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EDUCATION

Podcast Contributor Show Notes

Long Covid /

Post Acute Sequelae of SARS Co-V 2 (PASC)

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Social Media Handles:

- **Twitter:** @LetMeIntubateU

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Objectives: To explore the presentation, diagnosis, and management of Post Acute Sequelae of SARS Co-V 2 for front-line clinicians in primary care, urgent care, and emergency department settings

Sample Tweet: Covid isn't going anywhere, & neither is #longcovid. More & more of our patients are suffering with long covid / #PASC. We sit down with expert @LetMeIntubateU to learn all about this syndrome & how front-line clinicians can best manage it. [insert link and screenshot of artwork]

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Patient Support Groups:

Survivor Corps. <https://www.survivorcorps.com>

Body Politic. <https://www.wearebodypolitic.com/covid19>

Long Covid Support. <https://www.wearebodypolitic.com/covid19>

Tags:

Infectious disease ID, Pulmonary

*****DO NOT PUBLISH BELOW HERE*****

Introduction: Story of a patient with long covid

Main Talking Points:

1. What is the actual *name* of this syndrome? It's changed over time!

Post-Acute Sequelae of Covid-19 (PASC) Syndrome

Formerly called long-haulers, long-covid, post-covid

2. How do we define it?

>4 weeks of symptoms that are presumed from covid-19 is subacute version of it, >12 weeks is chronic form

3. What do we know about the percentage of covid patients who are affected by this?

Some pre-publications (sorry for even citing these) suggest that up to 80% of patients may have symptoms of PASC. Although currently published work suggest anywhere from 30-50% will have ongoing prolonged symptoms.

4. Is there a "typical" demographic emerging?

In a recent Lancet publication looking at 6 months symptoms, it looks like women are more likely to have diffusion impairment on PFT, a trend towards CT scan findings, more anxiety and depression, and msk symptoms.

Similarly, older adults have worsening diffusion impairment, CT scan findings, and msk symptoms.

5. How did you become interested in it? You literally created a clinic for these patients at your institution!

Serendipitously, I was building a post-ICU clinic at the start of my first year on faculty here. Within 9 months it became clear that the greatest population in need of post-ICU follow up was our COVID-19 patients since our ICU's quickly filled with these patients and every patient on ECMO had covid. Then gradually i started to get patients reaching out to me that had covid but never were critically ill that wanted to see me. Again, it became very apparent how much this population of people needed someone familiar with COVID to participate in their care.

6. What causes it? What are some of the main theories right now?

Direct viral toxicity? Endothelial damage? Prolonged inflammatory response??
Cytokine production? Pro-coagulant state? Immune dysregulation?

Survivors of SARS COV 1 and MERS had similar long term symptoms

7. Let's talk about how our patients may present with long covid. Which symptoms are most commonly associated with this syndrome?

I most commonly see shortness of breath and "brain fog" or other neuropsychiatric symptoms. Typically patients present several months after their acute illness with ongoing symptoms and failure to recover to baseline or inability to return back to work.

As i had alluded to, there are sort of two overlapping phenotypes of this presentation. One is the group that was in the ICU and critically ill on a ventilator or on ECMO for this illness. I typically see those patients in my clinic and follow up with them routinely. This is in contrast to those that were not critically ill and often times did not even require hospitalization and these patients typically present out of frustration or concern for their ongoing symptoms

8. On a related note, what does the data so far tell us about how long these symptoms might last?

We don't know, only that the probability of ongoing symptoms probably goes down over time. But it also appears that there will be subphenotypes that emerge from this larger population. The group of critically ill covid patients who have some prolonged symptoms but then gradually recover. Those that were never critically ill but that have prolonged symptoms of covid-19. Reports are suggesting that patients with moderate disease may have the highest probability of prolonged symptoms whereas those with severe disease had acute symptoms but then recover and have a lower probability of prolonged symptoms.

9. Are there any risk factors we can identify?

Women? age?

10. What should our workup entail?

MultiID clinic

Symptom based workup

11. When do you find yourself reordering certain tests, e.g., repeating parts of the workup if the patient isn't feeling better?

I try not to, unless there has been a clinical change. Every test is limited. No test is perfect. The sensitivity/specificity of any test is not 100% and the diagnostic yield of any test is less than 100%. If I perform a CT scan to look for PE and there is no PE and the patient has ongoing symptoms 30 days later, i do not repeat the test. In some patients if i did, i would be repeating this test dozens of times. Instead, i continue

through the workup unless the patient has an acute change or decompensation that makes me suspicious that i need to repeat the test.

12. Let's move onto management. This can be a really challenging condition for our patients to live with. And we don't always know how to help them. How should we approach the treatment of long covid?

- a. Validating their experience, letting them know we believe them (YES)
- b. Targeted treatment of symptoms (YES) *(let's give examples)*
- c. Ongoing support like pulmonary rehab, PT, counseling, etc. depending on symptoms (YES)
- d. Encouraging participation in clinical trials

13. Are there any unusual medications or novel therapies being studied? *(e.g., ivermectin - this seems to be popping up everywhere these days! Or anything else)*

Ivermectin data is bad in acute covid

Some trials on antifibrotic therapy, although some of these studies have been stopped early for adverse outcomes

Vitamin B12

COVID-19 vaccine itself?

14. We're learning that the covid vaccine seems to help about a third of patients with long covid syndrome feel better. Is this legit? Why do we think this might help?

- a. **It might be legit**
- b. **Immune distraction?**

15. There is a large body of emerging literature on this subject. Are there any articles that you particularly like, that we should direct our listeners to?

16. Any patient resources or support networks that we could educate our patients about?

17. Closing pearls / top 3 take-home points you want front-line clinicians to know about this disease.

- a. **These prolonged symptoms are real**
- b. **It remains our job as front-line physicians to encourage vaccination, mask wearing, and social distancing while vaccine efforts are under way to prevent covid-19 illness in our patients**
- c. **A multiD approach to patient care is often needed**

Neda's Notes:

Terminology: lots of different terms, including

- Post acute covid syndrome (beyond 3 weeks of symptoms)
- Chronic covid (beyond 12 weeks)
- Long covid
- Long hauler

Fauci in late February: **Post Acute Sequelae of SARS-CoV 2**, or PASC, to be studied at NIH

Does not *require* having had a positive test

Symptoms:

- Many different symptoms, some of them vague
- Top symptoms (in order from recent studies) are fatigue, muscle or body aches, SOB, difficulty concentrating or focusing, inability to exercise, headache, difficulty sleeping, anxiety, memory problems
- July 2020 report from Survivor Corps

Prevalence:

- We're learning more as we go
- Anywhere from 10% to 75% of people have symptoms more than 3 months afterwards
- In a 1/21 *Lancet* Chinese cohort study of 1,733 patients assessed 6 months after discharge, 76% of patients had at least one symptom, mainly fatigue or muscle weakness, sleep difficulties, and anxiety or depression.
 - *"More severely ill patients had increased risk of pulmonary diffusion abnormality, fatigue or muscle weakness, and anxiety or depression. The seropositivity and titers of the neutralizing antibodies were significantly lower than at acute phase."*
- Early Italian data: 50% of patients had symptoms >8 weeks out
- Irish study: 50% of patients had symptoms at >10 weeks out (PLoS One 11/20)
- Covid Symptom Study: 10% had symptoms at >4 weeks (BMJ 10/20)
- New York/Mt. Sinai: 10% had symptoms at >8 weeks
- JAMA research letter: 30% at 6 months (JAMA Network 2/21 based on survey data of ~200 patients)

Predictive Factors:

Covid Symptom Study from Kings College - prelim data suggest:

- Female
- Elevated age
- Elevated BMI
- Asthma
- Multiple symptoms after 5 days

Pathophysiology: Several different theories

- Overactive immune response and neurovascular dysregulation
- SARS-CoV-2 binds to ACE2 and enters host cell and directly damages the target organ
- Leads to inflammatory cytokine cascade

Workup:

Organize approach based on systems; see infographic below

Management:

- Patient validation - "I am listening. I believe you."
- Expectation setting
- Clinically actionable approach

Potential Treatments:

- Anti-inflammatory/allergy -- antihistamines, steroids, NSAIDs, antibiotics, colchicine
- Antivirals / monoclonal antibodies -- leronlimab (Miravaroc), Singulair, ivermectin
- Supplements: niacin, omega 3 fatty acids, thymosine alpha one
- Mood / memory: Wellbutrin, Luvox, stimulants?
- Pulmonary interventions: ICS, albuterol

Patients have organized themselves into a few support groups that have grown quite large:

- Survivor Corps - Fauci has presented to them
- Body Politic
- Long Covid Support

BMJ Infographic: "Long Covid in Primary Care."

"Long covid" in primary care

Assessment and initial management of patients with continuing symptoms

Post-acute covid-19 appears to be a multi-system disease, sometimes occurring after a relatively mild acute illness. Clinical management requires a whole-patient perspective. This graphic summarises the assessment and initial management of patients with delayed recovery from an episode of covid-19 that was managed in the community or in a standard hospital ward.

An uncertain picture



The long term course of covid-19 is unknown. This graphic presents an approach based on evidence available at the time of publication.

However, caution is advised, as patients may present atypically, and new treatments are likely to emerge

Managing comorbidities

Many patients have comorbidities including diabetes, hypertension, kidney disease or ischaemic heart disease. These need to be managed in conjunction with covid-19 treatment. Refer to condition specific guidance, available in the associated article by Greenhalgh and colleagues

Safety netting and referral

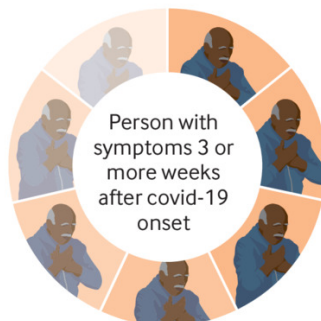
The patient should seek medical advice if concerned, for example:

- Worsening breathlessness
- PaO₂ < 96%
- Unexplained chest pain
- New confusion
- Focal weakness

Specialist referral may be indicated, based on clinical findings, for example:

- Respiratory** if suspected pulmonary embolism, severe pneumonia
- Cardiology** if suspected myocardial infarction, pericarditis, myocarditis or new heart failure
- Neurology** if suspected neurovascular or acute neurological event

Pulmonary rehabilitation may be indicated if patient has persistent breathlessness following review



Person with symptoms 3 or more weeks after covid-19 onset

Clinical assessment

04
Full history
From date of first symptom

Current symptoms
Nature and severity

Examination, for example:

- Temperature
- Heart rate and rhythm
- Blood pressure
- Respiratory examination
- Functional status
- Pulse oximetry
- Clinical testing

Assess comorbidities

Social and financial circumstances

Investigations

Clinical testing is not always needed, but can help to pinpoint causes of continuing symptoms, and to exclude conditions like pulmonary embolism or myocarditis. Examples are provided below:

Blood tests

- Full blood count
- Electrolytes
- Liver and renal function
- Troponin
- C reactive protein
- Creatine kinase
- D-dimer
- Brain natriuretic peptides
- Ferritin – to assess inflammatory and prothrombotic states

Other investigations

- Chest x ray
- Urine tests
- 12 lead electrocardiogram

Social, financial, and cultural support

Prolonged covid-19 may limit the ability to engage in work and family activities. Patients may have experienced family bereavements as well as job losses and consequent financial stress and food poverty. See the associated article by Greenhalgh and colleagues for a list of external resources to help with these problems

Medical management

- Symptomatic, such as treating fever with paracetamol
- Optimise control of long term conditions
- Listening and empathy
- Consider antibiotics for secondary infection
- Treat specific complications as indicated

Self management

- Diet
- Sleep
- Quitting smoking
- Limiting alcohol
- Limiting caffeine
- Daily pulse oximetry
- Attention to general health
- Rest and relaxation
- Self pacing and gradual increase in exercise if tolerated
- Set achievable targets

Mental health

In the consultation:

- Continuity of care
- Avoid inappropriate medicalisation
- Longer appointments for patients with complex needs (face to face if needed)

In the community:

- Community linkworker
- Patient peer support groups
- Attached mental health support service
- Cross-sector partnerships with social care, community services, faith groups

