Post-COVID19 perspectives for primary care

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General Internal Medicine
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Complex Chronic Diseases Program (CCDP)

We treat and manage Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, Fibromyalgia, and symptoms attributed to Chronic Lyme Disease.
Objectives

• Understand an approach to evaluation of patients with prolonged symptoms following SARS CoV2 infection
• Identify who requires additional evaluation
• Discuss approach to investigation of focal symptoms
• Identify patients who require referral to subspecialists
• (Treatment of post-COVID sequelae will not be discussed)

• Discussion of cases – mine and yours
Pathophysiology of SARS-CoV-2

1. **Direct cytotoxic effect**
   - Viral entry mechanism of SARS-CoV-2
   - Spike protein
   - Receptor-binding domain (RBD) of spike protein binds to ACE2

2. **Dysregulation of the RAAS**
   - Angiotensin I
   - Angiotensin 1-9
   - Angiotensin 1-7
   - Angiotensin II
   - Angiotensin II type 1 receptor
   - ACE2 downregulated

3. **Endothelial cell damage and thromboinflammation**
   - Endothelial cell damage and apoptosis
   - Endothelial inflammation
   - Fibrinolysis
   - Thrombin production

4. **Dysregulated immune response**
   - T cell lymphopenia
   - Inhibition of interferon signaling by SARS-CoV-2
   - Hyperactive innate immunity
   - Cytokine-release syndrome

- **Tissue injury/remodeling**
- **Inflammation**
- **Vasoconstriction**
- **Vascular permeability**

**Gupta 2020**
ACUTE COVID19

Nalbandian et al 2021

Subacute/ongoing COVID-19

Chronic/post-COVID-19

Fatigue
Decline in quality of life
Muscular weakness
Joint pain

Dyspnea
Cough
Persistent oxygen requirement

Anxiety/depression
Sleep disturbances
PTSD
Cognitive disturbances (brain fog)
Headaches

Palpitations
Chest pain

Thromboembolism

Chronic kidney disease

Hair loss

Week 12 6 months

Before symptom onset

Nalbandian et al 2021
Symptom Reports

Figure. COVID-19–Related Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Acute COVID-19 phase</th>
<th>Post-COVID-19 follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>Joint pain</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>Chest pain</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Cough</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Anosmia</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Sicca syndrome</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Red eyes</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Headache</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Sputum production</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Lack of appetite</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Sore throat</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Vertigo</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Myalgia</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>
10% of people infected with \textbf{SARS-CoV-2} will develop \textit{long COVID}, with persistent symptoms after 4 weeks.
COVID-19 – British Columbia numbers

<table>
<thead>
<tr>
<th>Cases</th>
<th>Recovered</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>148,000</td>
<td>145,000</td>
<td>1,759</td>
</tr>
</tbody>
</table>

https://ourworldindata.org/coronavirus-data
<table>
<thead>
<tr>
<th>What to call it?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post acute sequelae of COVID19 (PASC) – research term</td>
</tr>
<tr>
<td>Long COVID</td>
</tr>
<tr>
<td>Long-haul COVID</td>
</tr>
<tr>
<td>Post-acute COVID syndrome</td>
</tr>
<tr>
<td>Chronic COVID</td>
</tr>
<tr>
<td>(Myalgic encephalomyelitis/chronic fatigue syndrome?)</td>
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</tbody>
</table>
Definitions: timeline

There is no agreed-upon definition, but here is one from the CDC

**Acute COVID-19**: symptoms of COVID-19, up to four weeks following the onset of illness

**Post-COVID conditions**: broad range of symptoms (physical and mental) that develop during or after COVID-19, continue for ≥ 4 weeks, and are not explained by an alternative diagnosis
Most common symptoms

- Fatigue
- Brain fog
- Dyspnea
- Cough
- Painful joints or muscles
- Chest pain
- Depression or anxiety
- Headache
- Fever
- Palpitations
- Dizziness on standing
- Post-exertional malaise
Who gets long COVID?

• **SEX**: more common in women
  • Eg 23% of women and 19% of men still had symptoms 5 weeks after infection

• **AGE**: most common in younger to middle-aged adults
  • E.g. prevalence was 25.6% at 5 weeks for those between 35 and 49 years old

• **SEVERE COVID**: Patients with more severe acute symptoms were more likely; HOWEVER also seen in a large percentage of those with mild or even asymptomatic acute cases
Medically unexplained symptoms

“Everything has come back negative”

“There is nothing wrong with you”

Persistent symptoms and loss of function despite normal labs, imaging, electrophysiology, and other objective measures of organ function

NOT PSYCHOSOMATIC/SOMATIFORM
Pathophysiology of long COVID

• Organ damage resulting from acute phase infection?
• Complications from a persistent hyperinflammatory state?
• Ongoing viral activity?
• Inadequate antibody response?
• Worsening of co-morbidities?
• Extrinsic factors e.g. lockdown, isolation?
How to approach long-COVID patients

- Complete review of systems, screening for common symptoms
- Target investigations to patient symptoms
- Exhaustive investigations are not required to rule out objective end-organ disease
- Validate patient symptoms
- Refer to subspecialty for red flags or objective findings of disease
Approach to symptoms – what we do

- **Dyspnea, cough**: PFT, CT chest, echocardiogram, 6 minute walk test
- **Palpitations**: Holter, ECG
- **Chest pain**: ECG, exercise treadmill test, CCTA
- **Orthostasis**: orthostatic vitals, screen for POTS, am cortisol
- **Mood symptoms** – refer to Psychiatry (I am GIM!), trial of e.g. SSRI
Approach to Fatigue

• Review of focal symptoms to direct investigations

• Screening labs:
  • CBC + diff
  • Lytes, urea, creatinine
  • Mg, Phos, Ca
  • Fasting blood sugar
  • CRP Liver tests
  • CK TSH Ferritin Urinalysis
  • HIV HBV HCV FIT test

• >6 months fatigue, PEM, brain fog, unrefreshing sleep \( \equiv \) ME/CFS?
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When to refer

• Referral to subspecialty will depend on your access in your community, and your comfort with post-COVID patients

• NO referral: If a patient has normal investigations and symptoms are typical for long COVID, and are slowly improving

• We often refer to other specialists with objective findings of organ dysfunction (cardiac, respiratory, mental health, neurologic, dermatologic, thrombosis, voice dysfunction)

• I consider referral to the CCDP at BCWH in cases of severe fatigue, inability to work who have plateaued wrt recovery after 6-9 mo
Post-COVID19: Key points (CDC)

• The term “Post-COVID Conditions” is an **umbrella term** for the wide range of physical and mental health consequences experienced by some patients

• Objective laboratory or imaging findings should **not be used as the only measure** or assessment of a patient’s well-being

• Lack of laboratory or imaging abnormalities **does not invalidate** the existence, severity, or importance of a patient’s symptoms or conditions

• Approach treatment by **focusing on specific symptoms**

• Understanding of post-COVID conditions remains incomplete
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Post-COVID-19 Care & Recovery

Support your understanding and management of symptoms as you recover from COVID-19.
Questions/discussion

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