



# Similar presentation with other Corona viruses

- Middle Eastern Respiratory Syndrome (MERS) • Severe Adult Respiratory Syndrome (SARS)
- Both are the result of a corona virus
- Patients with these syndrome developed:
- Fatigue, myalgias, psychiatric conditions
- Present at 4-year follow-ups, as well as 7 and 15-years postinfection

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8146298/ accessed 07-01-2021 WRIGHT, 2023

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## What is the cause?

- Proposed that T-cell dysfunction may promote long COVID pathophysiology similar to what happens with autoimmune diseases
- 15-20% develop thyroid dysfunction
  Increased risk of developing Type I diabetes following COVID
  B-cells may also be involved in long COVID autoimmunity
- Other autoantibodies against interferons, neutrophils, connective tissues, cyclic citrullinated peptides, and cell nucleus are present in 10–50% of patients with COVID-19
- Gut microbiome disruption may also play a significant role
- Harbored Viral RNA x months

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC89499999/ accessed 07-01-2021

# Does Epstein-Barr Virus Play a Role?

- $\bullet$  One study showed that the COVID virus may reactivate the Epstein-Barr Virus
  - This virus is associated with mononucleosis and is also that to be the predominant cause of Chronic Fatigue Syndrome
  - Ordering an EBV Serology: 4 different markers to look for acute, recent, past or a reactivation may be the most helpful test to see if this virus is involved

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• EBV viral load is another potentially helpful test to obtain

https://health.ucdavis.edu/news/headlines/11-things-doctors-have-learned-about-long-haulcovid/2022/02?msclkid=cc7b54dcb35e11ec9e9cdee73cd750c4 wRIGHT, 2023

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# Autopsy Studies

- Lungs: diffuse alveolar damage similar to ARDS, end-stage pulmonary fibrosis, microthrombi, endothelial damage: all worse than that with influenza
- Heart: virus genome in cardiac tissue, intramyocardial inflammation, increased macrophages, T lymphocytes in the tissue
- Brain: acute hypoxemic damage in the cerebrum and cerebellum
- Renal: acute tubular necrosis

https://www.ncbi.nlm.nih.gov/books/NBK570608/?msclkid=b420b179b35a11eca2962546f297f8cd

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Differentiation (Terminology)	
Subacute or persistent COVID symptoms: u to 12 weeks from the initial infection	ıb
Chronic or Post acute Covid 19 syndrome: 7 weeks or longer of symptoms not attributab to other conditions	
https://www.ncbi.nlm.nih.gov/books/NBK570608/?msclkid=b420b179b35a11eca2962546f297f8cd	

# October 2021: World Health Organization Definition

• Term: Post Covid-19 Condition

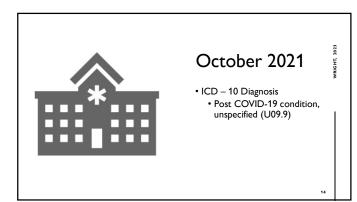
• "Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis."

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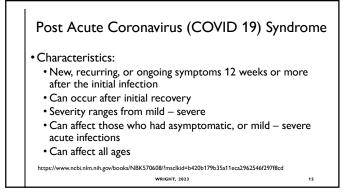
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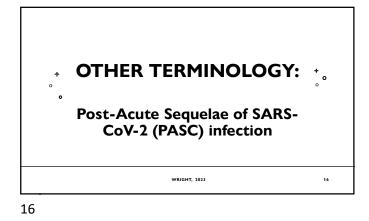
https://www.who.int/publications/i/item/WHO-2019-nCoV-Post\_COVID-19\_condition-Clinical\_case\_definition-2021.1 accessed 10-10-2021

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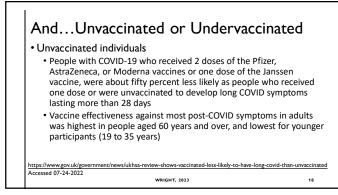


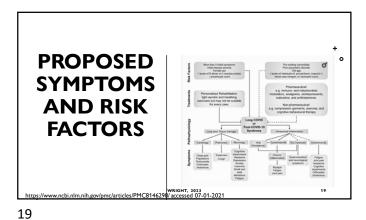
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 How Common is Post Acute Covid Syndrome?

 Image: Syndrome is post acute covid syndrome is post acute of post acute in a strain in this cohort of individuals with COVID-19 who were followed up to 9 months after illness, approximately 30% reported persistent symptoms.

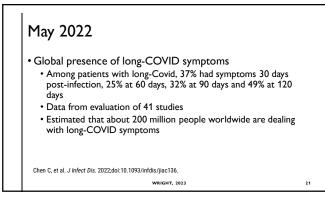
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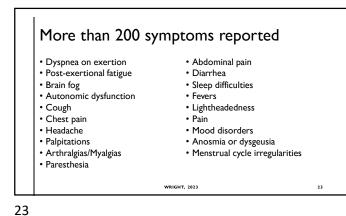
# Hospitalized Patients

- One half of people hospitalized with COVID-19 suffer at least one symptom 1 year after discharge
- Most common symptoms: fatigue and muscle weakness • Approximately 1/3 have persistent shortness of breath
- Increased rates of depression, anxiety, mobility issues

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01755-4/fulltext accessed 09-02-2021 WRIGHT, 2023

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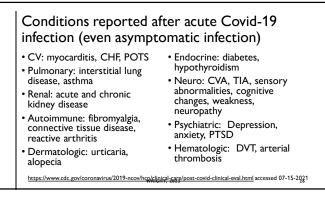
# New Study

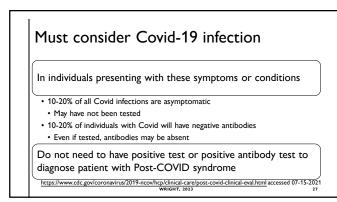
- Moderate to severe sleep disturbances and severe fatigue affect up to 40% of patients with long COVID, or post-acute sequelae of SARS-CoV-2 infection (PASC).
- These disturbances are particularly common among individuals of color (3x greater rate)

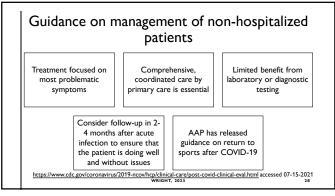
Dr. Pena, Annual meeting of the Associated Professional Sleep Societies; Sleep 2022 WRIGHT, 2023

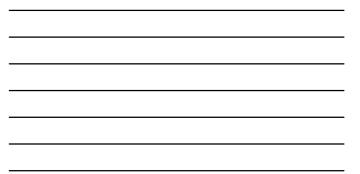
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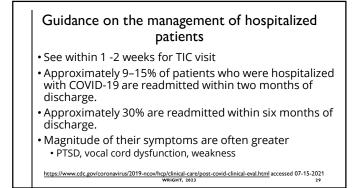
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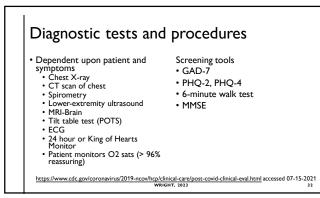


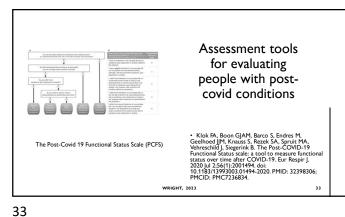




# Laboratory testing • Dependent upon patient and symptoms: • CBC with differential • OMP (glucose, liver, kidney, electrolytes) • D-dimer • BNP • TSH • AtC • Sed rate and CRP • ANA, RF, anti-CCP • Coagulation panel • Epstein Barr Virus Panel and viral load • Lyme • Vitamin D • CRP • Ferritin

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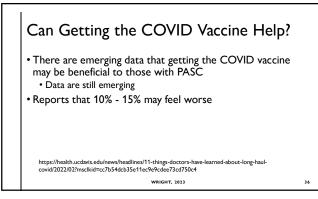
# Non-Pharmacologic Treatment Options

• Healthy diet

- Exercise plan: 30 minutes 5 days per week
- This has not been shown to worsen the symptoms/situation
- Acupuncture, Yoga, Tai Chi, Meditation (all being investigated)

https://health.ucdavis.edu/news/headlines/11-things-doctors-have-learned-about-long-haulcovid/2022/02?msclkid=cc7b54dcb35e11ec9e9cdee73cd750c4 wкюнт, 2023

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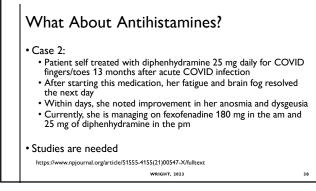
# What About Antihistamines?

- In a recent paper published in Journal of Nurse Practitioners, two patient case studies showed significant improvement in fatigue and improved ability to concentrate after taking diphenhydramine 50 mg. Patient took daily x 6 months and then transitioned to hydroxyzine 25 mg – with titration up to 150 mg daily.
- Patient maintained on 50 mg of hydroxyzine daily with elimination of fatigue, chest pain, recurrent rashes, brain fog and exercise intolerance

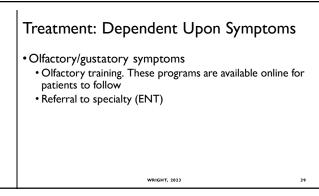
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https://www.npjournal.org/article/S1555-4155(21)00547-X/fulltext WRIGHT, 2023

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# Dyspnea: Must consider: pulmonary embolism Consider pulmonology referral Refer to: Pulmonary rehabilitation Vaccinate against influenza and pneumococcal infections Pulmonary function testing Steroids: mixed evidence Post acute COVID 19 specialty clinic

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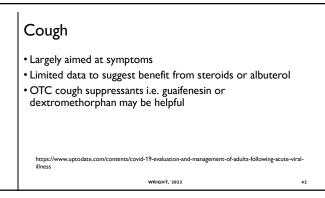
# Emerging Data

- Most have normal Chest Xray and CT scan
- However, using SPECT CT microemboli are detected; able to visualize using a radiotracer which parts of the lungs are not receive adequate blood supply
- Unfortunately, many don't meet criteria for anticoagulant treatment but should that change?

https://www.science.org/content/article/what-causes-long-covid-three-leading-theories accessed 07-27-2022
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# Mental Health

- SSRIs are likely to help many with Post Acute Covid 19 mental health symptoms i.e. anxiety/depression
- SSRIs such as fluoxetine which tends to be more energizing may be beneficial
- If pain is an issue along with depression/anxiety, consider SNRI for treatment

https://health.ucdavis.edu/news/headlines/11-things-doctors-have-learned-about-long-haulcovid/2022/02?msclkid=cc7b54dcb35e11ec9e9cdee73cd750c4 wRIGHT, 2023

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# Autonomic Dysregulation (POTS)

- POTS (orthostatic intolerance)
- Tilt Table Test
- Salt tablets 1 pill up to three times daily (3000-10000 mg daily)

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- $\bullet$  Fludrocortisone 0.1 mg 0.2 mg daily; max 1 mg daily
- Pyridostigmine 60 mg 120 mg every 8 hours (Myasthenia Gravis)
- Midodrine 10 mg three times daily (Pressor)
- Beta blocker (Metoprolol ER 25 mg once daily)
- Compression stockings

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# Other Treatments Being Looked At... • Blood washing also known as apheresis

- Little evidence to support; anecdotal evidence at best
- Not covered by insurance
- Procedure: blood removed through large needle from one arm, filtered to remove inflammatory proteins and lipids and returned to the other arm
- Hypothesis behind this is that COVID causes microclots, which are clogging capillaries and reducing oxygen
- Some are also turning to anticoagulants

<u>https://www.bmj.com/content/378/bmj.o1671</u> accessed 07-27-2022 wright, 2023

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# Other Treatments Being Looked At...

• Ritonavir boosted nirmatrelvir

• Anecdotal reports from individuals who have taken this

• At present, only indicated for those infected with acute COVID within 5 days of onset and at increased risk

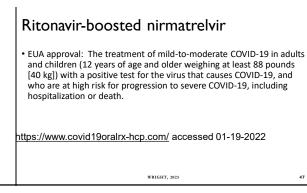
• Pfizer has being pushed to investigate further; study has been started

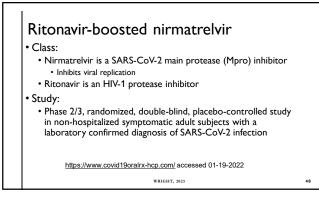
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• Concern re: rebound after completing treatment

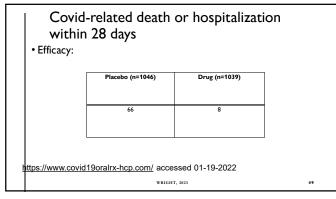
https://www.medscape.com/viewarticle/973538 accessed 07-27-2022 wRIGHT, 2023

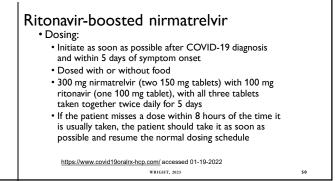
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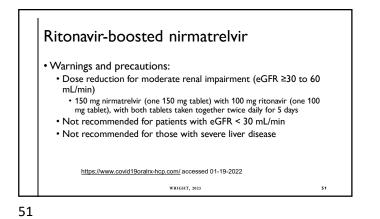












### Numerous Drug Interactions • Avoid with the following medications (CY3A cleared): • Alpha1-adrenoreceptor antagonist: alfuzosin • Analgesics: pethidine, piroxicam, propoxyphene • Antianginal: ranolazine • Antiarchurchenic actic during the second seco

pethidine, piroxicam, propoxyphene •Antianginal: ranolazine • Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine • Anti-gout: colchicine • Antipsychotics: lurasidone, pimozide, clozapine • Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine • HMG-CoA reductase inhibitors: lovastatin, simvastatin • PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH) • Sedative/hypnotics: triazolam, oral midazolam

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# CYP 3A Inducers

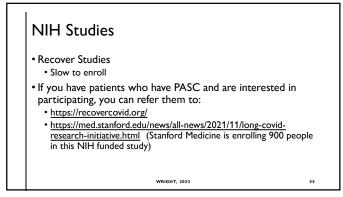
• Will result in decrease in levels and can result in reduced efficacy and drug failure

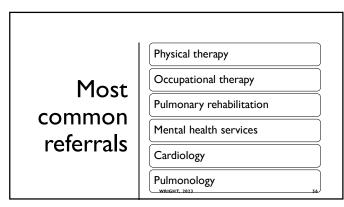
- Anticancer drugs: apalutamide
- Anticonvulsant: carbamazepine, phenobarbital, phenytoin
- Antimycobacterials: rifampin
- Herbal products: St. John's Wort (hypericum perforatum)

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# Ritonavir-boosted nirmatrelvir Adverse events (drug vs. placebo): Dysgeusia (6% vs. <1%)</li> Diarrhea (3% vs. 2%) Hypertension (1% vs. <1%)</li> Myalgias (1% vs. <1%)</li> 2% in the treatment group discontinued due to an adverse event; 4% in the placebo arm







# Evidence-based interventions

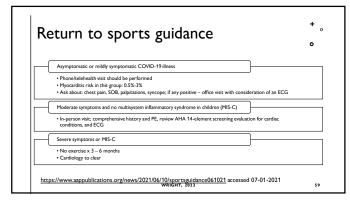
- Graduated return to exercise/activity
- Pulmonary rehab to improve breathing and strengthen respiratory muscles

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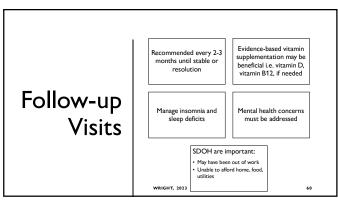
• Psychological support/interventions

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8146298/ accessed 07-01-2021

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# Post Acute Covid Clinics Numerous clinics are being developed across the country Multi-disciplinary clinicians/specialty NPs, PAs, MDs, Pulmonology, Cardiology, Physical Medicine, Psychiatry, Neurology, Physical Therapy, Occupational Therapy Many are closely studying their population and outcomes Expect significant amount of data over the next 1-2 years

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Resources	Long Covid Alliance (https://longcovidalliance.org/)
	Long Covid Kids (https://www.longcovidkids.org/)
	Center for Disease Control (www.cdc.gov)
	American Academy of Pediatrics (www.aap.org) www.ight, 2023

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