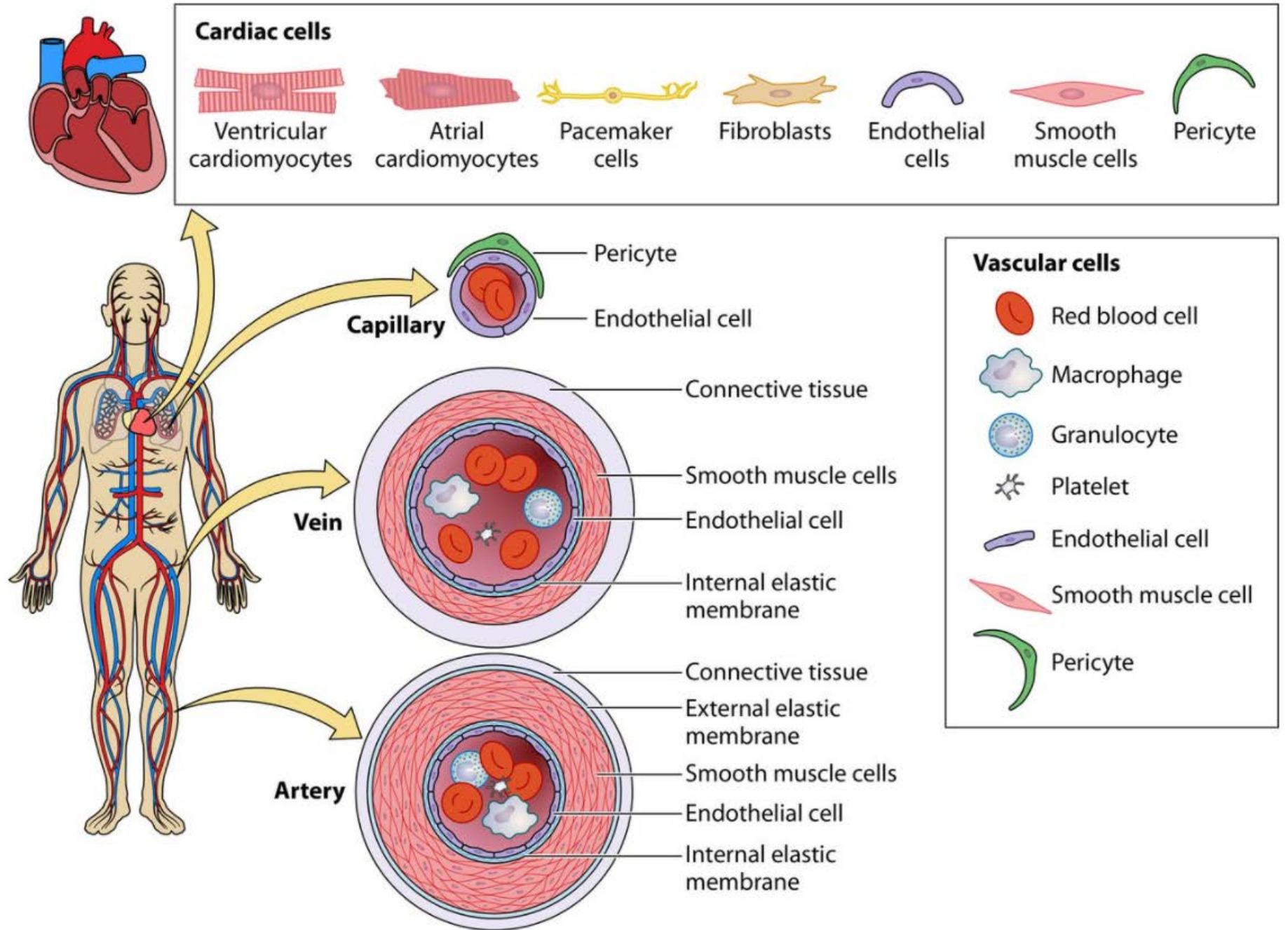
SARS-CoV-2 INVASION

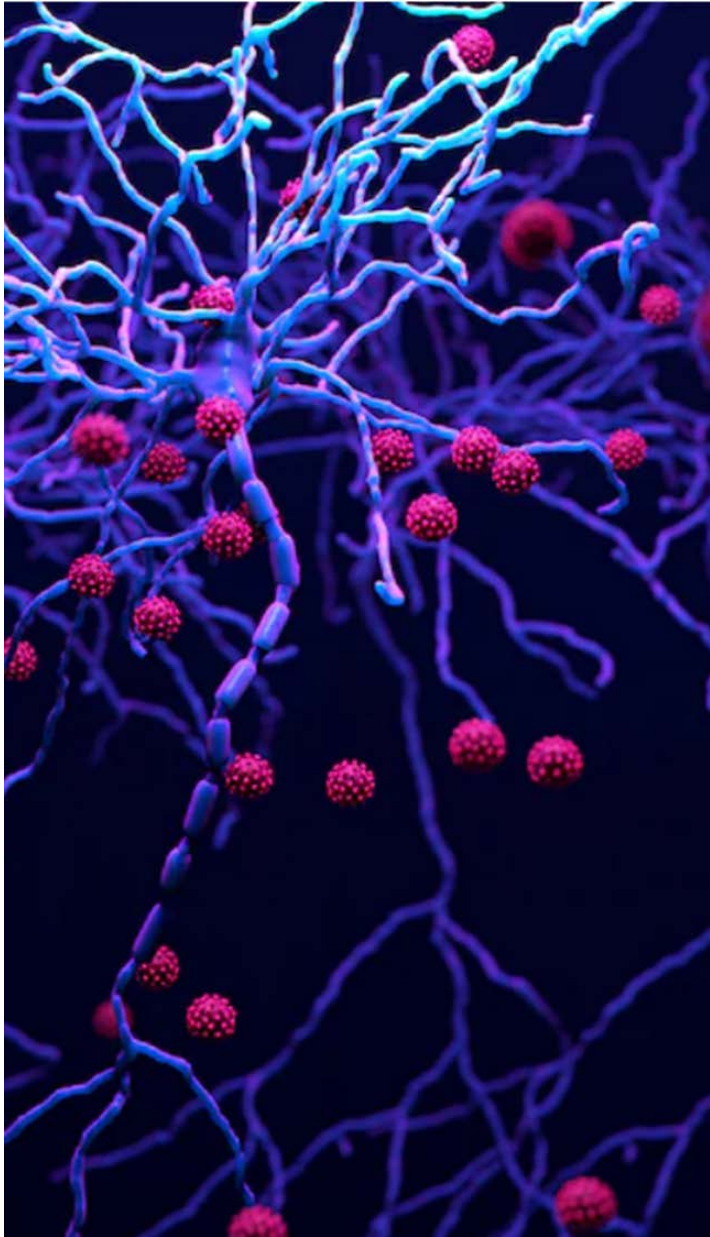
SARS-CoV-2 can take two pathways to involve the brain; direct and indirect pathways. (Wu Y et al., 2020)



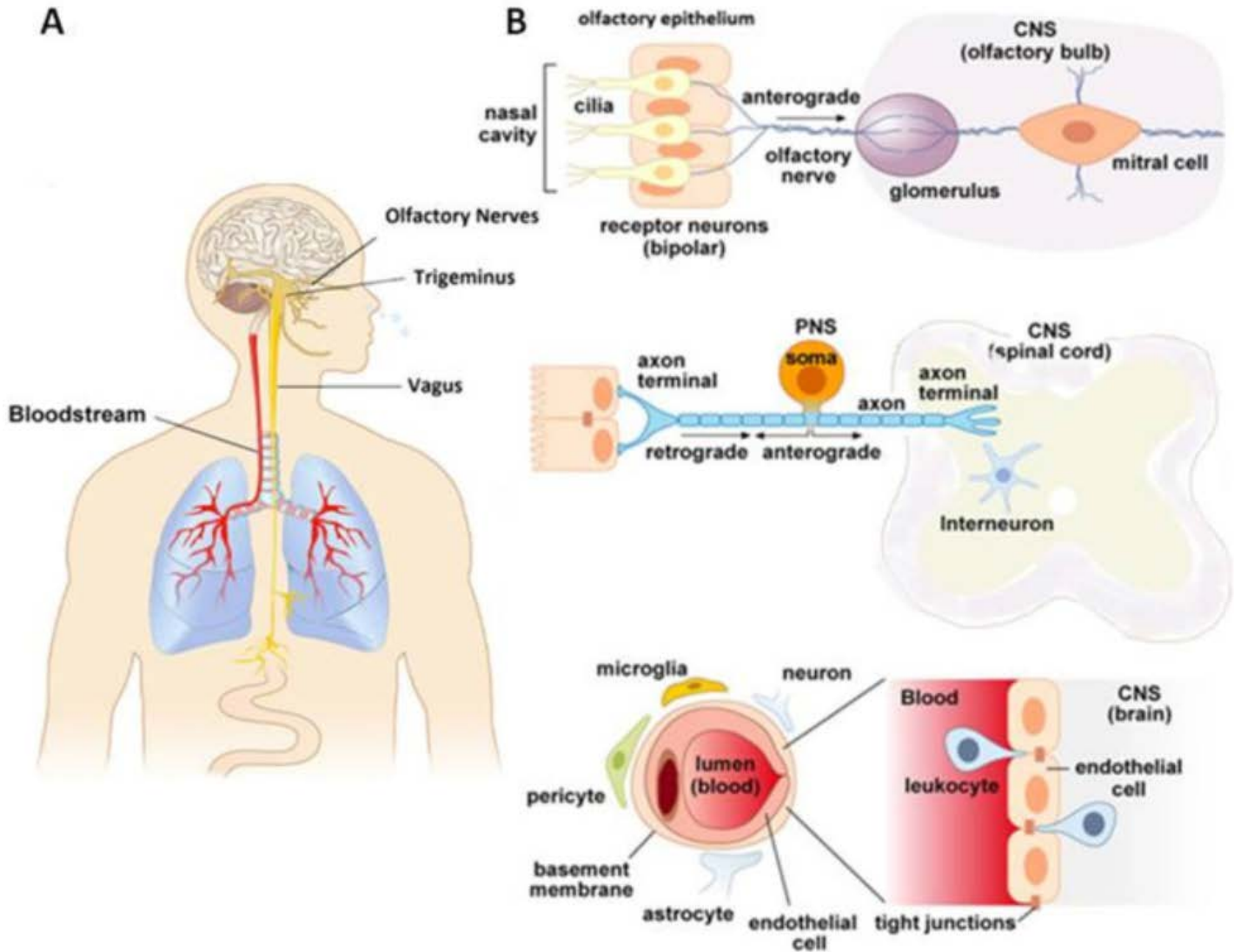


SEVERE ACUTE RESPIRATORY SYNDROME



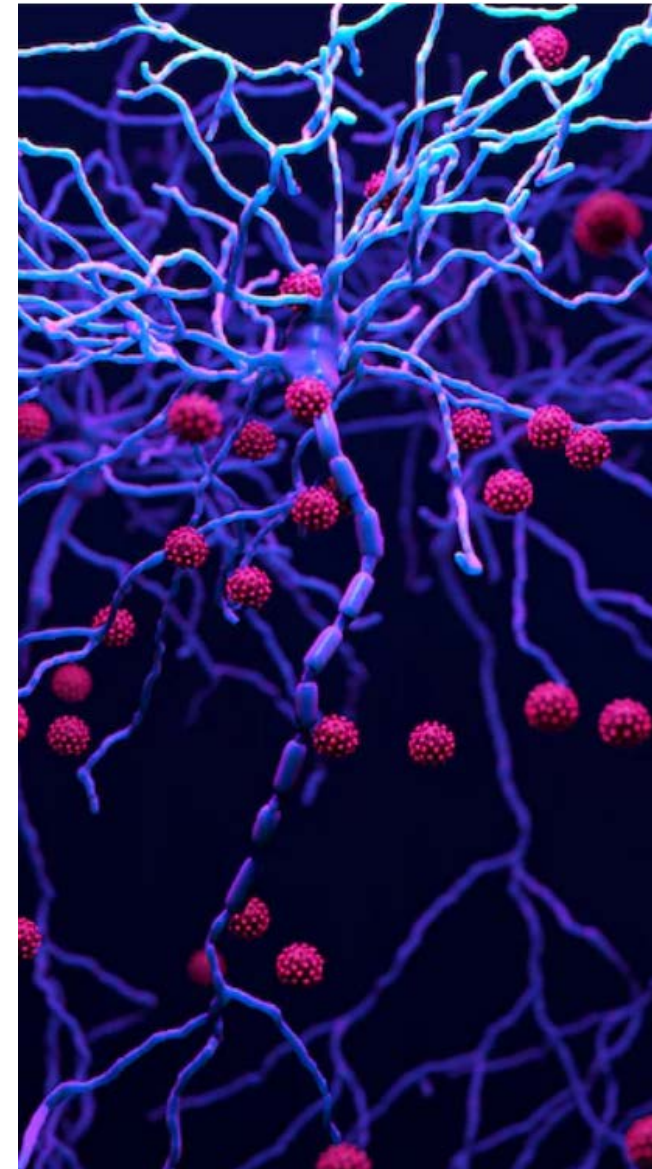
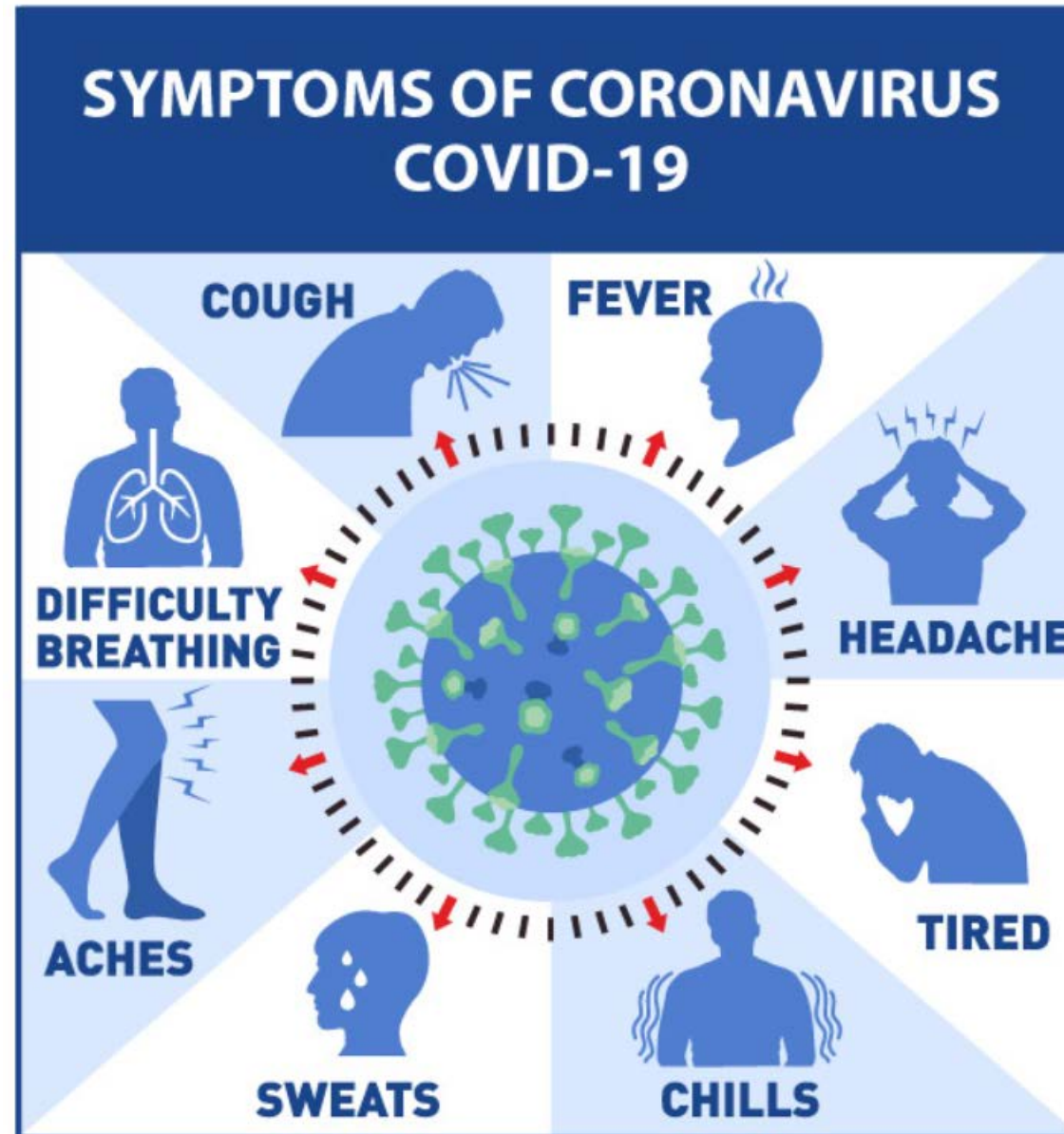


PATHOPHYSIOLOGY



A 3D visualization of a neural network. The image features a dense, branching structure of blue lines, resembling dendrites or axons, set against a dark blue background. Interspersed among these blue lines are numerous small, red, spherical nodes, which likely represent neurons or specific data points within the network. The overall appearance is that of a complex, interconnected system.

CLINICAL PRESENTATION



Clinical Presentation of Covid-19

Asymptomatic Infection

Absence of clinical signs and symptoms of the disease and normal chest X-ray or CT scan associated with a positive test for SARS-CoV-2

Mild Infection

Upper airway symptoms such as fever, fatigue, myalgia, cough, sore throat, runny nose and sneezing. Pulmonary clinical exam is normal. Some cases may not have fever and others may experience gastrointestinal symptoms such as nausea, vomiting, abdominal pain, and diarrhea.

Moderate Infection

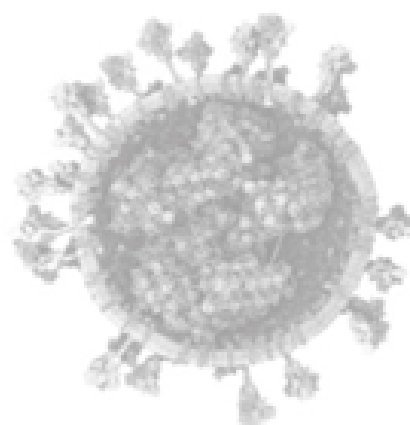
Clinical signs of pneumonia. Persistent fever, initially dry cough, which becomes productive, may have wheezing or crackles on pulmonary auscultation but shows no respiratory distress. Some individuals may not have symptoms or clinical signs, but chest CT scan reveals typical pulmonary lesions.

Severe Infection


Initial respiratory symptoms may be associated with gastrointestinal symptoms such as diarrhea. The clinical deterioration usually occurs in a week with the development of dyspnea and hypoxemia (blood oxygen saturation [SaO_2] <94%)

Critical Infection

Patients can quickly deteriorate to acute respiratory distress syndrome or respiratory failure and may present shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction.



RT-PCR cobas 6800 system -
Diagnostics Roche

277 

recovered from
symptomatic SARS-
CoV-2 infection

Pneumonia



182 Severe
inpatients

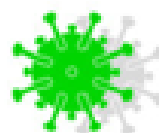


41 Non-Severe
Hospital at home

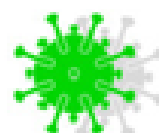
Mild cases



54 Outpatients



77 days (IQR 72-85) after disease onset



Post-Acute COVID Syndrome*

50.9%

(95%CI 45.0-56.7)

Severe inpatients 58.2% (95%CI 51.0-65.2)



Persistent
symptoms
& signs

- Fatigue 34.8%
- Dyspnea 34.4%
- Anosmia-dysgeusia 21.4%
- Cough 21.3%
- Headache 17.8%
- Mnesic complaints 15.2%



Imaging
study
abnormalities

18.9%



Standard
spirometry
abnormalities

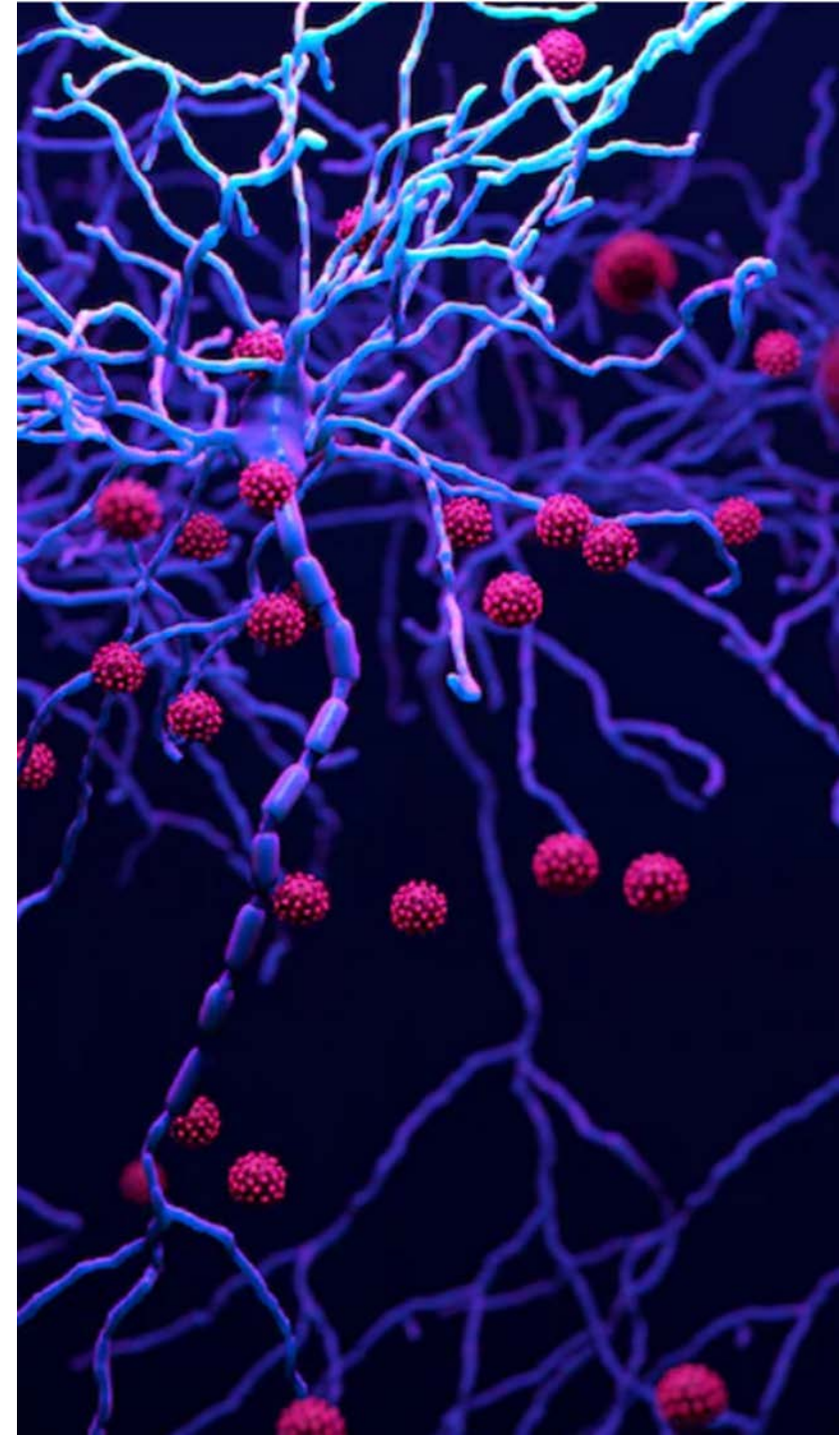
9.3%

A 3D rendering of a complex neural network. The structure consists of numerous blue, branching, fiber-like structures that resemble dendrites or axons, radiating from a central point. Interspersed among these fibers are many small, red, spherical nodes, some of which appear to be connected to the fibers. The overall appearance is that of a dense, interconnected web of neural pathways. The background is a dark, deep blue, which makes the glowing blue and red elements stand out prominently.

NEUROLOGIC SIGNS & SYMPTOMS

Acute neurologic symptoms associated with CoVID-19

- Anosmia
- Dysgueusia
- Myalgias
- Headache
- Fatigue
- Dizziness
- Cognitive dysfunction / "brain fog"



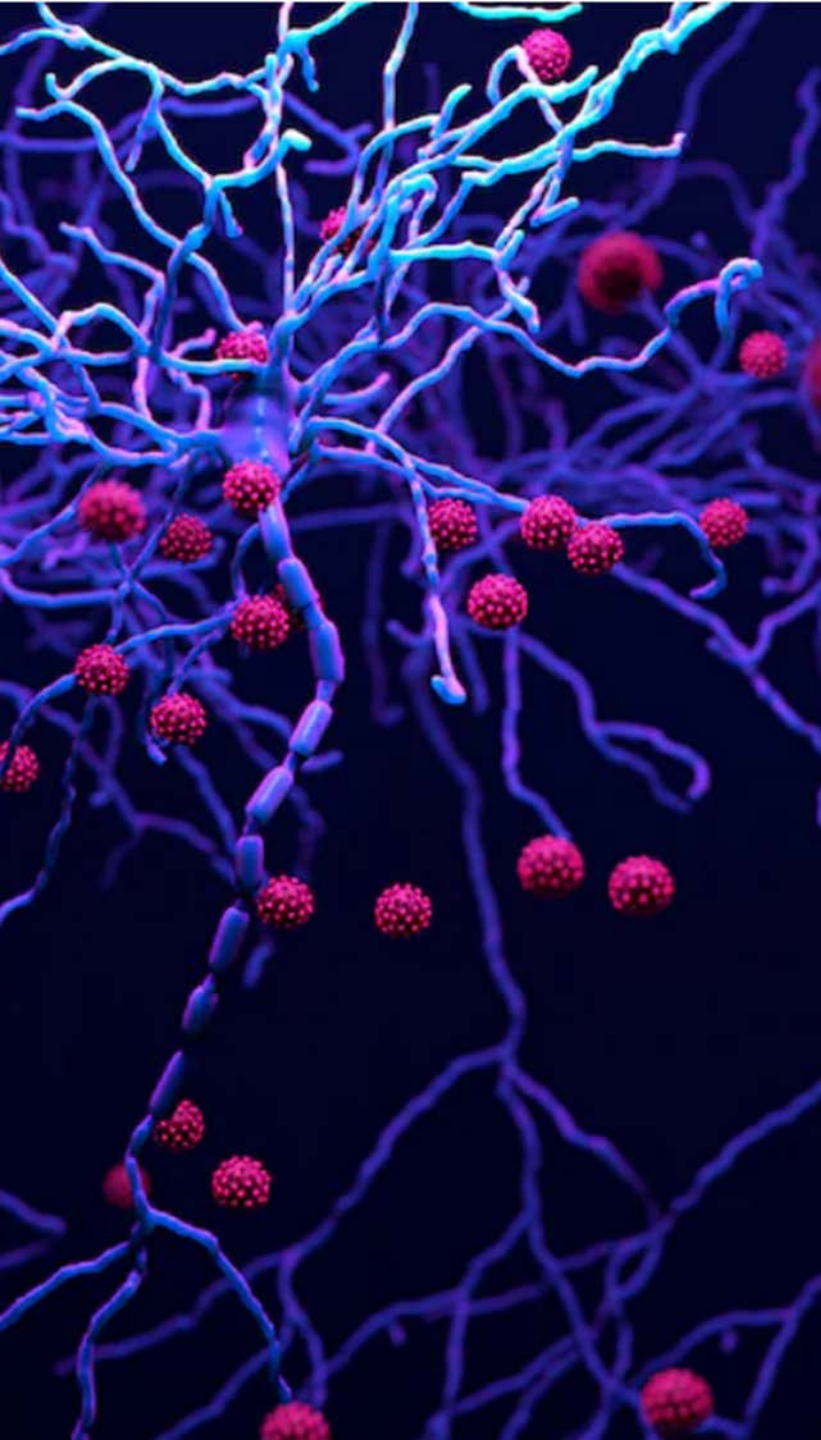
Acute neurologic symptoms associated with CoVID-19 (con't)

- **Encephalopathy / delirium**
- **Ischemic stroke / CNS vasculitis**
- **Intracerebral / subarachnoid / intraventricular hemorrhage**
- **Hypoxic-ischemic brain injury**
- **Seizures**
- **Acute disseminated encephalomyelitis (ADME) / Acute necrotizing encephalomyelitis**
- **Meningitis / encephalitis (including autoimmune encephalitis)**



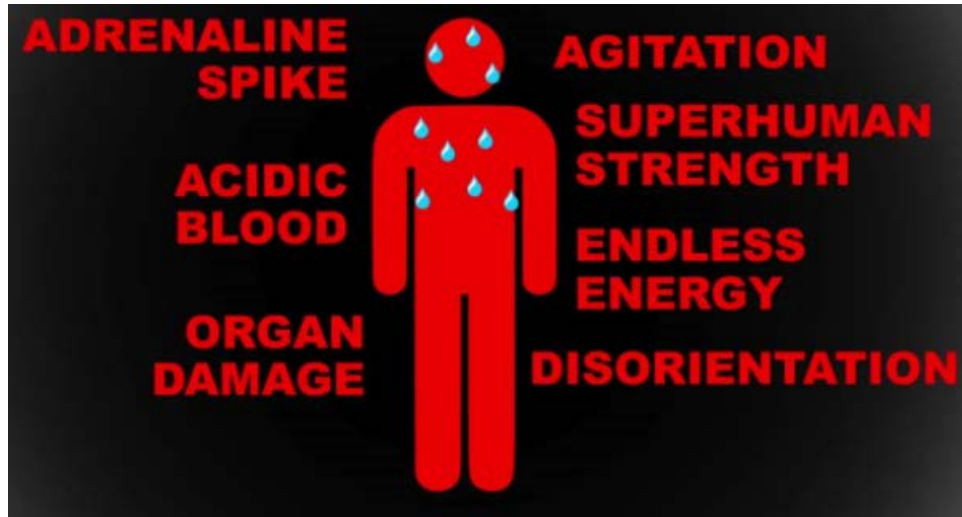
Acute neurologic complications: possible pathogenesis

- Direct infection of the CNS / PNS via direct invasion of nerves (i.e. olfactory bulb) or hematogenous spread
- Cytokine storm / inflammatory response (i.e., endothelitis)
- Systemic organ dysfunction (i.e. hypoxia, hypotension, hypercoagulable state, liver failure)
- Autoantibodies



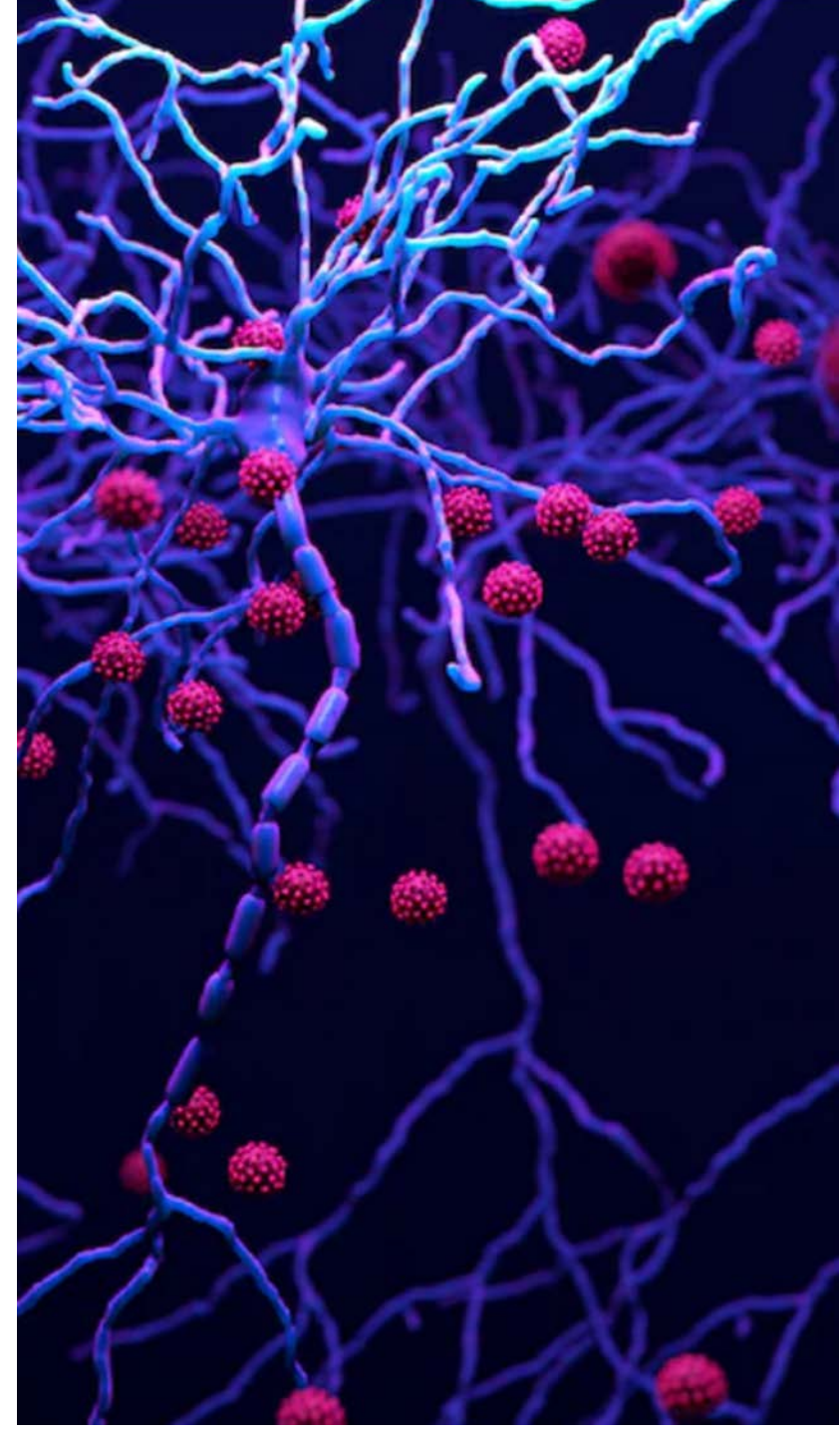
Neurologic complications of systemic CoVID-19 effects

- **Ischemic hemorrhagic stroke from coagulation disorder**
- **Ischemic stroke from depressed cardiac function**
- **Hypoxic ischemic brain injury from decreased pulmonary / cardiac function**
- **Critical illness polyneuropathy / myopathy**
- **Delirium and subsequent long term cognitive impairment**



PERTINENT CLINICAL ISSUES

- Agitated delirium
 - Malingering
- Over-diagnosis



A 3D visualization of a neural network. The background is dark blue. The network consists of numerous thin, branching blue lines that resemble dendrites or axons. Interspersed among these lines are many small, red, spherical nodes, some of which are larger and more prominent than others. The overall appearance is that of a complex, interconnected web of biological or computational structures.

CHRONIC COVID-19 SYNDROME [LONG COVID]



Long-term neurologic complications: possible pathogenesis

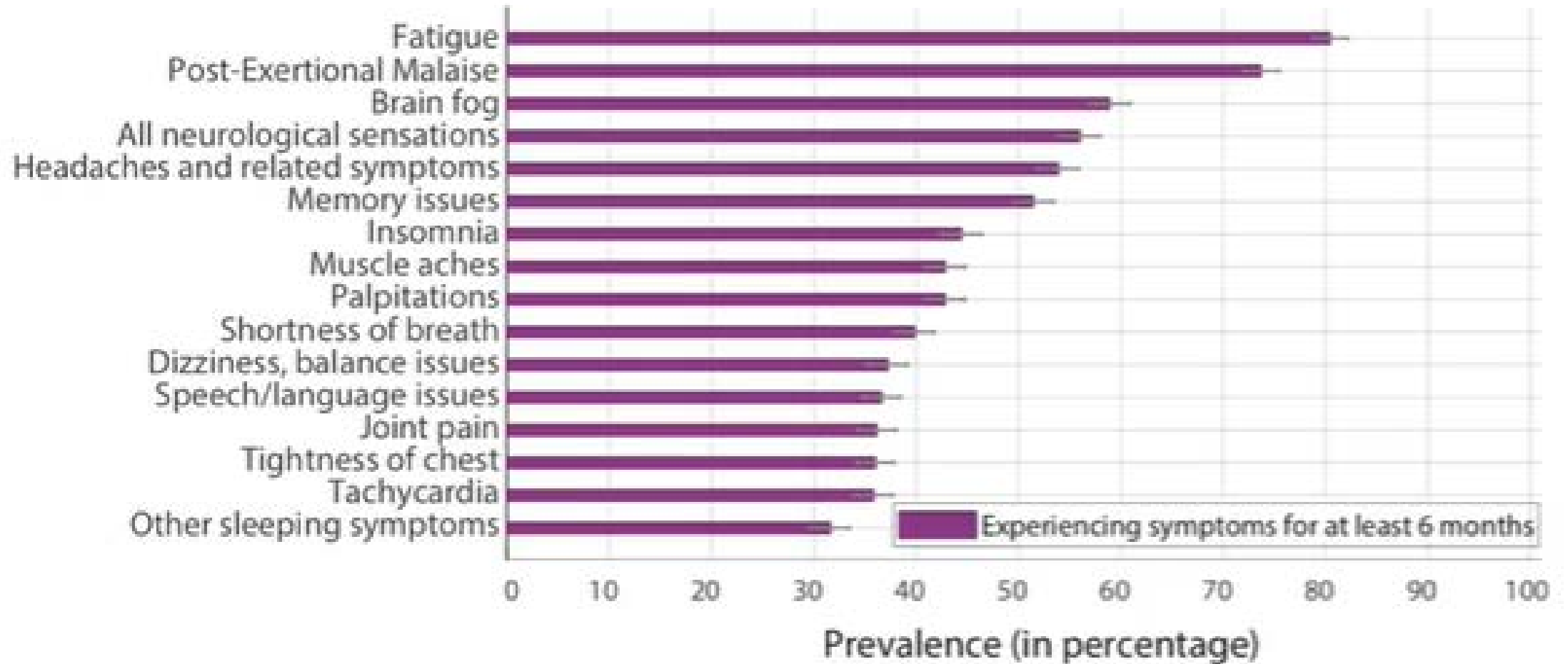
- **Ongoing cytokine activation / inflammatory response**
- **Autoimmune activity**
- **Degeneration of neurons / myelin from direct damage to the nervous system**

Long-term neurologic complications: possible pathogenesis (con't)

- **Movement disorders (tremor, myoclonus, ataxia, Parkinsonism)**
- **Limb stiffness / weakness / myalgias / tingling**
- **Peripheral neuropathy**
- **Autonomic dysfunction (syncope, palpitations)**
 - **Orthostatic intolerance syndromes**
 - **Orthostatic hypotension**
 - **Vasovagal syncope**
 - **Postural tachycardia syndrome (POTS)**
 - **Pupillary abnormalities**
- **Autoimmune encephalitis**
- **Psychiatric (anxiety, depression, PTSD)**



a. Remaining symptoms after month 6 (prevalence > 30%)



Post-Intensive Care Syndrome (PICS)

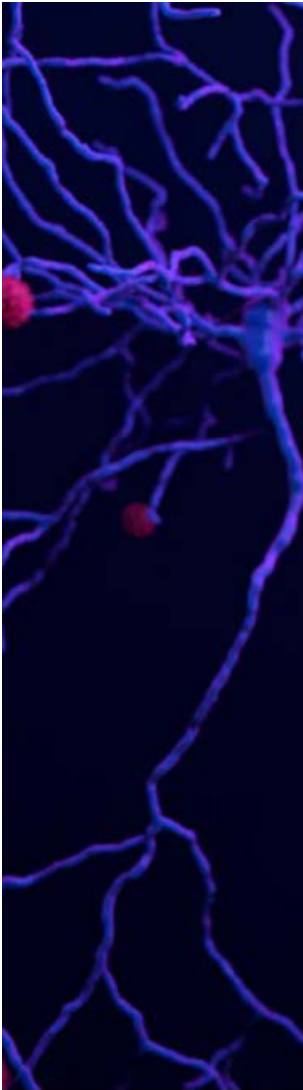
- **Occurs in up to 50% of ICU survivors**
 - **Physical symptoms: fatigue, weakness, pain**
 - **Cognitive symptoms: forgetfulness, difficulty concentrating**
 - **Psychiatric symptoms: depression, anxiety, PTSD**
- **Multidisciplinary PICS clinics are available at some institutions for symptomatic treatment**

A 3D visualization of a neural network. The background is dark blue. A complex network of thin, light blue lines represents dendrites or axons, branching out from a central point. Scattered throughout this network are numerous small, red, spherical objects with a textured surface, resembling neurons or synaptic terminals. The overall appearance is that of a dense, interconnected neural structure.

TREATMENT CONSIDERATIONS

WORK-UP OF LONG-TERM NEUROLOGIC COMPLICATIONS

- **Refer to a neurologist or multidisciplinary post-COVID clinic, and consider**
 - **Standard labs, + Bit B12 and thyroid studies**
 - **Rheumatologic labels if autoimmune process are suspected**
 - **MRI an MRA brain**
 - **LP (if GBS / myelitis / encephalitis) suspected**
 - **EMG / nerve conduction studies**
 - **EEG (if non-convulsive seizures are suspected)**
 - **Orthostatic testing**
 - **Cardiac work-up (EKG, echocardiogram, arrhythmia monitoring)**
 - **Psychiatric work-up (screening for PTSD, depression)**
- **If Post-Intensive Care Syndrome is suspected, refer to PICS clinic**





Long-term neurologic complications: treatment

- **Symptomatic treatment**
- **Immunomodulatory therapies if ongoing autoimmune response / autoimmune disorder suspected**
- **Multidisciplinary (neurology, psychiatry, PT/OT), etc) follow-up in a neurology or neuro-COVID clinic when possible**

RECOVERY: Comprehensive Post-COVID Center at Yale

Referral Pathway

Inpatients (pre-discharge)

Respiratory Assessment

- Ambulatory oximetry
- Pulse oximeter & incentive spirometry training

Functional Assessment

- Physical & occupational therapy evaluation
- Swallow evaluation

Care Coordination

- Arrange home services
- Address care barriers

Outpatients (ongoing sx)

- Referral by outpatient provider, occupational medicine provider, health system COVID-19 hotline, or self

Initial Assessment

Visit 1 (telehealth)

- Pulmonary consultation
- Subjective sx assessment
- Assess for extrapulmonary complications

Initial Diagnostics

- Repeat imaging (HRCT)
- PFTs, 6MWT
- Repeat selected labs

Visit 2 (face-to-face)

- Ongoing pulmonary care
- PT/OT assessment
- Subjective sx assessment
- Neurocognitive screening
- Mental health screening
- Additional subspecialty involvement

Subsequent Care

MD visits

- Planned 3, 6, and 12 mo or as needed per severity
- Extrapulmonary consultation as needed

Rehab

- PT/OT outpatient care
- Pulmonary rehabilitation

Lung function testing

- PFT & 6MWT at 3, 6, 12 mo
- CPET for selected patients

Additional diagnostics

- VQ or CTA chest
- Transthoracic Echo
- Cardiac event monitoring
- Functional cardiac imaging
- Neurocognitive testing

Disposition

Sx resolve & PFT normal

- Transition to primary care

Sx persist or PFT abnormal

- Non-specific phenotype → continue RECOVERY clinic
- Phenotype consistent with specific disease process → appropriate advanced lung disease program (e.g. interstitial lung disease, airways disease, pulmonary vascular disease)

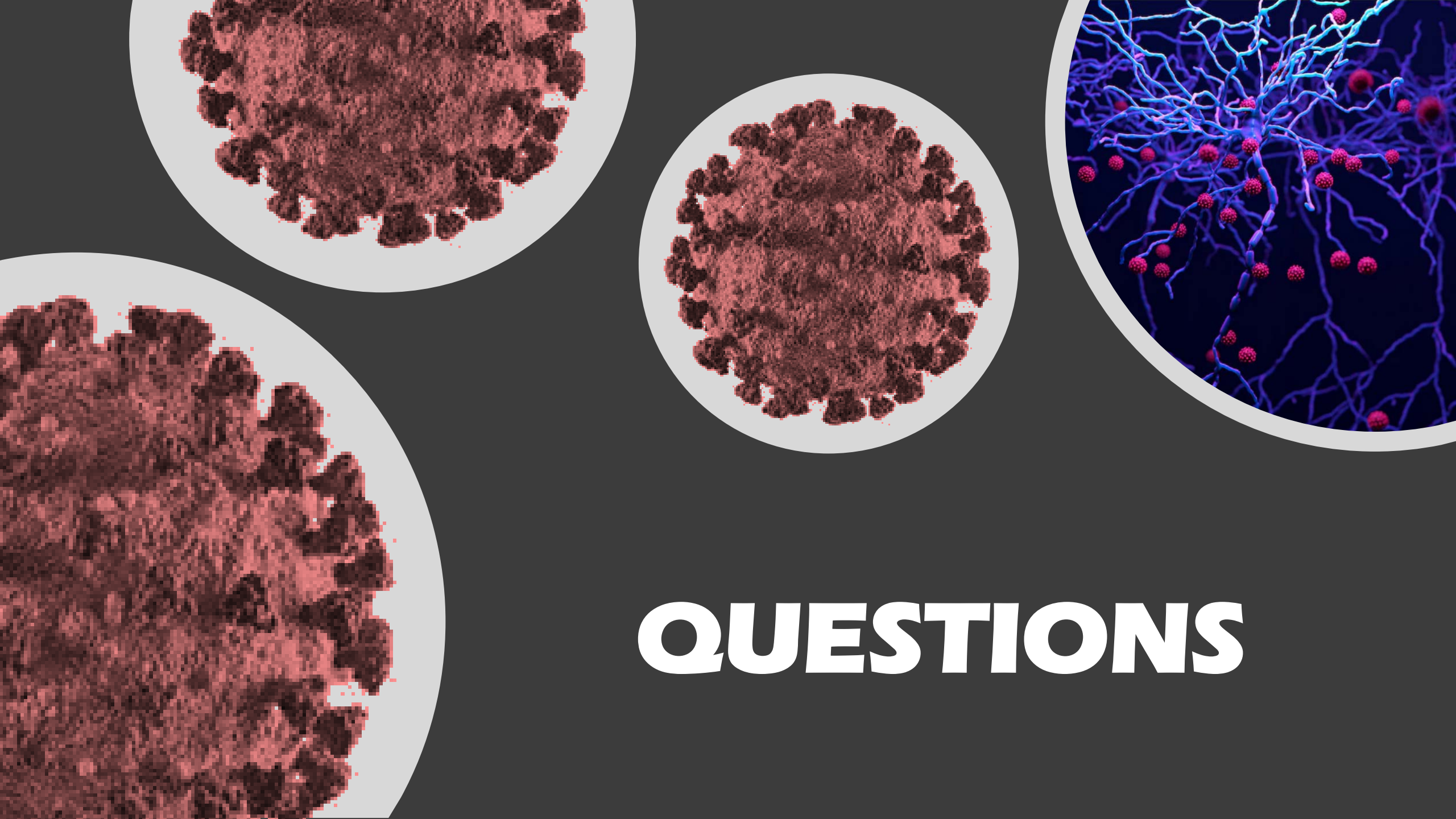
Multi-disciplinary discussion of active cases

Translational research efforts

Revision of clinic processes to meet patient needs and evolving evidence

WHAT WE CAN EXPECT GOING FORWARD

- Disproportionate morbidity and mortality numbers among AA and other people of color
- Expanded numbers of physical, mental and neurologic disabilities in the general population
- Extended periods of unemployment, compounding current economic, employment and wealth disparities currently in existence
- With current KNOWN CoVID-19 cases, a recent large scale chart review revealed that
 - 45 - 50% of those most seriously ill will have a variety of disabling symptoms 6 months later
 - 30% of all persons affected were symptomatic in 6 months
 - Taking a conservative low average of this overall group, in the US alone with 32million total cases in the US, >10M people will be left with some form of long-term sequelae



QUESTIONS



Appreciation



Contact Us



Central East (HHS Region 3)

MHTTC

Mental Health Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

a program managed by



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