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Review Article

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Current Stage of Knowledge and Research – Facts and Assumptions

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Abstract:

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic multisystem disorder characterized by persistent, debilitating fatigue lasting at least over six months and affecting multiple organ systems. Despite its classification by the WHO as a neurological disease since 1969, the precise pathogenesis remains unclear, and no definitive biomarkers exist. ME/CFS primarily affects adults aged 30–50, predominantly women, often triggered by infections such as Epstein–Barr virus or SARS-CoV-2, with a rising incidence following the COVID-19 pandemic.

Diagnosis is complex and based on exclusion of other conditions, relying heavily on clinical criteria, particularly the hallmark symptom of post-exertional malaise (PEM), a delayed, severe worsening of symptoms following exertion. The Canadian Consensus Criteria are commonly used in Europe, requiring at least five major and two of three minor criteria, including neurological, autonomic, and immunological disturbances.

Currently no causal, evidence-based cure exists. Treatment focuses on symptom management and patient education. The basic principle is the control of physical and mental activities and a careful energy management to avoid PEM, alongside supportive measures such as sleep hygiene, pain management, and psychosocial care. Pharmacological interventions address specific symptoms, with limited evidence for efficacy. Severe cases pose significant care challenges.

ME/CFS represents a substantial burden on patients and families, compounded by delayed diagnosis, lack of specialized care, and societal under-recognition. The current research aims to clarify pathophysiological mechanisms and identify biomarkers to enable targeted therapies. Until then, multidisciplinary, evidence-based management and improved awareness are essential to mitigate the disease's profound impact.

Key words: myalgic encephalomyelitis; chronic fatigue syndrome; me/cfs; infection triggers (epstein-barr virus; sars-cov-2); post-exertional malaise (pem); diagnosis by exclusion; canadian consensus criteria; symptom management

Introduction

History, possible causes, epidemiology, prevalence and pathogenesis

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic multisystem disease [1] [2]. It is defined as a condition persisting for more than six months in adults and affecting multiple organs or organ systems. As of September 2025, the full pathogenesis of the disease remains unresolved, and no specific biomarker detectable in routine clinical practice has yet been identified.

Since 1969, ME/CFS has been classified by the World Health Organization (WHO) as a neurological disorder and is currently coded as G93.3 in the ICD-10. Approximately two- thirds of ME/CFS patients are women, with a peak incidence between the ages of 30 and 50, thus affecting the life stage of highest productivity. In most cases (approximately 80%), the onset is preceded by an infection. Other precipitating events include prior surgical interventions, resuscitations, or trauma to the head and neck region. In the majority of patients no plausible trigger can be identified [1] [2] [3].

Potential infectious agents associated with the disease include Epstein–Barr virus (EBV), COVID-19 (with approximately 20% of Long COVID cases manifesting as ME/CFS), herpes simplex virus type 1 (HSV-1), human herpesvirus 6 (HHV-6), enteroviruses, influenza viruses, dengue virus, chikungunya virus, as well as bacterial pathogens such as Borrelia, Mycoplasma, Bartonella, Brucella, Chlamydia, and Legionella, in addition to rarer infections with fungi and protozoa such as Coxiella and amoebae [3].

Prevalence and incidence figures remain unreliable due to the complexity of the condition, the absence of biomarkers, and the challenging and time-

consuming diagnostic process, all of which contribute to a high number of undiagnosed cases as well as considerable rates of misdiagnosis. Notably, since the onset of the SARS-CoV-2 pandemic, there has been a marked increase in new ME/CFS diagnoses.

Current medical knowledge about the pathogenesis suggests dysfunction of both the central and autonomic nervous systems, potentially resulting from nerve fiber damage and neuroinflammation, as well as immune system impairment leading to increased susceptibility to infections and reactivation of latent viruses. Additionally, there are indications of impacts to the cardiovascular system (including endothelial cell dysfunction with capillary rarefication and impaired organ perfusion), muscle tissue damage with potential necrosis upon exertion and cerebral hypoperfusion (demonstrable via tilt-table testing and imaging), mitochondrial dysfunction across multiple cell systems (affecting energy production) and the gut microbiome [1] [3].

Ian James Martins discusses the importance of Sirtuin 1 (Sirt1) as a key diagnostic biomarker for chronic diseases, including NAFLD, diabetes, and neurodegenerative disorders, due to its role in regulating mitochondrial function, metabolism, and protein interactions. Sirt1's activation, particularly through diet, can enhance drug efficacy and manage disease progression by influencing amyloid beta metabolism and insulin resistance. Martins study highlights the need for precise proteomic diagnostics, focusing on Sirt1, to improve therapeutic interventions and avoid errors in drug metabolism and disease management [4].

It should be noted that a future laboratory diagnosis, revealing a mosaic of various changes, is likely to emerge (this is being intensively investigated in ongoing studies). Exemplary in this regard are the research findings particularly related to cerebrospinal fluid analyses by Iwasaki et al. (2025), which provide new insights into distinct immunological subtypes in ME/CFS. The differences identified by Iwasaki et al. (2025) can certainly be characterized as a significant contribution to understanding the pathogenesis of the disease and serve as a starting point for developing more targeted therapeutic strategies. The authors specifically highlight that the detailed characterization of disease subgroups is considered a promising approach [5].

It must be pointed out, however, that all these assumptions currently represent a certain degree of probability, but scientifically conclusive confirmation is still pending. Definitive evidence at the cellular or molecular level, however, remains outstanding. This can only be remedied by basic research in parallel to clinical trials, defining the disease more precisely and unmistakably in order to provide practicing physicians with useful guidance and to clearly visualize the dimension of the problem, moving away from estimated figures to a statistically accurate representation of prevalence and incidence, mortality and lethality. Such a development would also benefit the lack of public awareness and acceptance of the disease itself, which is often complained about by patients and their caregivers, as well as the allocation of funds, not only for further research, but also for securing the usually long- term care of the sick.

As for the current status, it appears that a diagnostic proof for ME/CFS will likely be integrated into diagnostics, as well as the differentiation of disease stages and potential therapies, in the near future. From daily clinical experience it can be confirmed, that the perception and acceptance of the illness as an independent somatic disease entity, possibly as a consequence of a previous infectious disease, is of great importance of those affected.

This must be seen in the light of the fact, that regardless of the specific proposed mechanisms of damage, the common endpoint is physical and cognitive impairment, ranging from mild limitations to complete bedbound status [1].

While significant improvement or recovery in adults is rare, disease severity can becategorized as follows: [2].

- *Mild*: able to work but with major restrictions
- *Moderate*: affecting around 65% of patients; largely homebound, work rarely possible
- *Severe*: light activities scarcely possible, largely bedbound, requiring substantial support
- *Very severe*: completely bedbound and dependent on full-time care, unable to perform basic activities, with a recommendation for complete sensory shielding.

Up to 60% of patients are unable to work. Only those with mild disease may be partially able to maintain employment, while approximately 25% are confined to their homes. Family members of patients may also experience considerable physical and psychological strain, often providing care without formal support. Life expectancy and quality of life may be reduced within the group of severe and very severe ill patients by deaths including heart failure, cancers (particularly lymphomas), and suicide [1].

II) Symptoms and Diagnostics

The diagnostic process first consists in obtaining a complete medical history and, where available, analyzing symptom diaries, followed by a physical examination, which may reveal cold, clammy extremities, Raynaud's phenomenon, mottled skin, elevated resting heart rate, reddened eyes, facial swelling, lymphadenopathy, and throat pain [1] [3].

A useful screening laboratory panel to exclude other, more readily identifiable diseases includes a complete blood count with differential, C-reactive protein (CRP), ferritin, HbA1c, lipid profile, protein C, lipoprotein(a), homocysteine, creatinine, creatine kinase (CK), liver enzymes, lactate dehydrogenase (LDH), bilirubin, electrolytes including phosphate, thyroid peroxidase antibodies (TPO-Ab), thyroid-stimulating hormone (TSH) with free T3 and free T4, immunoglobulin subclasses, antinuclear antibodies (ANA, and if positive extractable nuclear antigens [ENA]), antineutrophil cytoplasmic antibodies (ANCA), anticardiolipin antibodies, prothrombin, angiotensin-converting enzyme 2 (ACE-2), celiac antibodies, and N-terminal pro–B-type natriuretic peptide (NT-pro-BNP). This work-up can reveal deficiencies or abnormalities that may justify further targeted diagnostics (e.g., endocrine axis testing). However, in many cases, no relevant abnormalities are found - apart from, for example, autoantibodies against various receptors, which currently have no therapeutic relevance - so the primary function of this diagnostic panel is to exclude other disease entities [1] [3].

ME/CFS is therefore a classic diagnosis of exclusion. Before the diagnosis can be made, a range of neurological, psychiatric, endocrinological, and metabolic disorders must be thoroughly ruled out if they could plausibly explain the patient's symptoms. In the absence of a validated biomarker, diagnosis relies on scoring systems and established international criteria.

Diagnostic criteria must always include the cardinal symptom of post-exertional malaise (PEM). PEM is defined as a disproportionately severe deterioration in overall condition and pre-existing symptoms, without physiological recovery, triggered by exertion - often perceived as minor - whether physical, cognitive, emotional, orthostatic, or sensory. PEM may occur immediately after exertion, but more commonly develops 12 to 72 hours later and can be accompanied by so-called "crashes" (onset of new symptoms). By definition, PEM lasts at least 14–24 hours; however, the worsening can persist much longer and carries the risk of permanent deterioration. PEM helps distinguish ME/CFS from depression and burnout: in the latter, reduced drive is typical and physical activity does not cause deterioration, whereas in ME/CFS it does. Moreover, ME/CFS patients are often motivated and show little reduction in drive [1] [2] [3].

PEM must also be differentiated from fatigue of other etiologies, particularly following internal medical illnesses. Important differential diagnoses for fatigue include diseases further outlined in table 1.

Fibromyalgia, irritable bowel syndrome, endometriosis, and Hashimoto's thyroiditis are frequent comorbidities in ME/CFS [1] [3].

Rheumatology	Polymyalgia rheumatica (PMR), collagenoses, systemic lupus erythematosus (SLE), Sjögren's syndrome, sarcoidosis, ankylosing spondylitis, and psoriatic arthritis.
Endocrinology	Diabetes mellitus, hypothyroidism, Addison's disease, hypercalcemia.
Infectious diseases/Immunology	Post-infectious states, neuroborreliosis, AIDS, chronic sinusitis, chronic hepatitis, mast cell activation syndrome, immunodeficiencies such as common variable immunodeficiency (CVID).
Hemato-Oncology	Anemia, iron deficiency, malignant diseases and their treatments
Gastroenterology	Inflammatory bowel disease (IBD), celiac disease, primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC).
Neurology and Psychiatry	Depression, somatic symptom disorder, multiple sclerosis (MS), myasthenia gravis, hypermobile Ehlers–Danlos syndrome (hEDS), Parkinson's disease, Alzheimer's disease, sleep disorders (particularly obstructive sleep apnea syndrome [OSAS]), cervical spinal stenosis/whiplash injury, attention-deficit/hyperactivity disorder (ADHD), and autism.
Others	Fatigue secondary to heart failure, renal failure, medication side effects, and mitochondrial myopathy.

Table 1: Differential Diagnoses for Fatigue

(Own version 2025, based on Hoffmann et al. 2024 & Renz-Polster/Scheibenbogen 2022)

Whereas the underlying mechanisms of PEM, which is not exclusively a symptom of ME/CFS, are not fully understood, the literature agrees, that it cannot be considered a potential cause of death and that PEM is naturally depending on the subjective assessment of the patient, but is anyway part of the assessing CCC and IOM criteria [6].

In Europe, the Canadian Consensus Criteria (CCC) are most frequently applied for diagnosis in adults, as they are more specific than the Institute of Medicine (IOM) clinical criteria, which are more commonly used in the United States. [1] The five major criteria and the three minor criteria are outlined in table 2 [1-3,7].

Major criteria	*Pathological fatigue*	Disproportionate exhaustion that does not improve adequately with sleep or rest (with careful consideration of differential diagnoses as described in Table 1 above).
	PEM	Assessed, for example, by repeated handgrip strength measurements with a dynamometer; such tests are typically limited to research contexts (e.g., measurement of inappropriate blood lactate accumulation). Exercise testing should be avoided, as it may worsen the disease.
	Sleep disturbances/unrefreshing sleep	May be supplemented by overnight pulseoximetry or polysomnography if OSAS is suspected.
	Pain (head, muscle, joint, bone, neuropathic)	Important differentials include migraine, cervical spine disorders, peripheral neuropathy, neuroborreliosis, and orthopedic causes. If small fiber neuropathy is suspected, skin biopsy may be indicated; if there are signs for hypermobile Ehlers–Danlos syndrome, the Beighton score should be assessed.
	Neurological/cognitive impairments	Memory and concentration deficits, confusion, attention difficulties. Imaging studies investigating cerebral hypoperfusion in ME/CFS are ongoing in multiple trials.
Minor criteria	*Autonomic nervous system disturbances*	Orthostatic intolerance in postural orthostatic tachycardia syndrome (POTS) and orthostatic hypotension (diagnostically and differentially useful tests include the Schellong test, 10-minute standing test, tilt table testing, 24-hour blood pressure, and ECG monitoring), marked pallor, dizziness, gastrointestinal or urinary disturbances, pupillomotor abnormalities, and palpitations.
	Neuroendocrine disturbances	Dysregulated body temperature, cold/heat intolerance, febrile sensations, cold extremities, weight changes, abnormal appetite, and impaired stress response. Abnormal findings warrant evaluation of TSH, growth hormone (GH), the gonadotropic axis, the adrenocortical axis, and insulin resistance.
	Immunological disturbances	Lymphadenopathy, sore throat, allergic tendencies, persistent flu-like malaise, reactivation of latent viruses, hypersensitivities/intolerances, mast cell

Table 2: Canadian Consensus Criteria

(Own version 2025, based on Hoffmann et al. 2024; Renz-Polster/Scheibenbogen 2022; Carruthers et al. 2003; Hainzl et al. 2024)

In adults, a minimum illness duration of six months is required to distinguish ME/CFS from the (not uncommon) post-infectious fatigue state. All five major criteria and at least two of the three minor criteria must be met to establish a diagnosis of ME/CFS [7]. For ease of diagnosis, supportive questionnaires and scoring tools exist for each criterion.

After clarifying the diagnosis in the prescribed way, additional tools can be used to assess disease severity (e.g., the Bell score, with repeated assessments being useful for monitoring), symptom frequency (e.g., the Munich–Berlin Symptom Questionnaire [MBSQ]), and functional capacity (e.g., FUNCAP55) [1]

Without accurate diagnosis and appropriate treatment, the patient's condition may deteriorate. On average, it takes around five years for a diagnosis of ME/CFS to be established [1]. This delay may be due to the often-non-specific nature of symptoms, particularly in the early stages, as well as to the fact that the disease and its diagnostic process are insufficiently known among the medical profession and are often not recognized as a distinct disease entity. There is a lack of continuing

education on ME/CFS, and the condition is addressed only peripherally in university curricula. Consequently, patients often feel misunderstood by physicians, which can severely strain the therapeutic relationship.

As of September 2025, Austria has no specialized ME/CFS facilities. As a result, even after diagnosis, appropriate treatment is often unavailable. By contrast, Germany, though not yet with comprehensive nationwide coverage, offers the Immunodeficiency Outpatient Clinic at Charité Berlin (no age restrictions) and the Chronic Fatigue Centre for Young People at the Technical University of Munich (for patients up to 20 years of age).

Diagnostic work-up is further complicated by the lack of suitable centers and the shortage of specialists, leading to uncoordinated evaluations. Moreover, patients' mobility and ability to plan daily activities may be severely limited by the disease (e.g., geographically distant facilities may be inaccessible or impossible to attend) [2].

III) Therapeutic Approaches

Currently, there is no therapeutic cure for ME/CFS. The focus is primarily on education, self- management, symptomatic treatment, and empathetic psychosocial support [1].

a) Non-pharmacological Intervention

The most important tool in non-pharmacological therapy is "Pacing." Pacing involves individual energy management throughout the day to avoid post-exertional malaise (PEM). The goal is to prevent exceeding

personal limits [1]. This requires attentiveness to both physical and psychological boundaries, with breaks taken before and after exertion [2]. Support can be provided through tools such as diaries and wearables (e.g., smartwatches) [1].

In the future, AI could play a significant role in supporting pacing and general ME/CFS management.

It is important to emphasize that the goal of pacing is not to increase exertion limits, but to stabilize the patient's overall condition, enabling the feasibility of other therapies. Therefore, the principle of "Pacing first" applies, alongside the best possible symptom-oriented treatment and therapy for comorbidities. However, once the condition reaches a severe stage, pacing can become almost impossible, as basic activities (e.g., eating, drinking, speaking) can trigger PEM [1-3,8].

Other strategies include sleep hygiene, relaxation techniques (such as autogenic training, meditation, breathing exercises), stress reduction, coping mechanisms, physiotherapy (for pain management and circulatory activation, tailored to individual needs), cautious manual therapy, massage, occupational therapy, and dietetics (for intolerances, dietary adjustments, nutritional deficiencies, later evaluation of swallowing difficulties, pureed food, meal replacements, parenteral nutrition, preventing weight loss). For therapists, home visits, teletherapy, or practices with minimal sensory stimuli are recommended (e.g., seating/lying options, minimal waiting times, dimmable lighting, barrier-free access, air filters, masks) [1,2,3].

Supportive tools for sensory shielding can include noise-canceling headphones, acoustic filters, dark sunglasses, room darkening, screen filters, and sleep masks. Adequate hydration (especially before getting up), electrolyte solutions, increased salt intake, compression stockings, and abdominal binders can alleviate symptoms of orthostatic dysfunction. Regarding nutrition, a protein-rich diet of 1g/kg body weight with sufficient unsaturated fatty acids is recommended. If deficiencies are detected, supplementation with iron, folic acid, vitamin B12, and vitamin D should be considered. Psyllium husks may help with irritable bowel symptoms [3].

Patients often take supplements to correct deficiencies and improve energy metabolism. However, there are few clinical studies showing clear benefits in this area. ME/CFS patients likely experience disturbances in mitochondrial energy production, as well as deficits in amino acids, vitamins, and lipids, meaning temporary supplementation with ribose, vitamin B1, B2, B12, NADH, Coenzyme Q10, and carnitine could be helpful, potentially improving symptoms. It is typically recommended to try supplementation for 4 weeks, monitor tolerance, and then reevaluate the individual's condition [9].

While ME/CFS is not a psychiatric disorder, psychological comorbidities (such as depression and anxiety) may occur, often due to the severity of the illness, stigma, potential social isolation, and/or financial difficulties. These should be addressed and treated adequately (e.g., pharmacologically with antidepressants or SSRIs, if necessary). Psychotherapy should primarily assist with coping with the illness and does not have a curative approach [1]. Additionally, support groups and online forums can help patients process their illness [3].

In the workplace, more flexible models are needed, tailored to each individual's situation, such as flexible working hours, sufficient breaks, single-person offices, home-office options, quiet spaces, and the possibility to work while lying down. This approach allows certain patients to remain in the workplace or regain workability after periods of limited mobility [10].

Financial and social security is also crucial for patients, as many are partially or fully unable to work. Depending on the individual case, disability pensions, nursing allowances, medical devices (e.g., walkers, electric wheelchairs), and additional support services may be necessary. However, these services are often complicated by bureaucracy and the lack of societal recognition of the illness, adding further burden to patients [1].

Severely affected patients are bedridden and highly sensitive to external stimuli, presenting significant therapeutic challenges. Additionally, there is limited research data on those severely affected by the disease. These patients rely heavily on appropriate caregiving staff and adequate spatial arrangements, particularly in regard to nutrition (e.g., feeding tubes), personal hygiene, and sensory shielding [8].

b) Pharmacological Interventions

Many medications used for ME/CFS are prescribed "off-label," requiring specific informed consent. Additionally, this patient group tends to experience more side effects from therapies, so a critical risk-benefit analysis should be performed beforehand, with regular reevaluations of the treatment. Lactose-free medications and gluten-free diets should only be used when there is verified lactose intolerance or clinically confirmed celiac disease. Over the course of the illness, however, other intolerances may emerge [1].

At the beginning of pharmacological therapy, it is generally recommended to start with a low dose (e.g., using compounded prescriptions) and gradually increase it. Depending on the response and side effects, dose reductions or discontinuation trials can be conducted [2].

Across all therapeutic trials, it can be observed that very few causal approaches are available among a variety of symptomatic treatments: [1,2,3].

- For alleviating orthostatic dysfunction/POTS, cardioselective beta-blockers, Ivabradine, Pyridostigmine, or Fludrocortisone can be considered. For sleep disturbances, Melatonin, Dibondrin, Tryptophan, Pregabalin, and low-dose antidepressants (e.g., Trazodone, Doxepin, Trimipramine, and Mirtazapine) may be effective. In pain management, the proven multimodal WHO step scheme is used, sometimes supplemented with a situation-specific use of Pregabalin or Gabapentin. Low-dose Naltrexone may also be indicated for chronic pain.

- For allergic symptoms or mast-cell overactivity, an antiallergic therapy with H1+H2 antihistamines in combination (similar to the treatment for systemic mastocytosis) may be attempted, and possibly a mast cell stabilizer such as Cromoglicic acid or Ketotifen may be administered.
- For herpesvirus infections and recurrences, the use of Aciclovir or Valaciclovir is recommended.
- Long-term antibiotic therapy with Azithromycin or Minocycline may sometimes alleviate symptoms in the early stages of the disease, likely due to their immunomodulatory and anti-inflammatory effects.
- Furthermore, it is generally agreed that ME/CFS patients (like healthy individuals) should receive all recommended vaccinations. Infections must be treated empirically

or in accordance with antibiogram data. The use of immunoglobulins remains a topic of discussion and is certainly effective in cases of IgG deficiency or immune defects, but such cases may be distinct from ME/CFS.

There are also reports of low-dose Aripiprazole (0.2-2 mg/day) being effective in improving fatigue and cognitive deficits in ME/CFS. One hypothesis is that the neuroinflammation believed to occur in ME/CFS may be mediated by dopamine D2 receptor agonists, which is where the action of Aripiprazole is thought to intervene [11].

There is less evidence for hyperbaric oxygen therapy, anticoagulants, and rheological agents such as Vericiguat and Sulodexide. These treatments aim to prevent or treat microcirculation disturbances caused by microthrombi [1].

In particularly severe cases, experimental treatments such as immunoadsorption or B-cell depletion with Rituximab and Cyclophosphamide are under investigation. These highly invasive therapies are subject to strict indications [3].

In the event of an acute flare-up caused by overexertion or infection, diagnostic evaluation should be initiated, and adequate fluid intake should be provided. Sensory shielding should also be prioritized in this situation. Benzodiazepines (e.g., Alprazolam) may be given short- term, but long-term use requires consideration of the risk of addiction [8].

Recommended guidelines with more detailed information on the pharmacological and non- pharmacological treatment of ME/CFS for patients and healthcare providers can be found on the websites and publications of Charité University Medicine Berlin [12], the German and Austrian ME/CFS societies [1], the National Institute for Health and Care Excellence (NICE) in the UK [13], and the Centers for Disease Control and Prevention (CDC) in the USA [14].

Additionally, the German Society of Neurology (DGN) advocates for a balanced, interdisciplinary, and scientifically grounded approach that considers not only immunological but also psychosomatic and functional aspects. In light of the absence of approved causal therapies, transparent patient education is essential, alongside the development of appropriate care structures and psychiatric support, in order to adequately address the significant psychological burden many patients face [15], However, the recognition of the syndrome as an organic neurological disease should be acknowledged, according to the WHO and newly revisited for the ICD-11 classification beyond dispute [16].

IV) Conclusion

ME/CFS is a multisystem disorder that presents significant challenges for both patients and their treating physicians due to its severe impact on those affected, the absence of biomarkers, the lack of widespread specialized care, and the limited number of reliably effective therapies. The suffering of patients and their families, as well as their entire social environment, can be considered substantial, and the existing deficit in the recognition of the illness exacerbates these issues.

This inevitably gives rise to the justified demand for continuing education, training, and, above all, evidence-based, certified case management for individuals with ME/CFS within the public health and social systems of developed nations. These systems should have sufficient resources for both the research into the underlying causes of the illness and the development of therapy and care options. Current research is underway and must necessarily focus on identifying the triggers of the disease and understanding its pathophysiology in order to develop targeted therapies for ME/CFS patients.

It can be stated that there is sufficient evidence that, according to the WHO definition, ME/CFS is unequivocally a somatic condition that meets all criteria of a chronic illness, although distinguishing it from psychosomatic disorders can sometimes be difficult on a case-by-case basis. The authors of the guidelines believe that while psychological comorbidities often and understandably occur, they are concomitant as a consequence of the underlying condition and not its cause.

Regarding the issue of recognition of the disease by authorities and healthcare institutions, it can be outlined that the challenges mainly stem from its diverse manifestations, the lack of visible presence of affected individuals in public life (which is a characteristic of the illness), and the continued absence of a singular biomarker or pathognomonic imaging.

In summary, the condition represents a complex, chronically debilitating illness with poorly understood and difficult-to-define symptoms that is increasingly coming into the focus of both political and medical attention. Despite intensive research efforts, no reliable biological markers or effective therapies have been identified to date. The neurological community remains critical of the term “encephalomyelitis,” as inflammatory processes in the central nervous system are generally not detectable in ME/CFS. The clinical presentation overlaps with numerous medical and psychiatric conditions, which further complicates diagnosis. Many studies on ME/CFS suffer from methodological limitations, making interpretation difficult and contributing to the lack of evidence-based treatment options.

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