LONG COVID WEB

LONG COVID WEB ECHO
SESSION SUMMARY from 12 Dec 2025

(i) KEY PRESENTATION: Update on Long COVID Trials by Dr. Angela M. Cheung, MD, PhD, FRCPC, CCD

Around 400 million people worldwide and 3.5 million in Canada experience long COVID, causing significant economic losses and work incapacity. The condition involves immune dysregulation, inflammation, endothelial dysfunction, viral persistence, thrombotic microclots, mitochondrial dysfunction, and microbiome issues, with complement activation as a central connector leading to cell damage and post-exertional malaise.

The presentation was an update on Long COVID trials in Canada and abroad, and illustrated the continued impact of Long COVID, its multi-system effects, and potential pathogenic mechanisms linked by complement activation.

No trials reviewed demonstrated efficacy in treating established long COVID, underscoring the priority of prevention via acute-phase strategies alongside core symptom management such as rest and pacing.

Trials covered in the presentation:

- Stop PASC trial (Paxlovid vs placebo, 155 participants)
- PAX LC trial (Paxlovid vs placebo, 100 participants)
- RSLV132 trial (RNase enzyme vs placebo, 100 participants)
- Outsmart Long COVID trial (AER002 monoclonal antibody vs placebo)
- BLOC trial (Rovuna vs placebo, 119 participants)
- RECOVER trial (BC007 vs placebo, 30 participants)
- RECLAIM trial (Ibudilast and pentoxifylline vs placebo, 460 participants)
- Ritatolimod trial (double-stranded RNA analog vs placebo, 66 participants)
- Nicotinamide riboside supplement trial (37 vs 21 participants)
- ACTIV-6 metformin trial (prevention, 11,000 participants)

The Q & A discussion following the presentation addressed trial limitations, prevention strategies, ongoing research, off-label treatments, and diagnostic challenges.

Trial Limitations:

- Concerns raised about short treatment durations potentially missing effects.
- Lack of patient phenotyping leading to heterogeneous groups that dilute phenotype-specific outcomes.
- Episodic nature of symptoms complicating trial design, similar to other conditions like HIV or Lupus.
- Response defended use of sensitive SF36 scale, which detected clinically meaningful improvements (5-point threshold as meaningful clinical difference) in many participants.
- 6-month follow-up data confirmed no differences between treatment and placebo groups.
- Improvements plateaued after 2-month treatment, prompting questions on optimal dosing and duration.

- Trials answer primary outcomes but raised many other questions, including endotype variations (e.g. autoimmune, reactivation of old infections like EBV)..

Metformin for Prevention:

- Dosage and frequency: 500 mg starting with once a day with gradual titration over 6 days to full dose 1500mg per day for tolerance.
- Treatment duration: Limited to acute infection phase (e.g. 2 weeks in COVID-OUT trial with stepped increase, and more recently with data from ACTIV6).
- Observational data supported trials, showing benefits in those already on metformin.
- Purpose: Prevention of long COVID during acute COVID, not treatment of established cases.
- Not recommended long-term or dose increases for pre-existing users without acute infection.

Off-Label and Patient Experiences:

- Some patients travel to USA for maraviroc and similar; only case series noted, no completed efficacy trials.
- Pentoxifylline: Patients insist on continuing despite RECLAIM results due to perceived gains, especially young with high D-dimers; possible anticoagulant role.
- Clinicians make individual decisions; drug safety allows flexibility despite trial data.

Ongoing Research:

- 827 trials on clinicaltrials.gov, plus European registry; covers antivirals, monoclonals, etc.
- Current focus is on viral persistence(e.g. use of pemgarda) but our speaker favors immune dysregulation rather than viral persistence causing issues.
- Blood samples from trials shared for endotype research via long COVID networks.
- Vaccine-related side effects (long COVID-like) under study, including spike protein.

Diagnostic Tests:

- Remains clinical diagnosis based on history, like migraine.
- No reliable biomarkers (e.g. spike protein lacks one-to-one correlation).
- Commercial tests unreliable with false positives/negatives; not FDA or Health Canada approved.

(ii) CASE PRESENTATION:

A 47-year-old female with a history of migraines, gluten intolerance, and three COVID-19 infections (2020-2021) developed severe long COVID after the third episode, resulting in bedbound fatigue, post-exertional malaise (PEM), orthostatic light-headedness (positive 10-minute stand test: HR 65→120 bpm, BP 100/60, tolerated only 4 minutes), worsening migraines unresponsive to prior treatments, migratory myalgias without joint involvement, cognitive/memory decline, sensory hypersensitivities, 25 lb weight loss, rashes, food intolerances, and shortness of breath; elevated D-dimer with otherwise normal labs, MRI head, ECHO, and PFTs; currently on long-term disability from Service Canada work, self-managing with OTC famotidine/loratadine/Benadryl/Tylenol and supplements (magnesium, vitamin D, iron, probiotics, CoQ10/ubiquinol, fibre); diagnoses include long COVID, ME/CFS post-COVID, postural orthostatic tachycardia syndrome (POTS), and migraines.

ECHO members discussed this case, and covered the following points:

- Clarification on famotidine, loratadine, and Benadryl: Used for suspected mast cell activation syndrome (MCAS), self-initiated after researching the condition post-long COVID onset.
- Migraine medications discontinued after trying multiple options under neurologist guidance due to intolerable side effects after 3 years of illness; patient unwilling to retry.
- Patient completed full pacing, energy management, and energy envelope programs via physiotherapy and occupational therapy; no longer boom-busting but remains bed-bound seeking marginal gains.
- Importance of assessing patient's pacing knowledge, daily application, and energy envelope understanding to tailor interventions.
- For POTS with low blood pressure (e.g., 100/60) and medication sensitivity: Recommend non-pharmacological approaches including up to 2 teaspoons salt daily (per Canadian Consensus), increased water, and compression garments; reference CMAJ article by Dr. Satish Raj*; note lower BP challenge in long COVID vs. typical POTS.

  *Raj, S. R., Fedorowski, A., & Sheldon, R. S. (2022). Diagnosis and management of postural orthostatic tachycardia syndrome. *CMAJ, 194*(10), E378–E385. https://doi.org/10.1503/cmaj.211373
- Modafinil suggested for severe fatigue/debilitation (e.g., inability to shower); monitor BP/HR as it may increase both; small ME/CFS trials support use.
- Midodrine suggested for POTS with low BP (per Canadian Cardiovascular Society guidelines); monitor BP/HR; use on top of non-pharmacological standards.
- Dragon Well Tea (specific green tea variety, long thin leaves, highly caffeinated, available at Asian stores for under $10): 1 tsp steeped in hot water, morning use for migraine prevention (better than acute treatment); has basal calming effect despite caffeine; avoid late day.
- Medications like modafinil/midodrine complement, not replace, compression stockings, legs-up-wall resting, fluids, and salt.

- CoQ10: Monitor for hypotension side effect; consider variable dosing and tolerance; all nutraceuticals have side effect profiles needing caution.
- Connect with community of lived experience peers via multidisciplinary programs (physio, OT, group pacing sessions); highly valuable for strategies, support, and reducing isolation.
- Limit caffeine (coffee/tea) as diuretic worsening orthostatic intolerance; do not count toward fluid goals despite total intake (e.g., 2L all caffeinated ineffective); small amounts ok for joy but prioritize water prescription.
- Use soups/other palatable sources to meet high fluid goals (e.g., 3L water challenging).
- Pacing is foundational ("the magic to help everything else" according to the Patient Partner on the Hub team) enabling medications/other treatments to work; requires life changes beyond pills.
- Taurine: Depleted in long COVID (hamster/human studies by Edmonton/Alberta group); studied for brain/nerve function; ongoing RECLAIM platform trial (Edmonton PI Dr. Grace Lam, Quebec sites incl. Dr. Alain Piché, overall PI Lawrence Richer, co-I Gavin Oudit; pediatric extension); search clinicaltrials.gov.
- Curcumin (turmeric active ingredient): Used by some for anti-inflammatory/antioxidant effects.

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

Friday January 16, 2026
Topic: Management strategies for Postural Orthostatic Tachycardia Syndrome
Speaker: Dr. Satish Raj

Submit your de-identified cases (PROJECT ECHO) to: Christine.chan@uhn.ca
Keep up-to-date with session topics: https://www.longcovidweb.ca/echo