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ME
ANZMES

GP Care Plan for Severe-Very Severe ME/CFS and Long COVID

and associated conditions e.g. dysautonomia

Introduction:

Severe and Very Severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) and Long COVID are complex, multisystem diseases that profoundly impact an individual's functional ability and overall quality of life. **An estimated 25% of the 65,000 Kiwis with ME/CFS are housebound or bedridden, many requiring 24/7 care just to survive,** highlighting the extreme level of disability experienced. GPs are crucial in navigating care for these patients, who often face a healthcare system unfamiliar with their condition. A patient-centered approach is essential to prevent harm and improve quality of life.

Severe ME/CFS and Long COVID present with a wide array of debilitating, fluctuating symptoms. GPs must understand this is a systemic, multi-organ illness, requiring validation of the patient's experience. Patients experience extreme sensitivities (light, sound, touch, smells, temperature, chemicals, foods), profound weakness, and severe, constant pain (muscular, joint, nerve, headaches). Eating and digestion issues are common, including difficulty chewing/swallowing, food sensitivities, and GI problems. Cognitive difficulties ("brain fog") are prevalent, sometimes leading to non-verbal states. Sleep disturbances (unrefreshing sleep, altered patterns) are common despite profound fatigue. Autonomic dysfunction (dizziness, lightheadedness, POTS, temperature dysregulation) is frequent. Shortness of breath and persistent, unalleviated fatigue are also hallmarks.

Essential Clinical Guidance & Management Strategies: The T.E.A.M. Framework

This framework offers a concise guide to critical aspects of managing severe ME/CFS and Long COVID using the T.E.A.M. mnemonic for easy recall, and to ensure a patient-centred multi-disciplinary approach.

T - Teamwork and Titration: "Slow and Low" Approach

Having a multidisciplinary team approach is necessary when dealing with severe cases due to the complex nature and seriousness of the disease. Build a team of ME-aware nurses/nurse practitioners, district nurses, occupational therapists (OTs), physiotherapists (PTs), and dietitians, as well as specialists such as neurologists, rheumatologists, and mental health professionals, as needed.

Patients with Severe ME/CFS often have extreme sensitivities to medications. The understanding of ME/CFS pathophysiology such as dysregulation of the autonomic nervous system, mast cell activation, immune dysfunction, and mitochondrial issues provides a biological basis for heightened drug sensitivities and the need for individualised dosing. All these underlying issues can affect how drugs are processed and how the body reacts to them.[1] [2]

Action for GPs:

- **Foster a multidisciplinary team approach** collaborating with necessary professionals; and have effective communication and coordination within this team.
- **Consider the patients' capacity and communication preference** and ensure the whole team honours and accommodates these needs. Many severe-very severe patients are non-verbal or require a proxy to communicate their needs. Include this named advocate in all communication and recognise their expertise and intimate knowledge of the patient.
- **Pharmacotherapy must follow a "slow and low" approach** by initiating new medications at very small doses, often below standard, and increase gradually with vigilant monitoring

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[1] Bateman Horne Center (2022). Medical considerations when treating urgently i l patients with underlying myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). https://batemanhornecenter.org/wp-content/uploads/filebase/education/top_resources/ER-and-Urgent-Care-Considerations-for-MECFS-1.19.22-005.pdf

[2] Montoya, J. G., Dowe l, T. G., Mooney, A. E., Dimmock, M. E., & Chu, L. (2021). Caring for the Patient with Severe or Very Severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Healthcare (Basel, Switzerland), 9(10), 1331. https://doi.org/10.3390/healthcare9101331 https://pmc.ncbi.nlm.nih.go1v/articles/PMC8544443/

for adverse reactions - working closely with your patient throughout this process. This individualisation is critical due to altered drug metabolism or heightened sensitivity.[3] [4]
- **Simplify medication routines** for the patient to reduce cognitive load.

E - Exertional Intolerance

It's important to understand that in severe ME/CFS, everything causes pain and Post-Exertional Malaise in Very Severe ME/CFS. Post-Exertional Malaise (PEM), also known as Post-Exertional Symptom Exacerbation (PESE) in Long COVID, is the cardinal and defining characteristic of ME/CFS and Long COVID. It's a debilitating worsening of symptoms after even minimal physical, cognitive, emotional, or sensory exertion. PEM often has a delayed onset, typically 12 to 72 hours after exertion, and can last for days, weeks, or months for the patient. This delayed and multi-faceted nature means patients often don't connect their "crash" to the precipitating activity, leading to a harmful "push and crash" cycle. Symptoms can include new or increased sensory sensitivities (light, sound, smell), autonomic dysfunction, cognitive difficulties ("brain fog"), pain, and profound energy depletion. [5] [6] [7] Listening and validating the patient's experience with PEM/PESE is vital; and approaching management strategies as a 'team' is important so that they feel seen and understood.

Action for GPs:

- **Prioritise listening to the patient,** taking a thorough history that contrasts what they could do before they became unwell versus what they can do now, and validating their experience of PEM/PESE, and the biological basis of their energy limitations.
- Each patient has a **highly restricted energy capacity.** Recognise **Pacing** - the careful balancing activity and rest within their energy limits - as the cornerstone of ME/CFS management to prevent debilitating "crashes". [8]
  - GPs must understand that pushing beyond the energy limit, even slightly, can lead to severe and prolonged symptom worsening for a severe patient.
  - Pacing strategies must be highly individualised, as energy limits and symptoms vary greatly between severe patients and can change day-to-day. There's no one-size-fits-all approach so this is where teamwork comes in. Provide patients

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[3] Bateman Horne Center (2022). Medical considerations when treating urgently i l patients with underlying myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). https://batemanhornecenter.org/wp-content/uploads/filebase/education/top_resources/ER-and-Urgent-Care-Considerations-for-MECFS-1.19.22-005.pdf

[4] Montoya, J. G., Dowe l, T. G., Mooney, A. E., Dimmock, M. E., & Chu, L. (2021). Caring for the Patient with Severe or Very Severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Healthcare (Basel, Switzerland), 9(10), 1331. https://doi.org/10.3390/healthcare9101331 https://pmc.ncbi.nlm.nih.go1v/articles/PMC8544443/

[5] Friedberg, F., Bateman, L., Bested, A.C., Davenport, T., Friedman, K.J., Gurwitt, A., Jason, L.A., Lapp, C.W., Stevens, S.R., Underhill, R.A., Vallings, R. (2014). Chronic fatigue syndrome myalgic encephalomyelitis: Primer for clinical practitioners 2014 edition. International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis IACFS/ME.

[6] Rowe, P. C., Underhill, R. A., Friedman, K. J., Gurwitt, A., Medow, M. S., Schwartz, M. S., Speight, N., Stewart, J. M., Vallings, R., & Rowe, K. S. (2017). Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Diagnosis and Management in Young People: A Primer. *Frontiers in pediatrics*, *5*, 121. DOI.

[7] Maeda, K. I., Islam, M. F., Conroy, K. E., & Jason, L. (2023). Health outcomes of sensory hypersensitivities in myalgic encephalomyelitis/chronic fatigue syndrome and multiple sclerosis. *Psychology, health & medicine*, *28*(10), 3052–3063. DOI.

[8] PACING-Activity-and-Energy-Management-for-people-with-MECFS-and-Long-Covid-MAY-2023.pdf

with the means to prioritise essential activities while delegating or deferring non-essential ones to caregivers to conserve energy - consider **referral to services and specialists such as OT's and Homecare support etc.**

- **Create a low-stimulation environment** such as providing patients with a quiet, darkened room with minimal scents and consistent temperature, and educate them on the importance of this at home.
- Suggest **communication aids** if verbal communication is challenging.
- **Respect patient boundaries and autonomy,** always seeking consent. Having a calm, quiet approach is often more supportive to the patient.

A - Atrophy vs. Deconditioning: Understanding Distinct Muscle Changes

While severe ME/CFS leads to muscle atrophy, it's crucial to understand this is distinct from simple deconditioning caused solely by inactivity. Research shows muscle changes in ME/CFS and Long COVID differ from those induced by bed rest in healthy individuals, pointing to unique pathophysiological mechanisms like impaired oxygen delivery and blood vessel dysfunction, not just disuse.[9] [10] Unlike deconditioning, ME/CFS involves cardinal symptoms like Post-Exertional Malaise (PEM), widespread pain, and sensory sensitivities.[11] [12] [13] Treatment and management plans for severe ME/CFS must be highly individualised to each patient's unique needs - this plan must be a collaborative process with a multidisciplinary team. Overexertion can actually harm ME/CFS patients, particularly those severely impacted, as even routine basic daily activities can push them beyond their extremely limited energy reserves.[14]

Action for GPs:

- **Focus on gentle movement within the patient's severely restricted energy envelope** to maintain range of motion - not to "recondition" them. Also ensure any movement assistance is gentle and within the patient's energy envelope to prevent PEM. Avoid interventions based on the "deconditioning" hypothesis, such as Graded Exercise Therapy

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[9] https://www.healthrising.org/blog/2025/06/05/deconditioning-chronic-fatigue-long-covid-muscle/ and https://ammes.org/2025/06/10/skeletal-muscle-properties-in-long-covid-and-me-cfs-differ-from-those-induced-by-bed-rest/

[10] Jammes, Y., & Retornaz, F. (2019). Understanding neuromuscular disorders in chronic fatigue syndrome. *F1000Research*, *8*, F1000 Faculty Rev-2020. https://doi.org/10.12688/f1000research.18660.1

[11] Scheibenbogen C, Wirth KJ. Key Pathophysiological Role of Skeletal Muscle Disturbance in Post COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): Accumulated Evidence. J Cachexia Sarcopenia Muscle. 2025 Feb;16(1):e13669. doi: 10.1002/jcsm.13669. PMID: 39727052; PMCID: PMC11671797. https://pmc.ncbi.nlm.nih.gov/articles/PMC11671797/

[12] Van Campenhout, J., Buntinx, Y., Xiong, H.- Y., Wyns, A., Po li, A., Nijs, J., Aerts, J. L., Laeremans, T., & Hendrix, J. (2025). Unrave ling the Connection Between Energy Metabolism and Immune Senescence/Exhaustion in Patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Biomolecules, 15(3), 357. https://doi.org/10.3390/biom15030357

[13] Montoya, J. G., Dowe l, T. G., Mooney, A. E., Dimmock, M. E., & Chu, L. (2021). Caring for the Patient with Severe or Very Severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Healthcare (Basel, Switzerland), 9(10), 1331. https://doi.org/10.3390/healthcare9101331 https://pmc.ncbi.nlm.nih.go1v/articles/PMC8544443/

[14] Montoya, J. G., Dowe l, T. G., Mooney, A. E., Dimmock, M. E., & Chu, L. (2021). Caring for the Patient with Severe or Very Severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Healthcare (Basel, Switzerland), 9(10), 1331. https://doi.org/10.3390/healthcare9101331 https://pmc.ncbi.nlm.nih.go1v/articles/PMC8544443/

(GET), which is to gradually increase patients' physical activity levels - this is harmful and exacerbates PEM.[15] [16]
- The profound weakness, almost constant pain, and severe limitations to physical and mental activity can make it difficult or impossible for patients to reposition their bodies independently, which increases the risk of developing pressure sores, also known as pressure ulcers or bed sores.[17] **Help with regular repositioning** may be needed to prevent pressure sores in patients who are unable to turn over in bed. Movement can help maintain range of motion, prevent contractures, and decrease stiffness. Passive range-of-motion exercises and gentle stretching can also help, if touch can be tolerated.[18] Work with occupational therapists (OTs) and physiotherapists (PTs) if necessary.
- **Recommend energy-saving tools** such as bedpans and shower chairs.

M - Malnutrition & Nutritional Support: Addressing Physiological Causes

Severe ME/CFS can lead to problems with nutrition and hydration. Patients with Severe ME/CFS are at significant risk of malnutrition or unintentional weight loss.[19] This is not an eating disorder or psychological issue and there is no reliable evidence to justify refusal of nutritional support on the grounds of speculated psychological theories.[20] [21] [22] Malnutrition is a direct physiological consequence due an inability to swallow, severe gastrointestinal problems tolerating food impeding adequate oral intake, or being too debilitated to eat or drink.[23] Again, it is important to listen, observe and understand the patient's needs. Some very severe patients will require tube feeding, either enterally or parenterally. Malnutrition can lead to decreased immune system function, reduced muscle strength, delayed wound healing, increased risk of falls, and further exacerbation of energy levels and cognitive problems.[24]

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[15] Speight, N. (2020, July 14). The value of home visiting by the doctor. *Journal of Clinical Virology*, *129*, 104506. https://pmc.ncbi.nlm.nih.gov/articles/PMC7551866/

[16] NICE Revisions backed by evidence – ANZMES

[17] https://www.cdc.gov/me-cfs/hcp/clinical-care/me-cfs-clinical-care-for-severely-affected-patients.html

[18] Strategies to Counter Muscle Loss in Severe ME/CFS Patients https://www.postviralnutrition.com/blog/preserving-muscle-severe-mecfs.

[19] https://www.nice.org.uk/guidance/ng206/chapter/recommendations#care-for-people-with-severe-or-very-severe-mecfs

[20] As per 36.

[21] Edwards, J. (2024). Management of Nutritional Failure in People with Severe ME/CFS: Review of the Case for Supplementing NICE Guideline NG206. Qeios. https://doi.org/10.32388/T9SXEU

[22] Edwards, J. (2024). Management of Nutritional Failure in people with Severe ME/CFS: Review of the case for supplementing NICE Guideline NG206. Qeios. doi.org/10.32388/T9SXEU

[23] Baxter, H. et. al (2021). Life-Threatening Malnutrition in Severe ME/CFS. Healthcare, 9(4), 459. doi.org/10.3390/healthcare904059 | https://www.mdpi.com/2227-9032/9/4/459

[24] Dr. Charles Shepherd and Dr. Abhijit Chaudhuri (2020) Nutritional assessment in ME/CFS: NUTRITIONAL-ASSESSMENT-AND-MALNUTRITION-AUGUST-2020.pdf

Action for GPs:

- Look for **physical signs of possible malnutrition,** such as hair loss, changes in facial features (prominent cheekbones, sunken eyes), a red swollen tongue, loss of skin elasticity, brittle nails, and muscle wasting.[25]
    - Use a validated screening tool like the five-step **Malnutrition Universal Screening Tool (MUST)** to help to record and monitor BMI and recent weight loss, identifying individuals at high, medium, or low risk of malnutrition. It's important to note that overweight or obese individuals can also be malnourished if their diet is not healthy.[26]
- **Use the NICE Clinical Guideline on ME/CFS to assess if a patient meets the criteria for nutritional support.** It lists the nutritional problems which may be experienced by a person with severe ME/CFS.
    - If oral intake is insufficient, consider medical nutritional support like gastric tube feeding or intravenous (IV) fluids early to prevent critical electrolyte imbalances. The NICE Guidelines suggests *'Nutrition support for adults: oral nutrition support, enteral feeding and parenteral nutrition'* for any patients who are nutritionally compromised.
- **Anorexia nervosa is often incorrectly diagnosed** in Severe ME/CFS patients, especially when presenting with malabsorption.[27] **Parenteral nutrition** may be required, in such cases, refeeding syndrome should be considered.[28] Patients with severe ME/CFS may also require **gastric tube feeding** and intravenous administrations to avoid critical electrolyte imbalances, requiring total care in compatible homes or in nursing facilities.[29]
    - Gastric feeding may require modification due to orthostatic intolerance. The choice of feeding position (flat vs. head-up) should be based on individual safety assessment, with a flat position considered safe in some contexts.[30]
- Refer to a **dietitian experienced in ME/CFS** for tailored guidance and fostering a multidisciplinary approach, emphasising that restrictive diets are generally not advised.[31]
    - Common nutritional deficiencies or lower nutrient levels found in ME/CFS patients can include certain B vitamins (especially B1), vitamin C, magnesium, sodium, zinc, L-tryptophan, carnitine, coenzyme Q10, and essential fatty acids.[32]

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[25] Dr. Charles Shepherd and Dr. Abhijit Chaudhuri (2020) Nutritional assessment in ME/CFS: NUTRITIONAL-ASSESSMENT-AND-MALNUTRITION-AUGUST-2020.pdf

[26] Dr. Charles Shepherd and Dr. Abhijit Chaudhuri (2020) Nutritional assessment in ME/CFS: NUTRITIONAL-ASSESSMENT-AND-MALNUTRITION-AUGUST-2020.pdf

[27] As per 20.

[28] As per 19.

[29] Crosby, L.D., *et al.* (2021). Off-label use of Aripiprazole shows promise as a treatment for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): a retrospective study of 101 patients treated with a low dose of Aripiprazole. *J Transl Med* **19**, 50. https://doi.org/10.1186/s12967-021-02721-9

[30] Edwards, J. (2024). Management of Nutritional Failure in people with Severe ME/CFS: Review of the case for supplementing NICE Guideline NG206. Qeios. doi.org/10.32388/T9SXEU

[31] Dr. Charles Shepherd and Dr. Abhijit Chaudhuri (2020) Nutritional assessment in ME/CFS: NUTRITIONAL-ASSESSMENT-AND-MALNUTRITION-AUGUST-2020.pdf

[32] https://me-pedia.org/wiki/Nutritional_deficiencies_in_ME/CFS

        - Nutritional deficiencies in severe ME/CFS: notable studies listed here: https://me-pedia.org/wiki/Nutritional_deficiencies_in_ME/CFS
    - Vitamin D levels will be low due to patients being housebound and not exposed to sunlight.[33]
- **Home-based services** should always be made available unless there are safety concerns. It's important to form a team of support for your patient. Nutritional support for severe ME/CFS often needs to be viewed in the context of long-term care, as intolerances are frequently a chronic problem.[34]
    - Home carers or family members can administer NG tube feeding with proper training and guidance from healthcare professionals. It's important for them to receive thorough instructions on how to prepare and administer the feed, as well as how to care for the tube and monitor for any complications.[35] [36] [37] Hospital admission for feeding problems is only justified if specific procedures require it.

Optimising Care Access: Telehealth & Home Visits

Ensuring safe and equitable healthcare access for Severe ME/CFS and Long COVID patients requires flexible care models. For many, moving from bed to car to clinic is akin to torture, causing extreme sensory overload, pain, and PEM. Severe patients are housebound and/or bedbound.

Home visits are a critical medical necessity, not a convenience. They enable essential physical examinations and phlebotomy within the patient's low-stimulation environment, preventing iatrogenic harm from clinic travel. Case studies have demonstrated there is benefit from ongoing home visits received by patients, for both moral support and symptomatic treatment.[38]

Telehealth is vital for patients too weak, cognitively impaired, or non-verbal for in-person visits. Communication via an approved proxy (caregiver or healthcare professional) is often essential and must be guided by the patient's explicit consent. In the USA, federal civil rights laws mandate telehealth accessibility for individuals with disabilities - New Zealand should follow this standard.

Proactively offer and facilitate home visits and telehealth appointments. Inform patients about Needs Assessment and Service Coordination (NASC) for publicly funded disability support. Establish preferred communication methods with patients and their approved proxy to ensure effective, patient-centered care.

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[33] Dr. Charles Shepherd and Dr. Abhijit Chaudhuri (2020) Nutritional assessment in ME/CFS: NUTRITIONAL-ASSESSMENT-AND-MALNUTRITION-AUGUST-2020.pdf

[34] Edwards, J. (2024). Management of Nutritional Failure in people with Severe ME/CFS: Review of the case for supplementing NICE Guideline NG206. Qeios. doi.org/10.32388/T9SXEU

[35] https://www.healthinfo.org.nz/index.htm?nasogastric-or-nasojejunal-tube.htm

[36] https://www.kidshealth.org.nz/tube-feeding/tube-feeding-tips-tricks-from-families

[37] https://www.homage.sg/services/nasogastric-tube-reinsertion/

[38] Speight, N. (2020, July 14). Severe ME in Children. *Healthcare (Basel)*, *8*(3), 211. https://pmc.ncbi.nlm.nih.gov/articles/PMC7551866/

Emergency Preparedness

Emergencies pose significant risks to patients due to extreme fragility and sensory sensitivities. To help best equip the patient and caregiver, GPs can;

- Advise caregiver to create an Emergency Information Sheet in case of hospitalization (diagnosis, symptoms, meds, allergies, sensory needs, contacts)
    - You can provide them with this Patient Health Information Form: Health Information Form_V5
- Recommend caregivers create a Crash Care Kit (earplugs, eye mask, electrolytes, meds, communication aids).
- Suggest caregivers to have power backup for essential equipment the patient may need.
- Advise caregivers to develop an evacuation plan, including safe lifting/moving strategies.
- Encourage patients to have a caregiver backup list.

Key Resources for GPs:

Utilise reputable, evidence-based resources such as:

- Know M.E. Series - CME: https://anzmes.org.nz/new-cme-accredited-series-for-health-professionals/
- MyHealthHub - CME: Navigating the Complexities of ME/CFS and long COVID, Dr. Cathy Stephenson and Fiona Charlton https://myhealthhub.co.nz/navigating-the-complexities-of-me-cfs-and-long-covid-2/
- ANZMES Health Hub for Healthcare Professionals: Medical Professionals – ANZMES
- ANZMES Severe-Very Severe ME/CFS and Long COVID Resources: Severe-Very Severe ME/long COVID Resources
- Centers For Disease Control and Prevention - ME/CFS Clinical Care for Severely Affected Patients: ME/CFS Clinical Care for Severely Affected Patients | ME/CFS | CDC

Understanding Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a long-term, complex, multi-systemic and debilitating condition characterised by profound fatigue, post-exertional malaise (PEM), cognitive dysfunction, unrefreshing sleep, autonomic issues, and widespread pain. It often develops following viral infections, environmental triggers, or other stressors, leading to immune system dysfunction, mitochondrial impairment, and neurological disturbances. It affects the nervous, endocrine, autonomic, cardiovascular, and immune systems.[39] With over 100-200+ potential symptoms, the condition's impact can vary greatly, making diagnosis and management highly individualised. Roughly 25% of all ME/CFS cases are categorised as mild, 50% as moderate-severe and 25% as very severe.[40] [41]

ME/CFS significantly impacts patients' quality of life, with many experiencing severe disability and requiring ongoing symptom management through medications, pacing strategies, and supportive therapies. Despite its prevalence, ME/CFS remains underfunded and misunderstood, emphasising the need for greater awareness, research investment, and accessible treatment options.

Post-Exertional Malaise (PEM)

Post-Exertional Malaise (PEM), also referred to as post-exertional symptom exacerbation (PESE) in the context of long COVID, is a debilitating response to normal, every-day activities in people with ME/CFS. For individuals with severe-very severe ME/CFS or LC, this can be triggered by sensory overload, such as exposure to light or even simple conversations.[42] [43] [44] Repeated episodes of PEM can exacerbate these already severe symptoms, and even minimal exertion can lead to significant setbacks for the patient's health and wellbeing.[45] [46] [47] PEM occurs due to immune system dysregulation, a malfunctioning energy production system, impaired mitochondria with insufficient energy metabolism in muscles. [48] [49] [50]

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[39] Grach, S.L., Seltzer, J., Chon, T. Y., & Ganesh, R. (2023). Diagnosis and management of myalgic encephalomyelitis/chronic fatigue syndrome. *Mayo Clinic Proceedings, 98*(10), 1544-1551. Link.

[40] Chang, C.J., Hung, L. Y., Kogelnik, A.M., Kaufman, D., Aiyar, R.S., Chu, A.M., Wilhelmy, J., Li, P., Tannenbaum, L., Xiao, W., & Davis, R.W. (2021). A Comprehensive Examination of Severely Ill ME/CFS Patients. *Healthcare*, *9*(10), 1290. DOI.

[41] As per footnote 1.

[42] Friedberg, F., Bateman, L., Bested, A.C., Davenport, T., Friedman, K.J., Gurwitt, A., Jason, L.A., Lapp, C.W., Stevens, S.R., Underhill, R.A., Vallings, R. (2014). Chronic fatigue syndrome myalgic encephalomyelitis: Primer for clinical practitioners 2014 edition. International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis IACFS/ME.

[43] Rowe, P. C., Underhill, R. A., Friedman, K. J., Gurwitt, A., Medow, M. S., Schwartz, M. S., Speight, N., Stewart, J. M., Vallings, R., & Rowe, K. S. (2017). Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Diagnosis and Management in Young People: A Primer. *Frontiers in pediatrics*, *5*, 121. DOI.

[44] Maeda, K. I., Islam, M. F., Conroy, K. E., & Jason, L. (2023). Health outcomes of sensory hypersensitivities in myalgic encephalomyelitis/chronic fatigue syndrome and multiple sclerosis. *Psychology, health & medicine*, *28*(10), 3052–3063. DOI.

[45] Friedberg, F., Bateman, L., Bested, A.C., Davenport, T., Friedman, K.J., Gurwitt, A., Jason, L.A., Lapp, C.W., Stevens, S.R., Underhill, R.A., Vallings, R. (2014). Chronic fatigue syndrome myalgic encephalomyelitis: Primer for clinical practitioners 2014 edition. International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis IACFS/ME.

[46] Rowe, P. C., Underhill, R. A., Friedman, K. J., Gurwitt, A., Medow, M. S., Schwartz, M. S., Speight, N., Stewart, J. M., Vallings, R., & Rowe, K. S. (2017). Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Diagnosis and Management in Young People: A Primer. *Frontiers in pediatrics*, *5*, 121. DOI.

[47] Maeda, K. I., Islam, M. F., Conroy, K. E., & Jason, L. (2023). Health outcomes of sensory hypersensitivities in myalgic encephalomyelitis/chronic fatigue syndrome and multiple sclerosis. *Psychology, health & medicine*, *28*(10), 3052–3063. DOI.

[48] https://www.meresearch.org.uk/research/the-connection-between-energy-metabolism-and-immune-regulation-in-me-cfs/

[49] Bateman Horne Center: https://batemanhornecenter.org/wp-content/uploads/filebase/education/top_resources/ER-and-Urgent-Care-Considerations-for-MECFS-1.19.22-005.pdf

[50] https://ammes.org/tag/impaired-muscle-energy-metabolism/

Long COVID

Long COVID is characterised by persistent, unexplained symptoms following infection with COVID-19 (SARS-CoV-2) lasting more than 12 weeks and not explained by an alternative diagnosis.[51] Both conditions share symptoms such as extreme fatigue, cognitive dysfunction, and post-exertional symptom exacerbation (PESE), with up to 50% of long COVID cases fitting the diagnostic criteria for ME/CFS.[52]

- **COVID developing to ME/CFS**
- Up to 50% of long COVID cases fit the diagnostic criteria for ME/CFS.[53] Using data from a long COVID research initiative run by the US National Institutes of Health (NIH), the incidence of ME/CFS is now considered 15 times higher than pre-pandemic levels, and that people with a history of COVID are almost eight times as likely to develop the chronic condition.[54]

Dysautonomia

Dysautonomia is an umbrella term for disorders that affect the autonomic nervous system (ANS), which regulates involuntary bodily functions like heart rate, blood pressure, digestion, and temperature control.[55] When the ANS malfunctions, individuals may experience symptoms such as dizziness, fainting, abnormal heart rates, unstable blood pressure, and fatigue.[56]

Common Types of Dysautonomia:

1. **Orthostatic Intolerance (OI)** – A condition where the body struggles to regulate blood pressure and circulation upon standing, leading to dizziness, lightheadedness, and sometimes fainting.[57]
2. **Postural Orthostatic Tachycardia Syndrome (POTS)** – Characterized by an excessive increase in heart rate upon standing, often accompanied by fatigue, nausea, and chest pain. POTS primarily affects individuals assigned female at birth between ages 15–50.[58]
3. **Inappropriate Sinus Tachycardia (IST)** – A condition where the heart rate is persistently elevated without an apparent cause, leading to palpitations, dizziness, and anxiety.[59]

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[51] Abramoff, B., Joshi, S., Herman, E., Silver, J. (2024). BMJ Best Practice: long COVID. Straight to the point of care. Link.

[52] As per footnote 1 & 3.

[53] As per footnote 1 & 3.

[54] https://www.iflscience.com/people-whove-had-covid-could-be-almost-8-times-as-likely-to-develop-mecfs-77612?s=03&fbclid=IwY2xjawH9RcZleHRuA2FlbQIxMQABHdL_9nu-DJuPWUrAfSoT16bBhzDiWhnfxgX3E6eqYshXDYz2xHZi2aEJiQ_aem_oBwZAag9KRFaIljqeu5LGw

[55] https://ccisupport.org.nz/wp-content/uploads/2021/11/19-Dysautonomia-October-2021.pdf

[56] https://www.healthline.com/health/types-of-dysautonomia

[57] Same as 14

[58] Same as 15

[59] https://www.eds.clinic/articles/types-dysautonomia-pots-oh-vasovagal-ist

4. **Neurally Mediated Hypotension (NMH)** – A reflex-mediated condition where blood pressure and heart rate suddenly drop, causing fainting. Triggers include prolonged standing, emotional distress, or pain.[60]

Dysautonomia can occur on its own or alongside other conditions such as ME/CFS, Ehlers-Danlos Syndrome, Lupus, and Parkinson's Disease.[61] While some forms are rare, others—like POTS and OI—are relatively common and can significantly impact daily life.

Mast Cell Activation Syndrome (MCAS)

Mast Cell Activation Syndrome (MCAS) is a chronic condition in which mast cells, a key part of the immune system, release excessive amounts of inflammatory mediators in response to triggers. These mediators can cause widespread symptoms affecting multiple organ systems, including skin reactions, gastrointestinal disturbances, cardiovascular instability, neurological symptoms, and respiratory issues.[62] MCAS is often associated with conditions such as ME/CFS, Fibromyalgia, Ehlers-Danlos Syndrome, and Long COVID.[63] Due to its complexity, effective management requires a combination of medications, mast cell stabilisers, antihistamines, and dietary modifications.[64]

Fibromyalgia

Fibromyalgia is a neurological and musculoskeletal disorder characterized by widespread chronic pain, fatigue, cognitive difficulties ("fibro fog"), and sleep disturbances.[65] It is believed to involve dysregulation of pain processing in the central nervous system, leading to heightened sensitivity to pain and sensory stimuli. Fibromyalgia is often associated with ME/CFS and other chronic illnesses, and treatment typically includes medications for pain relief, physical therapy, sleep management, and alternative therapies such as low-dose naltrexone (LDN), CoQ10, and magnesium supplementation.[66] [67]

Hypermobility

Hypermobility describes joints that stretch farther than normal. A subgroup may experience unstable joints, soft stretchy skin, recurrent hernias, dislocations or subluxations. Hypermobility can cause musculoskeletal pain, dysautonomia, cognitive dysfunction, and fatigue.[68] [69] Currently limited research suggests that Hypermobile Ehlers-Danlos Syndrome (hEDS) is the more common

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[60] Same as 18
[61] Same as 14
[62] https://www.mastcellaction.org/mcas-bibliography
[63] https://link.springer.com/chapter/10.1007/978-3-030-54165-1_21
[64] https://bestpractice.bmj.com/info/
[65] https://www.mdpi.com/2227-9059/12/7/1543
[66] https://www.mdpi.com/2227-9059/13/1/165
[67] https://www.frontiersin.org/journals/medicine/articles/10.3389/fmed.2021.666914/full
[68] Ganesh, R., & Munipalli, B. (2024). Long COVID and hypermobility spectrum disorders have shared pathophysiology. *Frontiers in neurology*, *15*, 1455498. https://doi.org/10.3389/fneur.2024.1455498
[69] https://solvecfs.org/new-study-using-solve-real-world-data-rwd-examines-joint-hypermobility-in-people-with-me-cfs/

disorder experienced by people with ME/CFS, versus classical EDS (a genetic connective tissue disorder).[70] [71] [72]

It is suggested that MCAS coupled with degranulation that occurs in both ME/CFS and long COVID results in hyperinflammation which damages connective tissue, worsening hypermobility.[73]

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[70] Mudie, K., Ramiller, A., Whittaker, S., & Phillips, L. E. (2024). Do people with ME/CFS and joint hypermobility represent a disease subgroup? An analysis using registry data. *Frontiers in neurology*, *15*, 1324879. https://doi.org/10.3389/fneur.2024.1324879

[71] Bragée, B., Michos, A., Drum, B., Fahlgren, M., Szulkin, R., & Bertilson, B. C. (2020). Signs of Intracranial Hypertension, Hypermobility, and Craniocervical Obstructions in Patients With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Frontiers in neurology*, *11*, 828. https://doi.org/10.3389/fneur.2020.00828

[72] https://www.ehlers-danlos.com/2017-eds-classification-non-experts/chronic-fatigue-ehlers-danlos-syndrome-hypermobile-type/

[73] https://ammes.org/tag/ehlers-danlos/