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LONG COVID: DIAGNOSTIC AND THERAPEUTIC PROTOCOL

As of November 2025

Only in cases of abnormal passive standing test

Basic diagnostics

Detailed medical history (supported by Symptoms questionnaire [https://www.neuropraxis-solothurn.ch/long-covid-solothurn-en])

Physical examination including neurological status, 10-minute passive standing test (NASA lean test) , ECG, temperature, respiratory rate, oxygen saturation, dermographism

Laboratory

Differential blood count, INR, pTT, fibrinogen, D-dimers, CRP, glucose, creatinine, electrolytes, transaminases, complement C3/C4, total protein, TSH, fT3, fT4, basal cortisol, ACTH, ferritin, holotranscobalamin, 25-OH vitamin D (target >120 nmol/L), autoantibodies against cardiolipin (IgG and IgM) and against beta2-glycoprotein (IgG and IgM), ANA, ds-DNA antibodies, urine status

In case of cardiac symptoms: CK, CK-MB, troponin I (hs), NT-pro-BNP

In case of gastro-intestinal involvement, also test total IgA, transglutaminase IgA antibodies, and calprotectin in stool

In children: always include transglutaminase IgA antibodies and total IgA

Depending on the situation: neurotransmitter receptor antibodies, lymphocyte subpopulations, MBL (mannose binding lectin), cortisol profile in saliva, immunoglobulins IgG, IgA, and IgM as well as IgG subclasses, cytokines TNF-alpha and interleukin-6 as well as soluble interleukin-2 receptor, SARS-CoV-2 IgG qn spike protein (immunity after infection or infection) and/or SARS-CoV-2 IgG nucleocapsid (immunity after infection), EBV-VCA-IgM and -IgG, EBNA-IgG. Vitamin B1, B6, folic acid, zinc

Treatment and advice, basics

- Exercise intolerance: Physical therapy and/or occupational therapy to learn pacing (not graded exercise therapy!)
- Mast cell activation syndrome (MCAS): Trial therapy: Fexofenadine 120-180 mg, H2 blockers; Daosin with meals (if food intake has a significant effect)
  If there is no response to fexofenadine, try ketotifen, cromoglicic acid (3 x 200 mg) or alpha-lipoic acid (2 x 200-600 mg)
- Nutritional advice: try a low-histamine diet for a few weeks
- Try dietary supplements: L-arginine 5 g 1-0-0 (with herpes reactivation, add L-lysine 1-3 g); liposomal vitamin C 500 mg 1-0-1; nattokinase 2000-8000 FU in the morning on an empty stomach; niacin "no flush" formulation 250-500 mg in the morning; vitamin D 1000-3000 IU/day (target >120 nmol/L); L-tryptophan 500 mg 1-0-1 on an empty stomach; N-acetylcysteine 600 mg 1-0-1; Zinc 15 mg 0-0-1; selenium 50 µg 1-0-0; quercetin 250-500 mg 1-0-1
- COVID-19 vaccination leads to an improvement in symptoms in about 25% of people with long COVID and can therefore be tried (not in post-vaccination cases!)
- Detailed advice on protection against further infection (wear FFP2 masks consistently in public indoor spaces; ensure good indoor air quality (ideally: air filters and regular ventilation!), if possible also in the classrooms of children of those affected; self-test before meetings)
- Orthostatic hypotension: BP drop >20 mm Hg systolic or >10 mm Hg diastolic
- Postural orthostatic tachycardia syndrome (POTS): Heart rate increase to >120/min or by >30/min (or >40/min between 12 and 19 years of age)

Even if the criteria for OH or POTS are not fully met, recommend non-pharmaceutical measures:

- Adequate fluid intake (at least 3 liters/day) with regular hydration, especially adequate fluid intake before getting up in the morning (up to 500 ml plus salt, e.g. broth)
- Adequate salt intake, approx. 8 g/day. Recipe for an electrolyte solution to drink throughout the day, especially in the morning: 250 ml fruit juice and 750 ml water with 0.5 level teaspoons of salt
- Get up slowly
- Class 2 (or 3) compression stockings, for women also a compressive abdominal belt
- Shower legs switching between warm and cool, cold foot baths in hot weather
- Avoid alcohol, drink little coffee
- Several small meals

Medication options:

- For POTS Ivabradine 2.5 mg 1-0-0, increase to 5 mg 1-0-0 after 7 days depending on effect/tolerability, possibly up to 7.5 mg 1-0-0 (ivabradine has no effect on blood pressure)
- For POTS and hypertension: Bisoprolol 1 x 5-10 mg, Nebivolol 1.25-5 mg, Labetalol 2 x 100-200 mg
- Other therapeutic options for POTS or orthostatic hypotension: Pyridostigmine 10 mg 1-0-0. If well tolerated, increase every 7 days to a maximum of 3 x 120 mg. Fludrocortisone 0.1-0.2 mg, midodrine 3 x 5-10 mg, vericiguat 2.5 to 10 mg, methylphenidate 3 x 5-10 mg, bupropion 150-300 mg, venlafaxine 37.5-300 mg, escitalopram 10 mg, pyridostigmine 2-3 x 10-60 mg, erythropoietin 10,000-20,000 IU/week subcutaneously or intravenously, octreotide 3 x 50-200 µg subcutaneously, clonidine 2 x 0.1-0.3 mg per os or 0.1-0.3 mg patch weekly
- For severe POTS, 1 liter of NaCl 0.9% intravenously over 1-2 hours weekly, titrate to 1 liter every 2-4 weeks up to 2 liters weekly

Therapy escalation

- Sensory or vegetative disorder: Referral to the neurology department of a central hospital to test for small fiber neuropathy
- Low dose naltrexone: Dissolve 1 tablet of naltrexone 50 mg in 50 ml of water (1 mg naltrexone/ml solution). Start with 0.5 ml in the evening, increase by 0.5 ml every 1-2 weeks to at least 1.5-2.5 ml, maximum 5 ml. If insomnia occurs as a side effect, take in the morning
- Low dose aripiprazole: Aripiprazole 1 mg/ml: Start with 0.1-0.25 ml daily, increasing by 0.1-0.25 ml every 1-2 weeks to a maximum of 2.0 ml. Take for several weeks
- Systemic corticosteroids: Prednisolone 20 mg for 5 days, followed by prednisolone 5 mg for 23 days
- For hypocortisolism, fludrocortisone 0.1-0.2 mg, possibly with 10-37.5 mg cortisone (equivalent) daily; consider endocrinological evaluation
- Hyperbaric oxygen therapy
- Intravenous immunoglobulins, HELP apheresis, immunoadsorption
- Anticoagulation: Aspirin 75 mg, clopidogrel 75 mg, and apixaban 2 x 5 mg combined with pantoprazole 40 mg. Caution: Inform patient about risk of bleeding, monitor closely!

Treatment of specific symptoms

- **Anosmia, dysosmia:** Structured smell training: smell scents (rose, lemon, eucalyptus, and clove) for 30 seconds in the morning and evening and imagine the scent. Medication: Zinc 2 x 50 mg, 1 puff of fluticasone nasal spray in each nostril or 32 mg methylprednisolone p.o. in the morning for 10 days, or vitamin A nasal drops 10,000 IU/day for 8 weeks
- **Fatigue, brain fog:** D-ribose 1-3 x 5-10 g (not for diabetes mellitus)
- **Insomnia:** Diphenhydramine 3-25 drops at night (a low dose is usually sufficient), melatonin 3-10 mg at night (often positive effect on brain fog), QUVIVIQ 25-50 mg 30 minutes before bedtime.
- **Cardiac symptoms:** always check for and treat POTS/postural hypotension. If the response is unsatisfactory, perform cardiological diagnostics, consider cardiac 3T MRI to diagnose myocarditis
- **Dyspnea:** POTS/postural hypotension? Respiratory physiotherapy. Try treatment with montelukast. Pulmonary evaluation, possibly VQ-SPECT/CT to check for ventilation or perfusion defects
- **Cognitive deficits:** POTS/postural hypotension? Bupropion 150–300 mg. Trial therapy with 1 mg guanfacine (Intuniv®) and 600 mg N-acetylcysteine at night; increase guanfacine (Intuniv®) to 2 mg after one month. MRI of the brain to rule out other causes. Neuropsychological assessment for objectification, possibly [18F]-FDG-PET to detect regional hypometabolism. Maybe try neurofeedback
- **Pain:**
  - Duloxetine 30-60 mg, amitriptyline or trimipramine 10-25 mg at night (not available in Switzerland: milnacipran)
  - Pregabalin 25-50 mg at night, if tolerated, increase dose to max. 300 mg daily, divided into three doses (smaller doses during the day)
  - Oxcarbazepine (start with 150 mg at night, increase to 2 x 600 mg) or lamotrigine (start with 25 mg in the morning, increase by 25 mg every two weeks to 3 x 100 mg; caution: exanthema, especially if the dose is increased too quickly!), alone or in combination with pregabalin
  - Topiramate, especially in cases of obesity (start with 25 mg at night, increase by 25 mg weekly up to 2 x 50-100 mg)
  - Tizanidine (2 mg at night, increase up to 2 x 4 mg), tramadol up to 4 x 50 mg, lidocaine patch for local pain
  - For pain patients with positive ANA test results, Plaquenil (caution: evaluate effectiveness only after several months)
  - Methadone or MST Continus®
- **Digestive problems:** Mast cell activation syndrome? Fexofenadine 120-180 mg daily, H2 blockers, Daosin with meals, nutritional counseling (low-histamine diet). Probiotics. If gastroscopy or colonoscopy is performed, histology with staining for mast cells (CD117)