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

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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

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

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 SpO₂, 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
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

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 (e.g., with nirmatrelvir/ritonavir) may reduce the risk of development of post-acute sequelae of COVID.

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