Long COVID, Post-Viral Syndromes and ME/CFS

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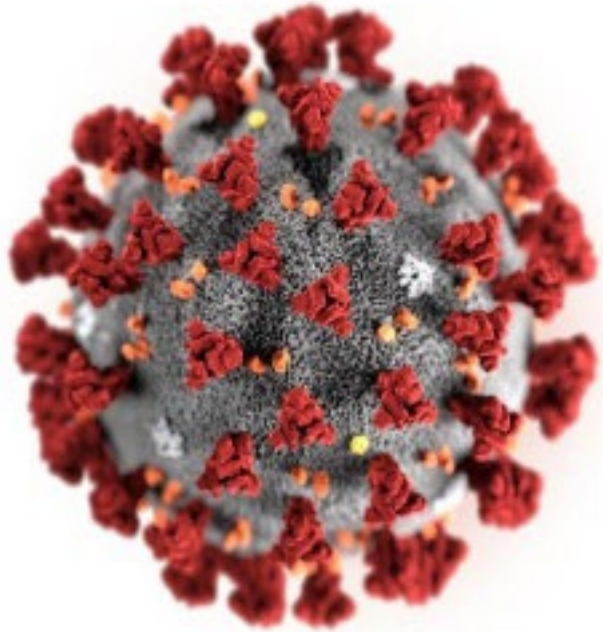
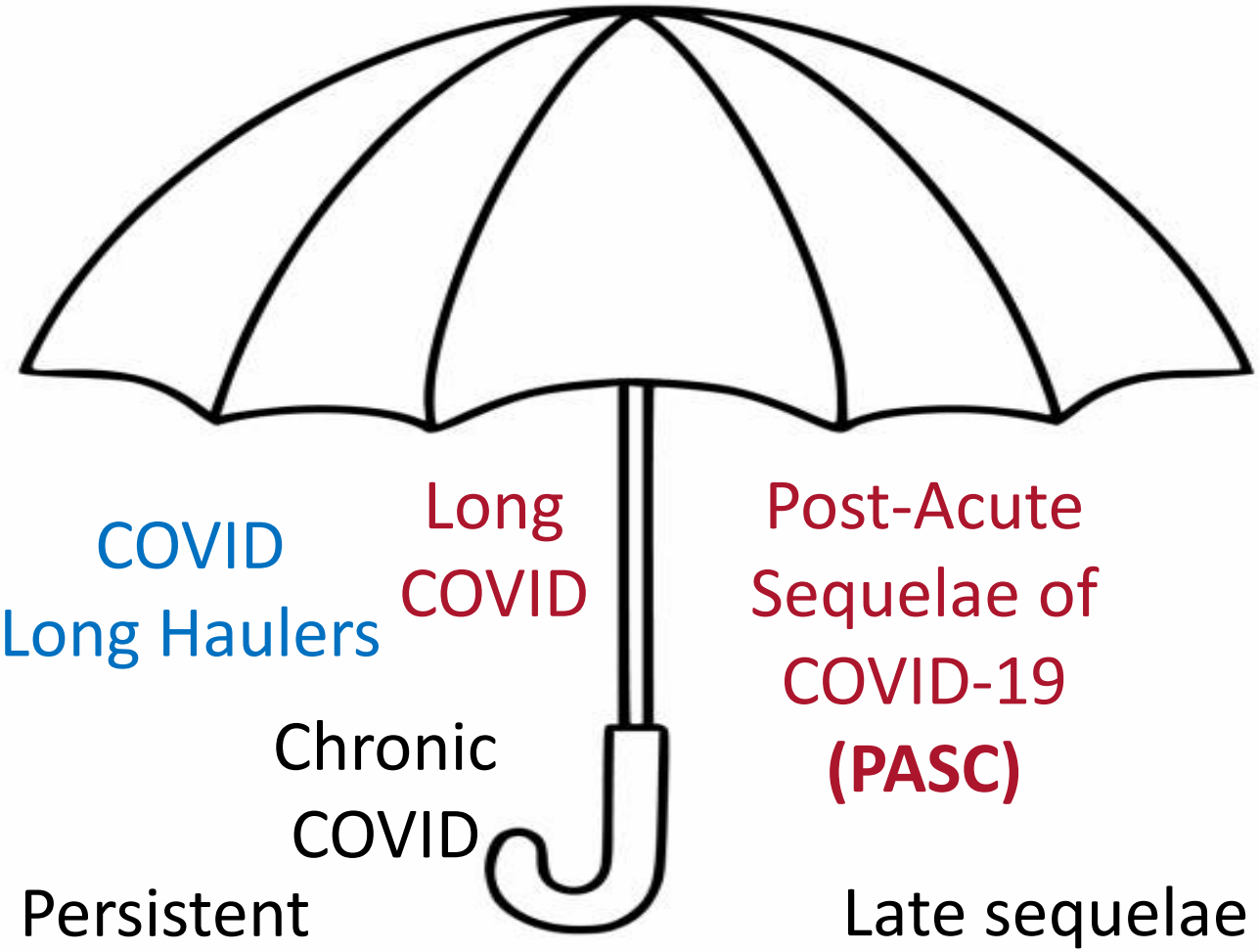
ACUTE COVID-19 IS KNOWN TO CAUSE WIDESPREAD ORGAN DAMAGE

- Lung
- Cardiac and vascular
- Neurologic complications
- Gastrointestinal and liver
- Kidney damage, chronic kidney disease



Post-COVID Conditions



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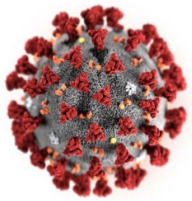
THERE ARE *ROUGHLY* **TWO MAIN GROUPS** OF LONG COVID:

People who had **severe** infection, hospitalization, post-ICU syndrome and/or lingering organ damage identifiable with objective markers.

People with **mild to moderate** infection but lack of recovery, or even increasingly worse symptoms and impairment, yet without apparent biological markers.

Right now, we call all lingering, unresolved, symptoms of acute COVID-19 some version of Long COVID, Long Haul COVID, Post-COVID, PASC or similar designations.

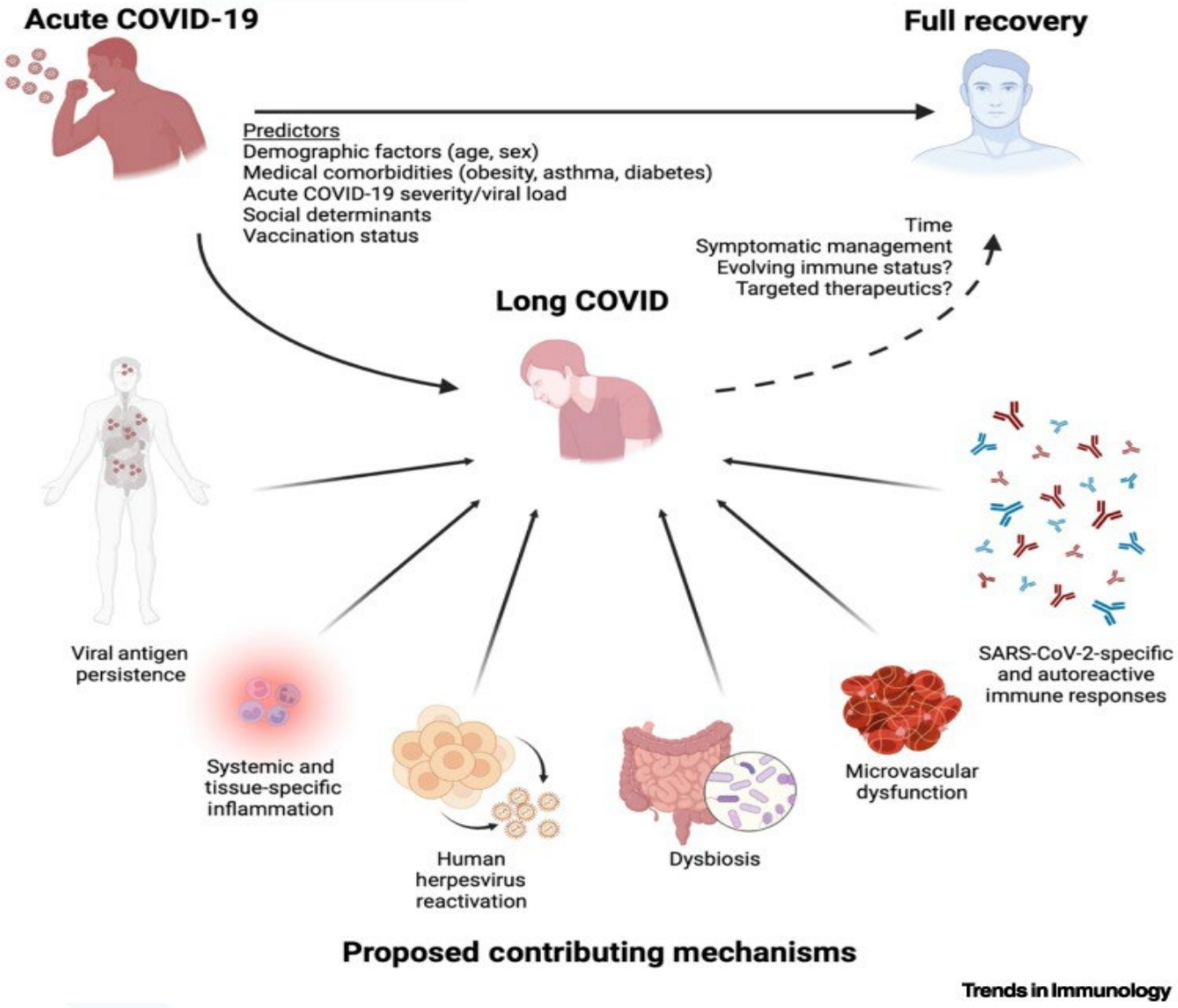
Hopefully, most patients will eventually recover, and only a small portion of these people will have permanent organ damage or eventually meet ME/CFS criteria.



WHAT CAUSES LONG COVID? …MUCH IS STILL UNCLEAR

There is a growing body of literature suggesting that **a combination of virus and host factors might contribute to PASC,** including:

- Viral antigen persistence
- Residual inflammation
- Herpesvirus reactivation
- Dysbiosis
- Microvascular and endothelial dysfunction, microclots
- Autoimmune phenomena



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Early clues regarding the pathogenesis of long-COVID. Peluso MJ, Deeks SG. Trends Immunol. 2022 Apr; 43(4): 268–270. doi: 10.1016/j.it.2022.02.008 PMID: 35272932

COMMON SYMPTOMS OF POST-COVID CONDITIONS (CDC GUIDANCE)

- **Fatigue**
- **Post-exertional malaise and/or poor endurance**
- **“Brain fog,” or cognitive impairment**
- **Palpitations and/or tachycardia**
- Dyspnea or increased respiratory effort
- Cough
- Chest pain
- Headache
- Arthralgia
- Myalgia
- Paresthesia
- **Impaired daily function and mobility**
- **Insomnia and other sleep difficulties**
- **Lightheadedness**
- Abdominal pain
- Diarrhea
- Fever
- Pain
- Rash (e.g., urticaria)
- Mood changes
- Anosmia or dysgeusia
- Menstrual cycle irregularities

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html

What is Myalgic Encephalomyelitis/Chronic Fatigue Syndrome? ME/CFS

- A chronic, debilitating, multisystem illness characterized by **central and peripheral nervous system disease, immune manifestations, and impaired cellular metabolism**.
- ME/CFS is thought to be a post-viral or post-infectious syndrome in most cases. Many Long- or Post- COVID cases meet ME/CFS criteria...

NEW ICD-10 CODES as of Oct 1, 2022:

- **G93.31 Postviral fatigue syndrome**
- **G93.32 ME/CFS, CFS, ME**
- **G93.39 Post infection and related fatigue syndromes**

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Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Essentials of Diagnosis and Management. Bateman L, Bested AC, Bonilla HF, et al [the US ME/CFS Clinician Coalition] Mayo Clin Proc. 2021 Nov;96(11):2861-2878. doi: 10.1016/j.mayocp.2021.07.004. Epub 2021 Aug 25. PMID: 34454716

Advances in Understanding the Pathophysiology of Chronic Fatigue Syndrome. Komaroff AL. JAMA. 2019 Aug 13;322(6):499-500. doi: 10.1001/jama.2019.8312. PMID: 31276153

ME/CFS CAN BE TRIGGERED BY A VARIETY OF PATHOGENS

- Infections documented to cause ME/CFS include **Epstein-Barr Virus, other herpesviruses, Parvovirus B19, West Nile Virus, enteroviruses, coronaviruses (including SARS CoV-2), and other *non-viral* pathogens as well.**

- People who meet ME/CFS criteria share the same core symptoms, but heterogeneity exists, likely due to the trigger, the systems affected, disease duration and the development of comorbid conditions. This heterogeneous illness is challenging to study.

By the time the diagnosis is made, often months or years later,

there is generally no definitive evidence left of the infectious trigger.

The COVID-19 pandemic has changed that due to worldwide scrutiny

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Advances in Understanding the Pathophysiology of Chronic Fatigue Syndrome. Komaroff AL. JAMA. 2019 Aug 13;322(6):499-500. doi: 10.1001/jama.2019.8312. PMID: 31276153

THE IOM (NAM) 2015 ME/CFS CLINICAL DIAGNOSTIC CRITERIA

The CORE criteria (all required for diagnosis) ***Must be moderate-severe and present >50% of time**

1) **Impairment of normal function, accompanied by fatigue, persisting >6 months**
2) **PEM: post exertional malaise***
3) **Unrefreshing sleep***
4) Plus at least one of the following:
   - **Cognitive impairment***
   - **Orthostatic intolerance**

Additional common but not CORE features of illness in the ME/CFS population:

- **Chronic pain** (headache, muscle and joint aches, hyperalgesia, central sensitivity)
- **Immune/inflammatory manifestations** (allergy, inflammation, chemical sensitivities)
- **Infection manifestations** (viral or atypical infections, sore throat, tender lymph nodes, low grade fevers)
- **Neuroendocrine manifestations**

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The IOM is now the National Academy of Medicine (NAM), which is part of the National Academy of Sciences, Engineering and Medicine.

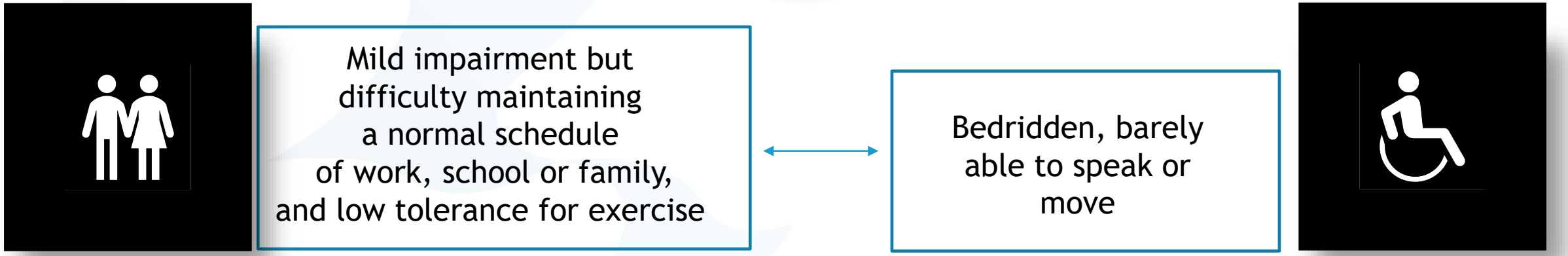
Beyond Myalgic Encephalomyelitis: Redefining an Illness. Institute of Medicine. Washington (DC): National Academies Press (US); 2015 Feb 10. ISBN-13: 978-0-309-31689-7ISBN-10: 0-309-31689-8

ME/CFS is distinguished from other types of chronic fatigue and post-viral illness by the degree of impairment/debilitation and the development of post-exertional malaise (**PEM**).

PEM is **illness relapse** due to activity or stressors. These stressors can be physical, cognitive, sensory, emotional or even being in upright posture.

PEM occurs in many patients with Long COVID as well.

ME/CFS illness severity and functional impairment ranges from:



IMPORTANT CO-MORBID CONDITIONS TO CONSIDER IN "LONG COVID" BEYOND OBJECTIVELY MEASURED ORGAN DAMAGE

- Cognitive impairment. ***Can be significant.***
- Orthostatic Intolerance (OI) and ANS dysregulation. Postural orthostatic tachycardia syndrome (POTS), orthostatic hypotension or other forms of dysautonomia. ***Common.***
- Mast Cell Activation Syndrome (MCAS): a ramped up allergic response system. ***Probably common.***
- Small fiber neuropathy (can lead to widespread pain, sensory sensitivities, orthostatic intolerance syndromes). ***Probably common.***
- Sleep apnea syndromes and other sleep disturbances.
- GERD and IBS, dysbiosis
- **Dx ME/CFS: if symptoms persist > 6 months and meet established criteria**

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Multisystem Involvement in Post-Acute Sequelae of Coronavirus Disease 19. Novak P, Mukerji SS, Alabsi HS, Systrom D, et al. Ann Neurol. 2022 Mar;91(3):367-379. doi: 10.1002/ana.26286. Epub 2022 Jan 18. PMID: 34952975

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MANAGING LONG COVID (AND ME/CFS)

- Provide understanding and support
- Teach “pacing” and activity management to prevent or reduce PEM
- Address severe symptoms sensibly, especially those that are “stressors”
  - Pain and headaches
  - Sleep disturbances
  - Orthostatic intolerance
  - Cognitive impairment
  - Anxiety, grief/loss (especially in the first 1-2 years of illness)
- Identify and treat “comorbid conditions” but remember that it generally won’t be a magic bullet for the whole illness
- Help patients build a “toolbox” of rescue medications and strategies to manage symptom flares and maintain some physical conditioning
- Remember that any other medical or mental health problem can occur in someone with Long COVID and ME/CFS

ICD-10 CODING IS IMPORTANT!

ICD-10 codes for PASC (Long COVID)

- **U09.9** All post- or long- COVID, COVID sequelae

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- G93.39 Post infection and related fatigue syndromes

Also new: POTS (postural orthostatic tachycardia syndrome)

- G90.A

MCAS (mast cell activation syndrome)

- D89.4x