



What cause CFS/ME?

-

WHAT SCIENCE AT PRESENT CAN TELL US

Analysed and compiled with CLAUDE 4.6, April 2026

By



Most Likely Cause of ME/CFS

THE PROMPT

Considering all relevant scientific papers recruiting the study participants according to the most strict criteria's like ccc, icc or seid, what's the most likely cause for cfs/me

INTRODUCTION

This is a rich and nuanced area. Here's a synthesis of where the science currently stands, focusing on studies using the most rigorous patient selection (CCC, ICC, SEID criteria):

Most Likely Cause of ME/CFS: Current Scientific Consensus

No single cause has been definitively established, but the weight of evidence from stringently recruited cohorts points toward a post-infectious autoimmune/neuroimmune disorder, likely triggered by a viral infection in genetically susceptible individuals.

VIRAL TRIGGER (STRONG, CONSISTENT EVIDENCE)

ME/CFS appears to emerge from an intricate web of genetic vulnerabilities and environmental triggers, notably viral infections, leading to a complex series of pathological responses.

About 10% of people with infectious diseases such as glandular fever (infectious mononucleosis) develop ME/CFS symptoms within 12 months, and 13–45% of people with Long COVID meet ME/CFS diagnostic criteria.

Studies have demonstrated a significant increase in antibodies to the herpesviruses EBV, HHV-6, and VZV in ME/CFS patients compared to healthy controls, with 72.5% of ME/CFS patients simultaneously co-expressing antibodies to multiple herpesviruses versus 31% of controls — and these levels cluster with moderate-to-severe fatigue.

AUTOIMMUNITY (RAPIDLY GROWING EVIDENCE — POSSIBLY CENTRAL)

This is arguably the most exciting and convergent area right now. Recent research increasingly underscores the role of immune dysfunction, including autoantibodies, in ME/CFS pathophysiology — particularly autoantibodies targeting β -adrenergic and muscarinic acetylcholine receptors, which are crucial for autonomic and cardiovascular regulation.

A 2025 Lancet study found that immunoadsorption (physically removing IgG antibodies from the blood) may improve symptoms in post-COVID ME/CFS patients, and the beneficial effects of IgG depletion suggest a significant role for autoantibodies and disturbed B-cell function in the condition's pathophysiology.

The leading hypothesis is molecular mimicry: a virus triggers an immune response, and the resulting antibodies cross-react with the body's own receptors (particularly those regulating blood flow, heart rate, and the autonomic nervous system), causing chronic dysfunction.

MITOCHONDRIAL AND METABOLIC DYSFUNCTION (CONSISTENT DOWNSTREAM FINDING)

Studies support a model of deficient ATP production in ME/CFS, compensated for by upregulation of immediate pathways upstream of Complex V, suggesting an elevation of oxidative stress — evidence of a distinct pathology that holds promise for developing diagnostic biomarkers.

Recent studies provide strong evidence for mitochondrial dysfunction specifically in skeletal muscle tissue. An electron microscopy study directly showed damage to mitochondria in ME/CFS patients' skeletal muscle, with a preferential subsarcolemmal localization. Another study found signs of skeletal muscle damage and regeneration in biopsies taken one day after exercise.

Whether mitochondrial dysfunction is a cause or a downstream consequence of the autoimmune/vascular disruption remains debated.

THE UNIFIED MODEL (CURRENT BEST SYNTHESIS)

ME/CFS appears to arise from a self-sustaining cycle of chronic inflammation, metabolic insufficiency, and neuroimmune imbalance — with immune alterations including reduced natural killer cell cytotoxicity, T-cell exhaustion, abnormal B-cell subsets, and diverse autoantibodies suggesting an autoimmune component, compounded by gut dysbiosis, HPA axis hypofunction, and endothelial dysfunction driven by oxidative stress and autoantibody-mediated receptor interference.

IN CONCLUSION

The most evidence-supported model is: a viral infection (often herpesvirus family or SARS-CoV-2) triggers a dysregulated immune response in genetically susceptible individuals, leading to persistent autoantibodies against autonomic receptors and a self-perpetuating cycle of neuroimmune dysfunction, vascular impairment, and mitochondrial energy failure.

The autoimmune angle is currently the most therapeutically promising — the 2025 Lancet immunoadsorption results being a key indicator — but the field hasn't yet converged on a single definitive mechanism, partly because ME/CFS likely contains biologically distinct subgroups.