Proposed Long-COVID workup and treatment approach from the clinics of Drs. Alex Truong, Tiffany Walker, and Thanushi Wynn – 01/23/2024

NOTE: This resource serves as reflection of our experience in working with Long-COVID patients.

Presenting Symptom	Diagnostic workup	Treatment
Syndrome consistent with long-COVID		Certizine 10mg BID (can trial other antihistamines, but at BID dosing) Famotadine 40mg BID Paced exercise tailored to Long COVID phenotype[1] Aggressive hydration Adequate sleep COVID vaccination and masking Vitamins that may help symptoms: - L-Arginine - Vitamin C - Alpha-lipoic acid - Vitamin D - Coenzyme Q10 - Tryptophan
Neuropsychiatric		
Brain fog/Cognitive dysfunction	Screen with MOCA or Digit Symbol Substitution Tool TSH, RPR, Vit B12, Vit D Referral to neuropsychology for further testing	Atomoxetine. Start with 40mg daily and titrate up by 20mg depending on persistence of symptoms and side effects. In some patients who report crashing in the early afternoon, BID dosing can be used. Other medications to consider: methylphenidate, dextroamphetamine/amphetamine, lisdexamfetamine, viloxazine, and guanfacine. Cognitive pacing counseling Referral to speech therapy or neuropsychology for cognitive rehabilitation therapy and compensatory training

Fatigue	TSH, RPR, Vit B12, Vit D	Physical therapy referral Aggressive hydration Pacing exercise with a balance of both endurance and strength building activities; monitor for post exertional malaise and modify physical or cognitive exertion, accordingly Consider use of stimulant or non-stimulant based ADD medication or stimulating SSRI such as Fluoxetine Low dose naltrexone (compounded)[2] - 1.5mg PO nightly x7 days - 3.0mg PO nightly x7 days - 4.5mg PO nightly onwards - Down titrate if symptoms worsen on higher doses
Post-exertional malaise	TSH, RPR, Vit B12, Vit D	Consider low dose naltrexone as above Physical and cognitive pacing
Anosmia/ageusia		Referral to pain management for possible stellate ganglion nerve blockade. Referral for smell retraining
Depression	PHQ-9 GDS short form	SSRI/SNRI
Anxiety	GAD-7	SSRI/SNRI Group therapy
Insomnia/sleep disturbances	PSG MSLT Screen for mood disorder	Melatonin Low dose Delta-8 supplement Quetiapine Trazadone SSRI/SNRI Low dose naltrexone (compounded)[2] - 1.5mg PO nightly x7 days - 3.0mg PO nightly x7 days 4.5mg PO nightly onwards - Down titrate if symptoms worsen on higher doses Referral to sleep medicine

Neuropathy/numbness and tingling	Vit b12, vit D, and TSH serum levels.	Consider brain imaging and referral to neurology if symptoms are associated with localizing weakness Trial Gabapentin/pregabalin Empiric initiation of vitamin D and B complex supplements.
Chronic pain		
Myalgia/arthralgia	ESR, CRP, RF, ANA w/ reflex, CPK, aldolase, myositis panel.	High dose NSAID (Ibuprofen 600mg TID w/ food) x2 weeks Gabapentin/pregabalin Low dose naltrexone (compounded) - 1.5mg PO nightly x7 days - 3.0mg PO nightly x7 days - 4.5mg PO nightly onwards - Down titrate if symptoms worsen on higher doses Avoid narcotics
Headaches/migraines	Consider brain MRI, especially if with localizing symptoms such as weakness or intractable nausea	Gabapentin/pregabalin Sumatriptan Low dose naltrexone (compounded) - 1.5mg PO nightly x7 days - 3.0mg PO nightly x7 days - 4.5mg PO nightly onwards Down titrate if symptoms worsen on higher doses Neurology referral
Chest pain	EKG and CXR	High dose NSAID (Ibuprofen 600mg TID w/ food) x2 weeks Can trial low dose naltrexone
Respiratory		
Dyspnea	PFTs, 6MW, chest imaging	Trial ICS or ICS/LABA with SABA Heart rate control if inappropriate tachycardia present with exertion.
	Abnormal chest imaging - Autoimmune workup	Consider biopsy. If results are consistent with organizing pneumonia or show active inflammation, then initiate treatment with corticosteroids x1-3months.

		If results are consistent with fibrosis without active inflammation, then treat with supportive care including supplemental oxygen, pulmonary rehab referral, and weight management.
	Normal chest imaging	Consider eval for cardiac dysfunction (TTE), pulmonary embolism (V/Q scan), Halter monitoring, and exercise testing (CPET) Consider pulmonary rehab
Cough	CXR Pulmonary function testing	Trial ICS or ICS/LABA with SABA Consider PO corticosteroids
Cardiac		
Tachycardia	D-dimer, fibrinogen, and iron studies. 6MW Check for orthostatic hypotension Tilt-table testing for possible POTS	Consider beta blocker (Toprol or Nadolol) or calcium channel blocker (diltiazem) Compression stockings
Gastrointestinal		
Nausea/vomiting		Bland diet PRN zofran, compazine, or reglan Consider trial of PPI or H2 blockade Consider probiotics[3] Consider GI referral for eval for possible gastroparesis
Diarrhea		High fiber, lactose free diet Imodium Consider probiotics[3] Consider GI referral or trial medications for IBS-D[4]
Constipation		Bowel regimen with Senna, Colace and prn Miralax. Consider probiotics[3] Consider GI referral or trial medications for IBS-C[4]
GERD		Famotidine 40mg BID Dietary and lifestyle changes

Other		
Dysautonomia	Tilt-table testing Check for orthostatic hypotension	Increased salt intake Compression stockings Recumbent physical activity with slow, stepwise progression to upright exercise as tolerated Consider[5] - Fludrocortisone - Midodrine - Propranolol - Clonidine - Pyridostigmine Consider referral to Cardiology to discuss ivabradine Consider referral to pain management for possible stellate ganglion nerve blockade.

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2. Bonilla H, Tian L, Marconi VC, et al. Low-dose naltrexone use for the management of post-acute sequelae of COVID-19. *Int Immunopharmacol*. Nov 2023;124(Pt B):110966. doi:10.1016/j.intimp.2023.110966

3. Liu Q, Mak JWY, Su Q, et al. Gut microbiota dynamics in a prospective cohort of patients with post-acute COVID-19 syndrome. *Gut*. Mar 2022;71(3):544-552. doi:10.1136/gutjnl-2021-325989

4. Marasco G, Cremon C, Barbaro MR, et al. Post COVID-19 irritable bowel syndrome. *Gut*. Dec 9 2022;doi:10.1136/gutjnl-2022-328483

5. Vernino S, Bourne KM, Stiles LE, et al. Postural orthostatic tachycardia syndrome (POTS): State of the science and clinical care from a 2019 National Institutes of Health Expert Consensus Meeting - Part 1. *Auton Neurosci*. Nov 2021;235:102828. doi:10.1016/j.autneu.2021.102828