LONG COVID WEB

LONG COVID WEB ECHO
SESSION SUMMARY from 13 Feb 2026

(i) KEY PRESENTATION: Unraveling Long COVID: Blood brain barrier disruption and neuropsychiatric symptoms by Dr. Alba M. Azola, MD

Dr. Azola, a specialist in physical medicine and rehabilitation focusing on long COVID and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), began her presentation with historical context for similar conditions.

She described neurasthenia from Dr. Osler's textbook as nervous system exhaustion with cognitive difficulties such as impaired attention and mental effort, mirroring long COVID brain fog. See: Osler, W. (1901). *The principles and practice of medicine: Designed for the use of practitioners and students of medicine*. D. Appleton and Co. https://www.loc.gov/item/tmp96029097/

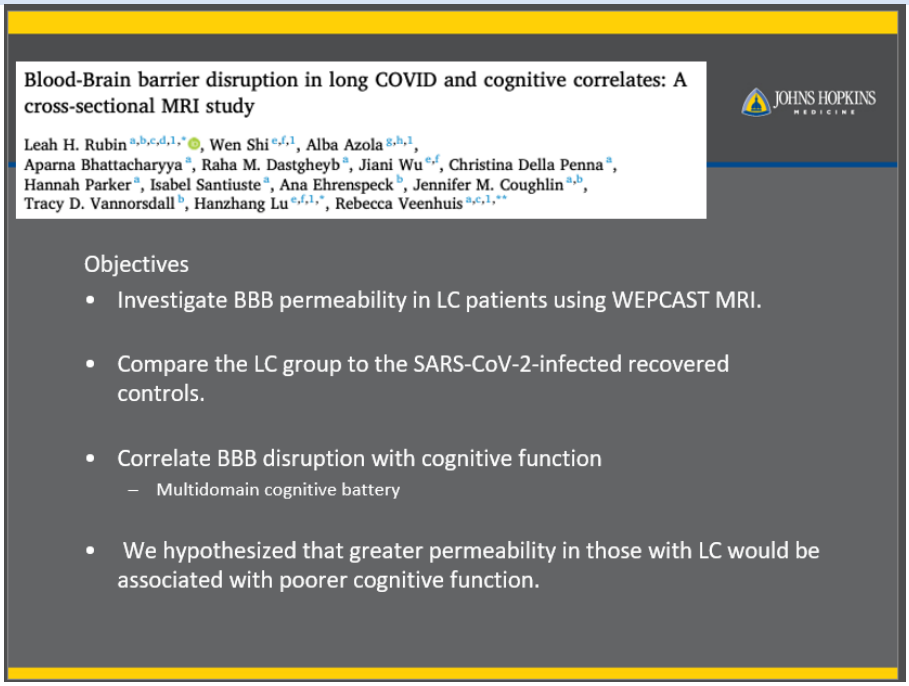
She highlighted outbreaks such as epidemic neuromyasthenia in Punta Gorda, Florida (1950s), the Royal Free Hospital event in London (1950s, coining myalgic encephalomyelitis), and the Lake Tahoe cluster (1980s post-Epstein-Barr virus), all featuring multisystem symptoms with fatigue and cognitive issues akin to long COVID's relapsing-remitting or progressive course.

She discussed the RECOVER Consortium's national U.S. study of nearly 10,000 participants, which defined post-acute sequelae of SARS-CoV-2 (PASC) using 12 symptoms distinguishing long COVID from never-infected controls, estimating 10% prevalence and four symptom subgroups; risk factors included lack of vaccination. See: Thaweethai, T., Jolley, S. E., Karlson, E. et al. RECOVER Consortium (2023). Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection. *JAMA*, *329*(22), 1934–1946. https://doi.org/10.1001/jama.2023.8823

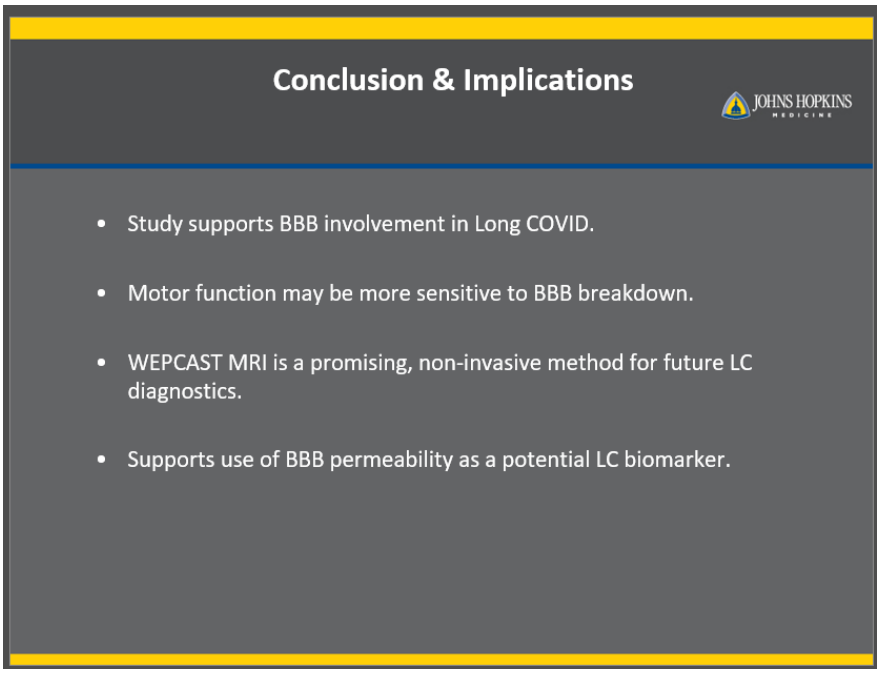
In her clinic's real-world validation with 130 long COVID patients versus 60 fully recovered SARS-CoV-2 controls (screened rigorously for fatigue, post-exertional malaise (PEM), brain fog, orthostasis, autonomic, and mast cell symptoms), the PASC score showed high specificity (100% positive cases were long COVID) but missed some patients, potentially underestimating prevalence. Combining loss of smell/taste, PEM, and reduced sexual desire/capacity yielded optimal sensitivity and specificity to aid clinical diagnosis.

Studies in neurocognitive mechanisms in long COVID were discussed, including neuroinflammation (e.g., Harvard TSPO PET showing microglial activation), neurotransmitter issues (low serotonin, high kynurenine; the NIH Goldstein CSF study with reduced catecholamines/dopamine at one year), vascular dysfunction (fMRI hypometabolism from endotheliitis), and the speaker's own blood-brain barrier (BBB) disruption study. See:

- Peluso, M. J., et al. (2024). Tissue-based T cell activation and viral RNA persist for up to 2 years following SARS-CoV-2 infection. *Science Translational Medicine, 16*(755), eadk3295. https://doi.org/10.1126/scitranslmed.adk3295
- Goldstein, D. S., Mina, Y., Walitt, et al (2024). Persistent Autonomic and Immunologic Abnormalities in Neurologic Post-Acute Sequelae of SARS-CoV2 Infection. *Neurology*, *103*(6), e209742. https://doi.org/10.1212/WNL.0000000000209742
- Rubin, L. H., Shi, W., Azola, A., Bhattacharyya, A., Dastgheyb, R. M., Wu, J., Penna, C. D., Parker, H., Santiuste, I., Ehrenspeck, A., Coughlin, J. M., Vannorsdall, T. D., Lu, H., & Veenhuis, R. (2025). Blood-Brain barrier disruption in long COVID and cognitive correlates: A cross-sectional MRI study. *Brain, behavior, and immunity*, *129*, 989–999. https://doi.org/10.1016/j.bbi.2025.07.024



The Blood-Brain Barrier in Long COVID study (97 long COVID vs. 31 controls, mean 30 months post-infection, mostly mild acute cases, highly disabled with 45% unable to work) used arterial spin labeling (ASL) MRI to measure global BBB permeability (PS metric). Long COVID patients had significantly higher permeability (even after age/sex/hospitalization adjustments), correlating with poor motor function (not other cognitive domains) and PEM presence; no differences in cerebral blood flow or volume.



The presentation concluded that blood-brain barrier disruption correlates with cognitive and motor impairments in long COVID patients, and that WEPCAST MRI offers a quantifiable, non-invasive tool to measure BBB permeability as a diagnostic and prognostic biomarker for future clinical applications.

(ii) CASE PRESENTATION:

The case discussion was of a 48 yo female who has severe symptoms of post-exertional fatigue and needs to do significant pacing. If she wants to wash her hair, she has to do minimal activity the day before and nothing else on the day of or the next day. She cannot cook a meal for herself. She has one hour of mental stamina per day for difficult things.

She has a university math degree but can't do basic arithmetic. Sleep is poor. She was started on low dose naltrexone, which has been helpful in that she didn't feel sick after exertion and recovery time seemed less, but improvement tends to plateau. She was also found to have orthostatic symptoms and was started on pyridostigmine with improvement.

Past history of ADHD diagnosis but stimulant medication made her focus worse, rosacea, high cholesterol, PCOS, GERD, bilateral sensorineural hearing loss, chronic urticaria.
She has been seeing physiotherapy.

Open Discussion – key points

The discussion focused on practical management strategies for dysautonomia, mast cell issues, and cognitive symptoms, and included off-label options tailored to patient needs.

Treatment Sequencing for Dysautonomia

Some clinicians noted pyridostigmine is usually third-line after beta blockers or volume loading, but early use makes sense for patients with constipation or hypertension who can't tolerate fluids. They advised low-dose titration (e.g., 15 mg, up to 3x/day) based on response and side effects like nausea or constipation, as many patients are highly med-intolerant.

Mast Cell Activation and Antihistamines

Views were expressed about rosacea and urticaria suggesting mast cell involvement, prompting recommendations for H1/H2 blockers like famotidine (BID for GERD/fatigue/headaches), loratadine (off-label 40 mg/day "allergist dose"), or rupatadine (up to 20 mg BID, titrate carefully; lactose warning). These help symptoms beyond allergies.

Non-Drug Therapies and Pacing

Occupational therapy (OT) was strongly endorsed for pacing, executive skills, somatic exercises, and home adaptations (e.g., shower stools, kitchen stools for orthostasis)—saving physical energy preserves mental stamina. Physiotherapy targeting thoracic outlet syndrome (scalenes/pecs for arm-elevation fatigue) was also suggested.

Brain Fog and ADHD-Like Symptoms

For brain fog when stimulants/non-stimulants (e.g., Intuniv/clonidine low pediatric doses) raise heart rate, options included low-dose fluoxetine (10 mg), amantadine/memantine (off-label, small studies support), or low-dose naltrexone (LDN; start low to 4.5 mg, up to 12.5 mg; fibromyalgia/ME-CFS

evidence emerging). LDN lacks guidelines but shows promise for fatigue/cognition; titrate individually.

Off-Label Prescribing Challenges

Clinical dilemmas were discussed relating to guidelines lag (no FDA/Health Canada approvals 6 years in), patients self-research amid misinformation, and that decisions must prioritize patient context over strict protocols. Clinicians need to balance evidence with "right patient, right dose."

**********NEXT SESSION**********

Friday 6 March 2026
Topic:
Pediatric Long COVID
Speaker: Dr. Lael Yonker

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