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Integrative Strategies for Long COVID

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Disclosures

Dr. Patterson is

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Served on CDC's Healthcare Infection Practices Advisory Committee

Has been a consultant to San Antonio Metro Health Department

Has been a co-investigator for the NIH Adaptive COVID-19 Treatment Trial (ACTT) studies at UT Health and UH

Was a sub-investigator for the Novavax SARS-CoV-2 vaccine trial at UT Health and UH

Has received income from Young Living Essential Oils

Has received honoraria from Medscape

Is a co-investigator for RECOVER NIH trial

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For more information, please visit <https://minorityhealth.hhs.gov/>

Learning Objectives

1. Define the nomenclature and major features of Long COVID that require management
2. Define Integrative Medicine
3. List some integrative medicine strategies for the management of Long COVID

Nomenclature Long COVID

- Post-Acute Sequelae of COVID-19 (PASC)
- Long Haul COVID, Post-COVID-19 Condition, Chronic COVID
- ICD-10-CM U9.09

- WHO Definition
 - Continuation or development of new symptoms **3 months** after initial SARS-CoV-2 infection, with these symptoms lasting for at least **2 months** with no other explanation
- CDC definition
 - Signs, symptoms, and conditions that continue or develop after initial COVID-19 or SARS-CoV-2 infection. The signs, symptoms, and conditions are present **four weeks or more** after the initial phase of infection
 - May be multisystemic; and may present with a relapsing– remitting pattern and progression or worsening over time, with the possibility of severe and life-threatening events even months or years after infection. Long COVID is not one condition. It represents many potentially overlapping entities, likely with different biological causes and different sets of risk factors and outcomes.

Key Features and Proposed Pathology

Fatigue	Metabolic, Mitochondrial
Post-exertional malaise (PEM)	
Brain fog	
Dizziness	Dysautonomia/Endothelialitis
Postural Tachycardia Syndrome (POTS)	
Gastrointestinal/SOB/Skin	Mast cell dysfunction
Anxiety/Depression	Mental/emotional

Integrative Medicine

- Approach to the ***whole*** patient
 - Body, mind, spirit
- Integration of *evidence-based* holistic therapies ***with*** conventional medicine
- Use of natural, non-invasive therapies when possible

Not complementary (parallel)

Not alternative (instead of)

Adaptogens

- Randomized placebo-controlled trial, n=100
 - Proprietary blend of adaptogens
 - Rhodiola, Elutherococcus, Schisandra
 - Supplementation X 2 weeks
 - Improvement in daily walk time, cough, decreased creatinine, decreased IL-6
 - compared to placebo

Karosanidze et al. Efficacy of adaptogens in patients with Long COVID.
Pharmaceuticals (Basel) 2022



Aromatherapy

- Randomized placebo-controlled trial, n=40 women
 - Proprietary blend
 - Thyme, orange, clove bud, frankincense
 - Inhaled twice daily X 2 weeks
 - Lower fatigue scores
 - Increased vigor, decreased mental fatigue compared to placebo

Food Supplements

- Randomized placebo-controlled trial, n=188
 - Fermented *Carica papaya* & *Morinda citrifolia* (noni) proprietary supplement, fermented & w honey
 - Plants known for immune-modulating, anti-inflammatory
 - 28 grams supplement twice daily X 20 days
 - Decreased clinical symptoms, IL-6, IL-8, nitric oxide metabolites compared to placebo

Supplement - Oxaloacetate

- Essential for gluconeogenesis/Krebs cycle.
 - Energy & mental focus
- Non-randomized controlled trial, n=43; 16 ITT
 - Anhydrous enol-oxaloacetate (AEO) 500 mg
 - Dosed 500 mg BID, 1000 BID, or 1000 TID X 6 weeks
 - Then, 500 mg BID or 1000 mg BID X 6 weeks
 - Decreased fatigue, dose-dependent

Natural sources – daikon radish, sacred lotus, cucurbita (gourd), tarragon



Cash & Kaufman. *J Trans Med.* 2022



Supplements & Olfactory training

- Randomized placebo-controlled trial, n=69, Rome
 - Ultra-micronized palmitoylethanolamide 700 mg & luteolin 70 mg (PEA-LUT) (anti-neuroinflammatory) and
 - Olfactory training (lemon, eucalyptus, rose, cloves)
 - Improved memory & olfaction compared to placebo

Natural sources PEA – egg yolks, peanuts

Luteolin – celery, parsley, broccoli, carrots, peppers, cabbage, apple skin

Supplement Stack

Supplement 'stack' may include

- High dose Vitamin C and D
- Niacin
- Quercetin
- Zinc
- Selenium
- +/- Magnesium

Nurek M et al *Brit J Gen Practice*. 2021

Medinger survey:

Modest improvements from

- Niacin
- Low histamine diets

Medicinger & Altmann. *Long COVID Handbook*



THE LONG COVID HANDBOOK



World-leading Expert Advice on Understanding,
Managing and Treating Long Covid

GEZ MEDINGER &
PROFESSOR DANNY ALTMANN



Probiotics

- Theoretical support of probiotics for COVID-19 therapy and longterm complications
 - Gut microbiota link to longterm manifestations
 - Probiotics may fight viral infections
 - May be an adjuvant therapy

Alenazy MF et al. *Metabolites*. 2022

Low Dose Naltrexone

- Observational study, no control. n=52
- LDN 1mg month one; 2 mg month two
- Improvement in 6 of 7 parameters
 - COVID-19 recovery
 - Limitation in activities of daily living
 - Energy levels
 - Pain levels
 - Concentration
 - Sleep disturbance
 - Improvement in mood – not significant

Inspiratory Muscle Training (IMT)

- Randomized controlled trial, n=281, UK & Denmark
 - Inspiratory muscle training X 8 weeks (Pulmonary Rehab)
 - Improved in breathlessness and chest symptoms
 - Improved resp muscle strength & aerobic fitness compared to placebo

Diaphragm Release + IMT

- Randomized controlled trial, n=52 men, Egypt
 - Diaphragm release + IMT
 - vs IMT alone X 6 weeks (Pulmonary Rehab)
 - Improved in breathlessness and chest symptoms
 - Improved resp muscle strength & aerobic fitness compared to placebo

Manual Diaphragm Release



Figure 1

Manual Diaphragm Release Technique. Source: Authors' own photo.

Rocha et al *J Physio* 2015

<https://www.youtube.com/watch?v=aJtGf4BtN>

cQ

Manual Diaphragm Release

How to release your own diaphragm



<https://www.youtube.com/watch?v=aJtGf4BtNcQ>



ENO (English National Opera) Breathe

- Randomized controlled trial, n=150, UK
 - Online breathing & wellbeing program, focused on breathing retraining using singing techniques
 - Welcome pack
 - Weekly online lessons
 - Focus group & emails
 - Online resources, self-directed
 - Lullabies, exercise videos
 - Improved mental health, breathlessness
 - Complementary integrated w standard care
 - Suitability of singing & music to address needs

ENO Breathe Welcome Pack

Participants receive a welcome pack, containing a welcome note from the ENO Breathe team and items including an ENO mug, tea, biscuits.



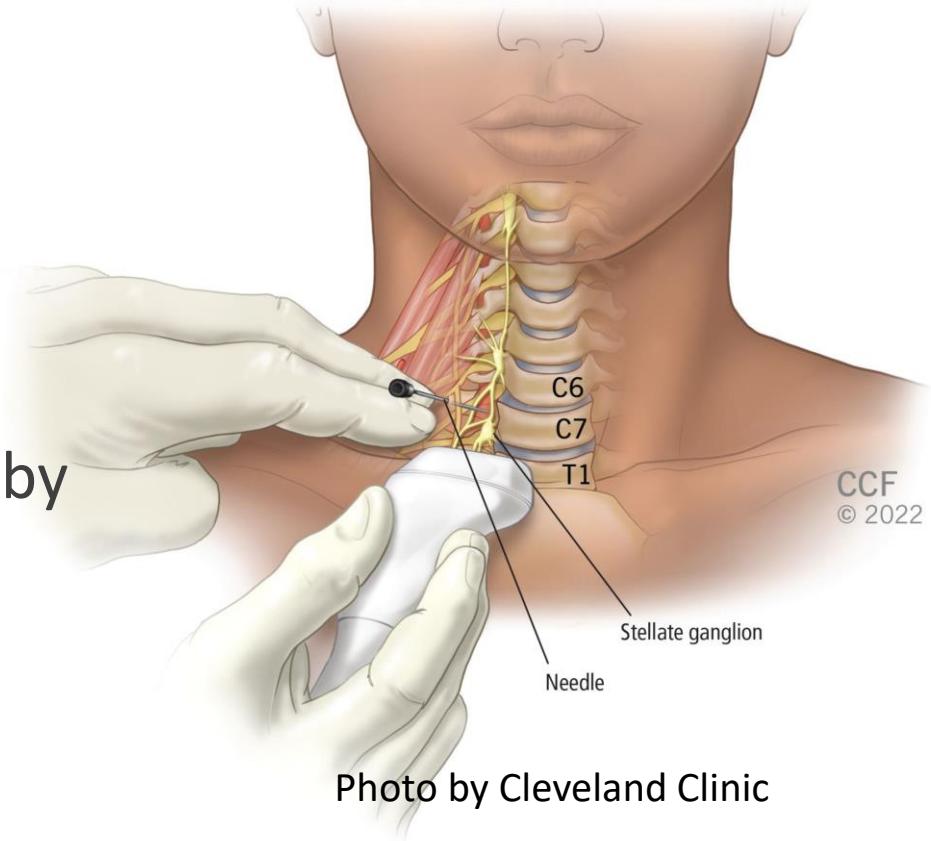
Philip et al. *Lancet Resp Dis.* 2022

ENO Breathe

“ENO Breathe is … so powerful because it responds to our illness humanely, openly, and richly, through emotions, embodiment, culture, art, ideas … whereas medical spaces (if we even manage to access them, which is hard enough) can be so alienating and emotionally and spiritually empty—so averse to treating the whole experience, the whole person. I felt that ENO Breathe has been healing for the trauma I have experienced and continue to experience: of having an unknown illness, not knowing if I will ever [be] getting better, and of receiving barely any medical care, for over a year.”

Stellate Ganglion Block

- Case series, 2 pts, US
- Addresses dysautonomia
 - Cervical autonomic chain activity blocked by local anesthetic
 - Allows regional autonomic nervous system to reboot



Acupuncture

- Treatment rationale follows that of acute infection
- Immune dysfunction
 - Expel pathologic Heat, clear Lung dampness
 - *Tai Yang* and *Yang Ming* zones
 - Nourish & mobilize qi
- Other focus, depending on pt's particular condition
- Publications to date are cases and rationale

Audette. *Medical Acupuncture*. 2022; Birch. *Integr Med Res*. 2021



ID Week, 2022

- NIH – *There is no specific treatment for Long COVID yet. You and your health care provider can work together to create a personal care plan to manage your symptoms and improve your quality of life.*

General Principles - Diet

- Anti-Inflammatory Diet, Mediterranean Diet
 - Low glycemic index, low saturated fat
 - Modulates inflammation
 - Improved lung function
 - Monosaturated and Polyunsaturated fats & Plant derived flavonoids
 - Decrease activation of NLRP3 inflammasome
- Severe infection is catabolic
 - Can lead to nutrient deficiencies—protein, B vitamins, Vitamin C, Cu, Zn, Fe

General Principles - Diet

- Foods rich in vitamins and minerals
 - Vegetables – dark/green, red/orange, legumes, other
 - Fruit
- Protein
 - 0.8 to 1.5 g/kg body weight daily, depending on age and other conditions

Alshuler. *Explore*. 2022

General Principles - Supplements

- Vitamin D
 - Anti-viral, anti-inflammatory
- Glutathione 250 – 1000 mg daily
 - Antioxidant, esp in lung epithelium
- Glutathione-generating compounds
 - Selenium (brazil nuts – natural source), n-acetyl cysteine, ginger
- Melatonin
 - Antioxidant, anti-inflammatory, immunomodulatory

General Principles - Supplements

- *Cordyceps sinensis* – medicinal mushroom, 1.5 – 3 g daily
 - Antioxidant, anti-inflammatory, increase NK cells
 - Increase exercise performance, decreased airway inflammation
- *Astragalus membranaceus* root, milkvetch, 4 – 60 gm daily
 - Antioxidant, increase immunity, modulate inflammation
 - Decreased fatigue, pain, nausea, improved sleep in cancer pts
- Garlic, *Allium sativa*, 600 – 900 mg dried garlic powder
 - Downregulates inflammatory cytokines, decreased cold/flu sx

General Principles – Breathing & Movement

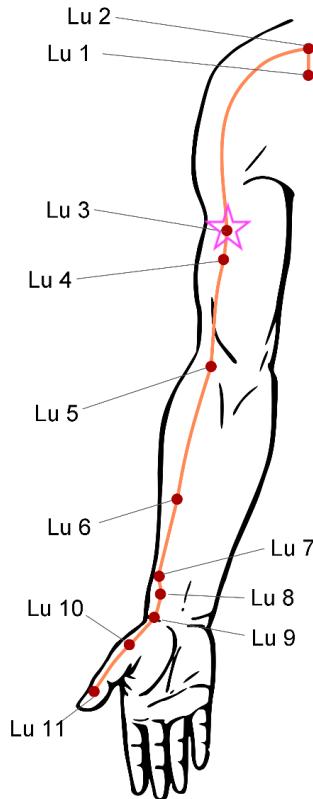
- Breathing exercises
 - Diaphragmatic breathing
 - Pursed-lip breathing
 - *Pranayama* – yoga breathing exercises
 - Tai Chi breathwork
 - Singing
- Pulmonary Rehab
- Movement – only as tolerated
- Qigong – improve lung function



Alshuler. Explore. 2022



Qigong



<https://spacetorelax.com/qigong-exercises-for-lungs-and-immunity/>

General Principles – Stress Management

- Mindfulness
 - Decreased stress and cortisol inflammation
 - Meditation, guided imagery, yoga, tai chi,
 - Incorporate deep breathing for vagal parasympathetic response.
- Creativity
 - Expressive writing – improved lung function, mental health, decreased pain

General Principles – Stress Management

- Aromatherapy
 - Stress relief
 - Lavender, geranium, others
 - Improved lung function
 - Eucalyptus (1, 8-cineole), peppermint (menthol)
- Sleep – Sleep hygiene, +/- melatonin
- Environment
 - Soothing sounds, green spaces
 - Supportive social interactions
 - Cool, lower humidity

RECOVER NIH Trial

PRevention, **E**valuation & **I**ncidence of **L**ong-term COVID in **S**outh **T**exas—OTA-21-015B:
PREVAIL South Texas: UT Health San Antonio



Prime:

UT Health San Antonio

Contact PI:

Thomas F Patterson

On behalf of MPIs:

Mark Goldberg

W Brian Reeves

Jennifer Potter

Sudha Seshadri

Barbara Taylor

Adult Cohort:

UT Health San Antonio

Case Western

Columbia

Emory

Harvard/Boston

Howard Univ

Mt. Sinai

Pacific NW Consortium

Stanford

U. Alabama Birmingham

Univ. of Arizona

UCSF

Univ. of Illinois

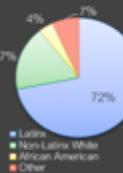
U. Utah/Mt. States Consortium

West Virginia U. Consortium

REGISTRIES

COVID

- N >12,000 with COVID
- All patients diagnosed with COVID-19 in county safety net system



CITY OF LAREDO

- N >42,000 with COVID
- All patients diagnosed with COVID-19 in city from public health surveillance



BEXAR Co. SURVEILLANCE

- N >100,000 COVID negative
- COVID negative contacts of known COVID cases identified in Bexar Co. contact tracing program and University Health

PREVAIL COHORT

CHARACTERISTICS

- 900 COVID+ (80% CIVOC, 20% Laredo)
- 100 COVID neg controls (Bexar Co surveillance)
- Anticipated demographics:
 - 76% Latino
 - Age: mean 42yo
 - Gender: 50% female

RECOVER MASTER PROTOCOL

- Recruitment and engagement by community health workers/promotores
- 7 Study visits over 3 years: CDE
- Symptom monitoring
- Blood and urine collection
- Clinical data collection

ANTICIPATED RESULTS

Based on preliminary data:

- Anticipated PASC: 37%
- Psychiatric comorbidity: 40% anxiety, 30% depression
- Economic or food insecurity: 45%

SCIENTIFIC STRENGTHS

1. Social Determinants of PASC

2. COVID-induced Trauma and Psych Disorders

3. Structural and Functional Brain Injury in PASC

4. Metabolism and Mitochondrial Dysfunction in PASC

5. Role of Inflammaging on Organ Injury in PASC

Margot Gage Witvliet - TED Talk

“Doctors didn’t listen to me....”

“*Make integrative medicine the norm.*”

- Listen
- Believe

