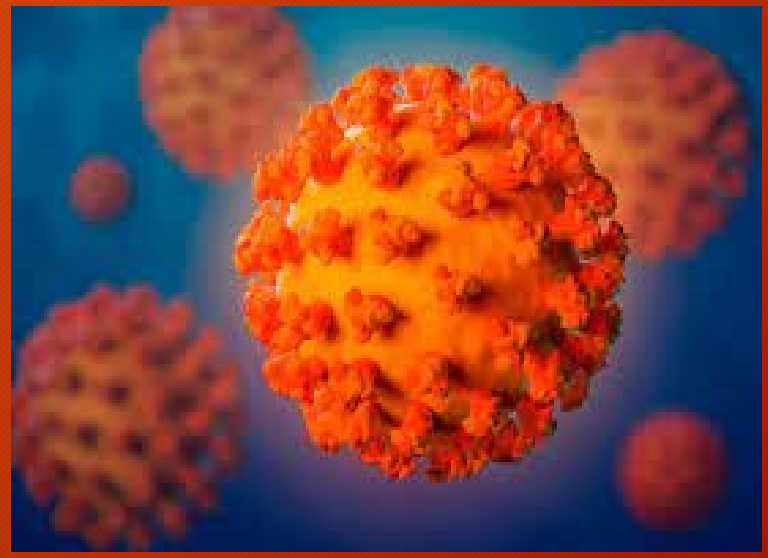
Post-acute Sequelae of COVID ("Long COVID")

Alithea Gabrellas, MD
Infectious Diseases Physician
Gallup Indian Medical Center

COVID: Terminology and Stages of Recovery

- **Acute COVID:** symptoms of COVID, up to 4 weeks following the onset of illness

- **Post-COVID condition:** Broad range of symptoms that develop during or after COVID, continue for more than 2 months (ie. 3 months from the onset of illness), have an impact on the patient's life and are not explained by an alternative diagnosis.



Post-COVID conditions cover a broad spectrum

- **Hospitalized patients:**
  - may have symptoms similar to the syndrome experienced by patients recovering from other critical illnesses known as post-intensive care syndrome (PICS)
  - survival and the frequency and severity of disability that COVID ICU survivors experience at six months appears to be similar to that experienced by non-COVID ICU survivors

Source: Clinical Outcomes Among Patients With 1-Year Survival Following Intensive Care Unit Treatment for COVID-19. Heeksakkers et al. JAMA. 2022. 327(6):559

Post-COVID conditions cover a broad spectrum

- **Outpatients (mild illness):**
  - data also suggest that a significant proportion of patients with mild disease may experience symptoms for up to several months, if not longer, following acute illness and often resolve by one year
  - **Common symptoms:** fatigue, dyspnea, chest discomfort, parosmia, cognitive difficulties, headache, depression or anxiety

Source: A Longitudinal Study of COVID-19 Sequelae and Immunity. Sneller et al. Ann Intern Med. 2022;175(7):969. Epub 2022 May 24.

How common is “Long COVID”?

- True prevalence is unknown due to varying definitions and analysis methods
- The largest study to date found that at 3 months, 6.2% of individuals who had symptomatic COVID had at least one of a predetermined set of 3 long-COVID symptom clusters
- A new analysis from the RECOVER trial puts the estimate at ~10%

Source: Estimated Global Proportions of Individuals with Persistent Fatigue, Cognitive and Respiratory Symptom Clusters Following Symptomatic COVID-19 in 2020 and 2020. Hanson et al. JAMA 2022; 328 (16): 1604

What causes “Long COVID”?

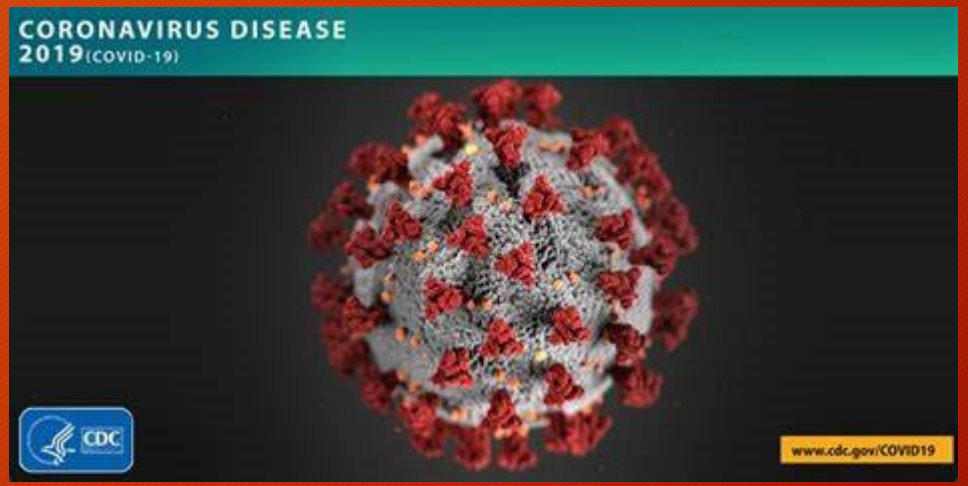
- Active area of research with no definitive answers yet
- SARS-CoV-2 viral particles may become active again, causing symptoms to reappear?
- Overactive immune cells may release high levels of inflammatory substances that can injure organs and tissues?
- The infection may cause the immune system to start making autoantibodies that attack a person’s own organs and tissues?

Who is more likely to develop “Long COVID”?

- People who experienced severe initial illness
- People who have underlying health conditions, such as diabetes, asthma, autoimmune diseases or obesity
- People who did not get a COVID vaccine
- People who experienced multisystem inflammatory illness (MIS) during or after COVID

Other factors that may play a role

- Female sex
- Older age
- Immune response to initial infection
- The SARS-CoV-2 variant that caused the initial infection
- Having a lower income or being unable to rest through the first few weeks after getting COVID also seem to raise the risk of long COVID

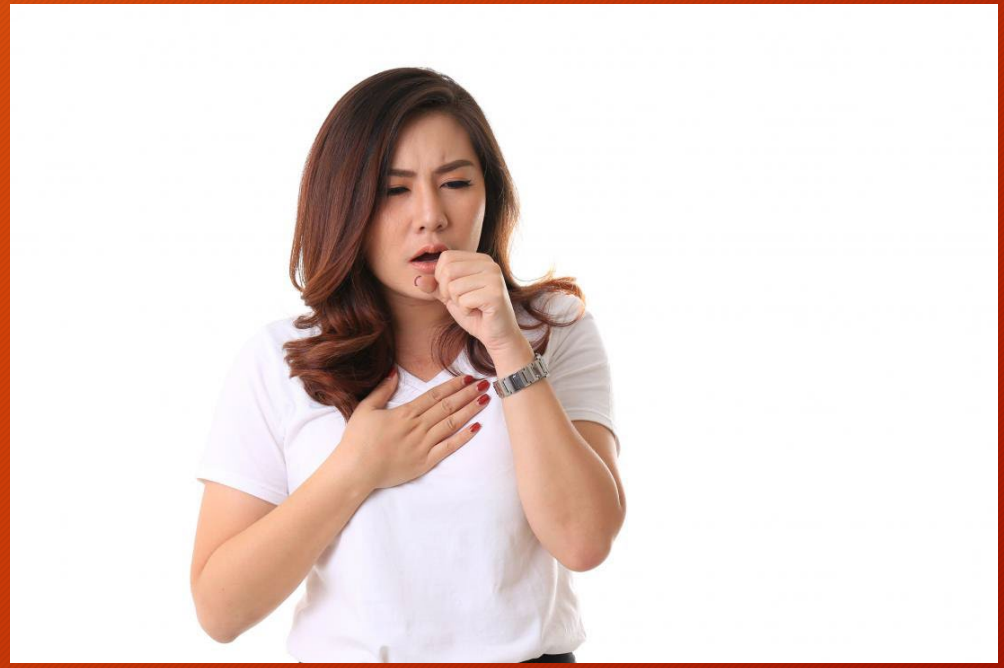


Evaluation of a patient with persistent symptoms

- For patients who are still having symptoms after 4 weeks or who have new or worsening symptoms, medical evaluation is recommended
- If cardiopulmonary symptoms are present, providers should evaluate for the development of late complications of COVID, such as secondary bacterial pneumonia, empyema, pulmonary embolism, or COVID-related myocardial injury or inflammation with chest imaging and EKG
- Check complete vital signs, with special attention to SpO_2, and in patients with orthostasis, pre-syncope or syncope, postural blood pressure (up to 10 minutes after standing) and pulse rate

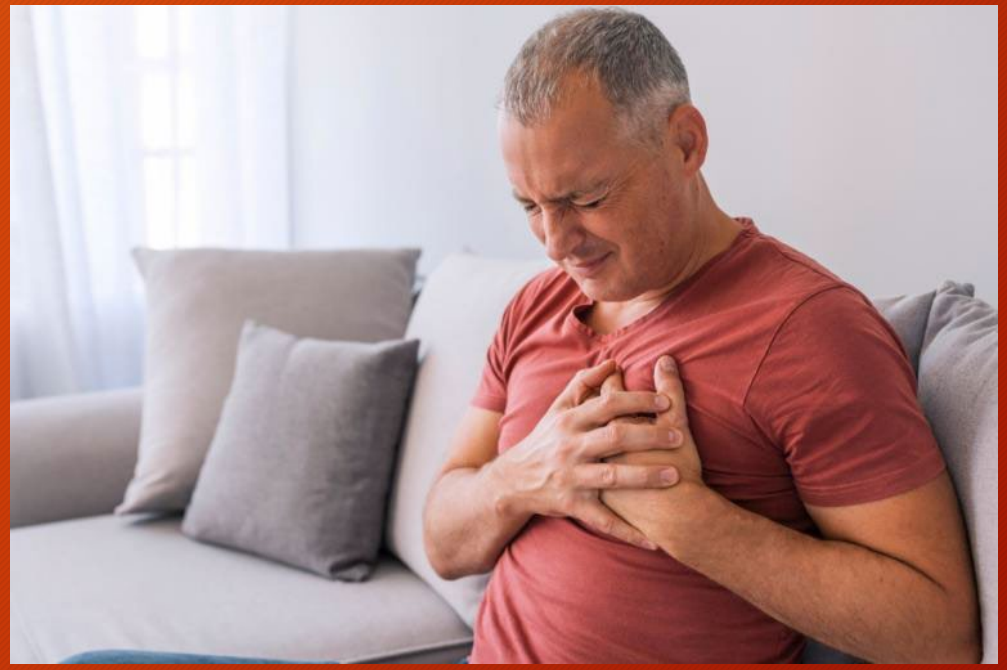
Management of specific Post-COVID symptoms: Cough

- Cough following recovery from acute COVID is managed in a similar fashion to cough in patients with postviral cough syndrome
- Supportive therapies (guaifenesin, benzonatate, dextromethorphan)
- If bronchospasm is present inhaled bronchodilators or glucocorticoids may help



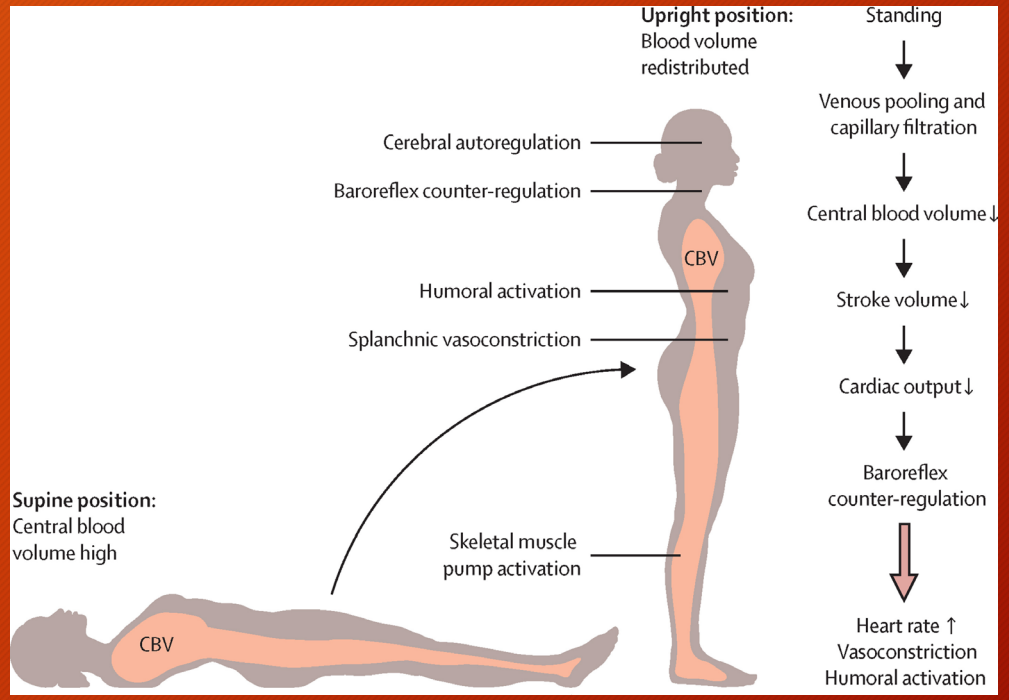
Management of specific Post-COVID symptoms: Chest discomfort/tightness

- May resolve slowly
- Does not necessarily require treatment unless interfering with patient's quality of life
- NSAID’s can be used if needed for more severe discomfort (as long as not contraindicated)



Management of specific Post-COVID symptoms:Orthostasis

- Some patients experience orthostasis and dysautonomia (unexplained sinus tachycardia, dizziness on standing) following COVID
- Compression stockings, abdominal binder, hydration, physical therapy, and behavioral modifications may help

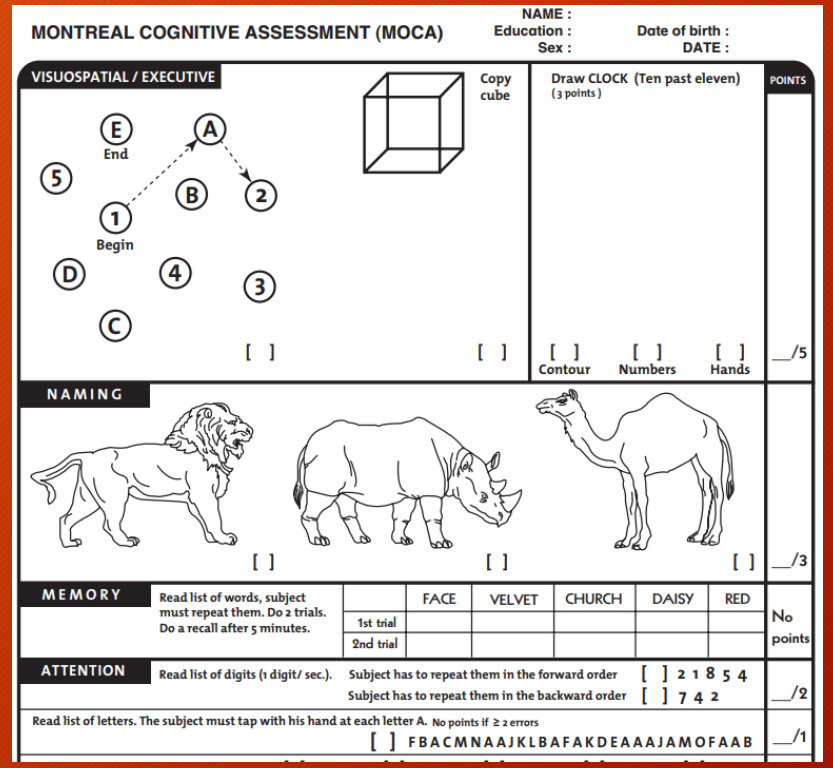


Postural Tachycardia Syndrome (POTS)

- Intermittent symptoms of orthostatic intolerance accompanied by excessive tachycardia without arterial hypotension
- Behavioral modifications and medications such as beta blockers, fludracortisone or midodrine are sometimes used in this condition

Management of specific Post-COVID symptoms: Neurocognitive Changes

- Screen patients who report memory and cognitive problems “brain fog” using formal testing such as the Montreal Cognitive Assessment (MOCA)
- Patients with scores indicating moderate-severe cognitive impairment may benefit from neuropsychological evaluation



MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE

Copy cube

Draw CLOCK (Ten past eleven) (3 points)

POINTS

E End, A, 5, B, 2, 1 Begin, D, 4, 3, C

[ ] [ ]

[ ] Contour [ ] Numbers [ ] Hands /5

NAMING

[ ] [ ] [ ] /3

MEMORY

Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2 /2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B /1

Management of specific Post-COVID symptoms: Smell and taste changes

- In most cases, symptoms resolve slowly over several weeks and do not require intervention except for education regarding food and home safety
- Persistent symptoms may respond to olfactory training programs

Management of specific Post-COVID symptoms: Fatigue and exercise intolerance

- Screen patients using a 6 minute walk test
- Encourage adequate rest, good sleep hygiene, fatigue management strategies
- Some patients may meet criteria for myalgic encephalomyelitis/chronic fatigue syndrome

Role of Physical Therapy

- Some have speculated that graded exercise therapy may not be appropriate for patients with COVID-related fatigue and debility given concern for worsening postexertional malaise (PEM)

- However, real world experience from multiple centers has demonstrated that a structured and supervised program can improve endurance and reduce fatigue and dyspnea for many patients

COVID and Diabetes

- Patients with type 2 diabetes are more likely to have serious complications, more ICU admissions, longer length of stay, and death from COVID
- Some studies suggest an increased incidence of diabetes after COVID
- Some of the newly diagnosed diabetes may be related to previously unrecognized diabetes, and approximately 50% of new-onset diabetes cases in the setting of COVID regressed to normoglycemia after recovery in one series
- An increase in the incidence of diabetes after COVID was also reported in children and adolescents <18 years of age

Source: Diabetes is a risk factor for the progression and prognosis of COVID-19. Guo et al. Diabetes Metab Res Rev. 2020
Source: Newly diagnosed diabetes vs. pre-existing diabetes upon admission for COVID-19: Associated factors, short-term outcomes, and long-term glycemic phenotypes. Cromer et al. J Diabetes Complications. 2022;36(4):108145. Epub 2022 Feb 4.

How can Post-COVID conditions be prevented?

- Several studies report lower rates of post-COVID symptoms in patients who are vaccinated
- Some data also indicate that early treatment of COVID (eg. with nirmatrelvir/ritonavir) may reduce the risk of development of post-acute sequelae of COVID

Source: Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers. Azzolini et al. Lancet Infect Dis. 2022;22(1):43. Epub 2021 Sep 1.

Ongoing areas of research on Post-COVID conditions

- NIH RECOVER has enrolled over 20,000 participants
- Obesity, Insulin Resistance, and PASC: Persistent SARS-CoV-2 infection and Inflammation in Human Adipose Tissue
- Pathophysiological Mechanisms of PASC: Inflammatory Mediators of Endothelial Dysfunction
- Role of Sleep in PASC Recovery and the Development of Immunological Memory
- Metabolic Dysfunction, Viral Persistence and Bioenergetic T-Cell Fatigue in Post-Acute SARS-CoV2
- Long-term Sequelae of SARS-CoV-2 Infection: Diabetes Mellitus