The Differences between M.E. and CFS

*M.E. (Myalgic Encephalomyelitis) describes a specific neuroimmune disease with clear defining features.

*CFS (Chronic Fatigue Syndrome) is a broad descriptive label based mainly on prolonged fatigue.

They overlap, but they are not equivalent.

Core Difference

*M.E. is defined by exertion intolerance and systemic dysfunction.

*CFS is defined primarily by long-lasting fatigue.

M.E. (Myalgic Encephalomyelitis)

What defines it

* Post-Exertional Neuroimmune Exhaustion (PENE) is central and required

* Multisystem illness involving:

* Neuroimmune dysfunction

* Autonomic nervous system dysfunction

* Impaired energy metabolism

* triggered by infection

* Symptoms worsen after physical, cognitive, or emotional exertion

* Worsening is often delayed and prolonged

Key features

* PENE lasting days, weeks, or longer

* Unrefreshing sleep

* Cognitive dysfunction

* Orthostatic intolerance

* Sensory hypersensitivity

* Fluctuating but often severe disability

How it’s understood

* Considered a distinct biological disease

* Recognized as neurological by the WHO (ICD-10 G93.3) or currently under Neurological 8E49

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CFS (Chronic Fatigue Syndrome)

What defines it

* Persistent fatigue lasting 6 months or more

* Fatigue is:

* New or unexplained

* Not substantially relieved by rest

* May include additional symptoms, but fatigue is the anchor

Key features

* Fatigue may be primary complaint

* Post Exertion Malaise (PEM) may or may not be present (depending on criteria used)

* Symptom set is heterogeneous

* Can include people with:

* Sleep disorders

* Depression

* Burnout

* Other chronic illnesses

How it's understood

* A syndrome, not a single disease

* Diagnostic criteria have varied widely over time

* Has been used as a catch-all label

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Why This Caused So Much Confusion

* In the late 1980s, M.E. outbreaks were re-labeled as CFS

* The name "chronic fatigue syndrome":

* Minimized the disease

* Shifted focus away from neurological and immune dysfunction

* Research cohorts became mixed, slowing progress

* Some diagnostic criteria did not require PEM

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Modern Criteria Try to Fix This

More recent definitions (e.g. International Consensus Criteria 2011) move closer to M.E. by requiring:

* Post-exertional Neuroimmune Exhaustion worsening

* Cognitive dysfunction

* Unrefreshing sleep

* Autonomic or immune features

But the name CFS is still widely used in practice.

Practical Reality Today

* Many patients diagnosed with “CFS” actually have M.E.

* Some people labeled CFS do not meet M.E. criteria

* This matters because:

* Exercise-based treatments may harm M.E. patients

* Management strategies differ significantly

people with M.E. meet some criteria for CFS, but not all people diagnosed with CFS have M.E.

*M.E. = specific neuroimmune disease with exertion intolerance

*CFS = broad fatigue-based syndrome

*Treating them as identical has caused misdiagnosis, mistreatment, and stigma.

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M.E. has well-documented cardiovascular and autonomic abnormalities.

CFS, as a broad fatigue-based label, does not require these findings.

What’s meant by “cardiovascular” in M.E.

This does not usually mean primary heart disease. It refers to circulatory, autonomic, and blood-flow regulation problems.

Common findings in M.E. include:

* Orthostatic intolerance

* POTS

* Neurally mediated hypotension

* Abnormal heart rate responses

* Excessive tachycardia on standing

* Reduced heart rate variability

* Reduced blood volume

* Impaired oxygen delivery

* Abnormal cerebral blood flow, especially on standing or exertion

* Poor recovery after exertion on cardiopulmonary exercise testing (CPET)

* Reduced VO_2 peak on day 2

* Abnormal anaerobic threshold

These findings are objective, reproducible, and align with patient symptoms.

Why this is tied to M.E. specifically

In M.E., cardiovascular and autonomic dysfunction are part of the core disease mechanism, contributing to:

* Post-exertional Neuroimmune Exhaustion (PENE)

* Exercise intolerance

* Cognitive dysfunction

* Lightheadedness, weakness, “crash” symptoms

They reflect system-wide failure to regulate energy and blood flow under stress.

CFS by contrast

CFS criteria (especially older ones):

* Focus primarily on chronic fatigue

* Do not require:

* Orthostatic intolerance

* Abnormal CPET findings

* Autonomic dysfunction

* Include a heterogeneous group of patients

Some people diagnosed with CFS do have these cardiovascular issues, but when they do, they are likely experiencing M.E. physiology.

Why this matters clinically

* Cardiovascular/autonomic dysfunction helps:

* Distinguish M.E. from nonspecific fatigue

* Explain why exercise can be harmful in M.E.

* Treating M.E. as “just fatigue” leads to:

* Inappropriate exercise prescriptions

* Symptom worsening

* Disease progression in some patients

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M.E. includes objective cardiovascular and autonomic dysfunction affecting blood flow and exertion tolerance; CFS, as a diagnostic label, does not require or define these abnormalities.

Brain imaging studies show meaningful differences, and the key point is not that CFS has “normal brains”, but that the imaging abnormalities consistently line up with M.E. physiology, not with fatigue alone.

*M.E. shows reproducible functional brain abnormalities involving:

*Blood flow

*Neuroinflammation

*Network connectivity

*Energy use

*CFS, as a broad fatigue-based label, includes people with and without these findings

When imaging abnormalities are present in “CFS” cohorts, they almost always correlate with:

* Post-exertional Neuroimmune Exhaustion

* Autonomic dysfunction

* Cognitive exertion intolerance

In other words: imaging tracks M.E., not fatigue.

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SPECT (Blood Flow)

Findings associated with M.E.

Global and regional cerebral hypoperfusion

* Reduced blood flow in:

* Brainstem

* Frontal and temporal lobes

* Worsening hypoperfusion on standing or after exertion

* Correlation with:

* Orthostatic intolerance

* Cognitive dysfunction

* Severity

Relevance to CFS

* SPECT abnormalities are not required for CFS diagnosis

* Mixed CFS cohorts show inconsistent results

* When abnormalities are present, patients usually meet M.E. criteria

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PET (Neuroinflammation & Metabolism)

Findings associated with M.E.

* Evidence of neuroinflammation, particularly:

* Brainstem

* Thalamus

* Limbic regions

* Abnormal glucose metabolism

* Microglial activation (in research settings)

Relevance to CFS

* PET abnormalities are not universal in CFS cohorts

* Strongest signals appear in patients with:

* PEM

* Autonomic dysfunction

* Post-infectious onset

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fMRI (Functional Connectivity)

Findings associated with M.E.

*Altered functional connectivity in:

*Default Mode Network

*Salience network

*Brainstem–cortical pathways

*Abnormal activation patterns during:

*Cognitive tasks

*Sensory processing

*Increased effort for basic cognitive tasks

Relevance to CFS

*fMRI findings are heterogeneous in fatigue-only cohorts

*Clear, consistent patterns emerge when:

*PEM is required

*Cognitive exertion intolerance is measured

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Why this Distinction Matters

*Brain imaging abnormalities are:

*Functional, not degenerative

*Often dynamic (worse with stress or exertion)

*This supports M.E. as:

*A disorder of brain–body regulation

*Not deconditioning

*Not psychiatric

CFS, without physiological anchors, cannot reliably show these patterns.

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Summary

Functional brain imaging (SPECT, PET, fMRI) consistently shows abnormalities in blood flow, inflammation, and neural connectivity in patients with M.E., particularly those with Ppost-Exertional Neuroimmune Exhaustion and Autonomic Dysfunction. These findings are not tied to fatigue itself and are not required for a CFS diagnosis. When such abnormalities appear in “CFS” cohorts, they almost always reflect underlying M.E. physiology rather than chronic fatigue alone.

Note:

Brain imaging does not validate “fatigue.” It validates the biological disease we call M.E.

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Core Point

M.E. (Myalgic Encephalomyelitis) is defined by pathology involving the brain and spinal cord (encephalo- = brain, -myelitis = spinal cord inflammation/dysfunction).

CFS (Chronic Fatigue Syndrome), by definition, does not require evidence of encephalomyelitis.

What’s meant “Encephalomyelitis” means in M.E.

It does not mean the same thing as acute, destructive encephalitis.

In M.E., evidence points to:

* Neuroinflammation (often low-grade, diffuse)

* Brainstem dysfunction

* Spinal cord signaling abnormalities

* Disrupted neuroimmune communication

* Abnormal sensory and autonomic integration

These are supported by:

* PET studies showing neuroinflammation

* SPECT studies showing cerebral hypoperfusion

* fMRI showing abnormal connectivity

* Clinical signs (cognitive dysfunction, sensory overload, autonomic failure)

This is why M.E. is classified by the WHO under neurological diseases (ICD-10 G93.3). Current WHO 8E49

Why CFS does NOT Include Encephalomyelitis

CFS is defined by:

* Chronic fatigue ≥ 6 months

* Optional associated symptoms

It does not require:

* Neuroinflammation

* Brainstem involvement

* Spinal cord dysfunction

* Objective neurological findings

As a result:

* CFS includes a heterogeneous population

* Some have M.E.

* Some have other causes of chronic fatigue

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Why the Names Matter

* The term CFS:

* Centers fatigue rather than pathology

* Allows inclusion without neurological disease

* The term M.E.:

* Reflects central nervous system involvement

* Explains symptom patterns (PENE) autonomic failure, sensory overload)

This naming difference is not semantic — it reflects different disease models.

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*M.E. involves dysfunction of the brain and spinal cord consistent with encephalomyelitis;

*CFS is a fatigue-based syndrome that does not require or define central nervous system pathology.

Important Nuance

* M.E. encephalomyelitis is often:

* Subtle

* Functional

* Neuroimmune-mediated

* It may not show up on routine MRI

* This does not invalidate the diagnosis

Bottom Line

* M.E. = neurological disease involving brain and spinal cord

* CFS = descriptive fatigue syndrome

* Treating them as identical has obscured biology and harmed patients

References

The ICC2011 Criteria specifically for Myalgic Encephalomyelitis
https://doi.org/10.1111/j.1365-2796.2011.02428.x

IOM/SEID 2015

Chronic Fatigue Syndrome CFS.

Note: The following paragraph is from the SEID/IOM 2015 paper.

“In considering which name would be most appropriate, the committee turned first to ME—“myalgic encephalomyelitis” or “encephalopathy.” Historically however, the diagnostic criteria for ME have required the presence of specific or different symptoms from those required by the diagnostic criteria for CFS; thus, a diagnosis of CFS is not equivalent to a diagnosis of ME.” https://www.nap.edu/nap-cgi/skimchap.cgi?recid=19012...

Fukuda / CDC 1994 CFS Criteria

Our guidelines include recommendations for the clinical evaluation of fatigued persons, a revised case definition of the chronic fatigue syndrome, and a strategy for subgrouping fatigued persons in formal investigations. https://www.acpjournals.org/.../0003-4819-121-12...

The ICPRIMER 2012 - a diagnostic tool for the ICC 2011.
https://www.investinme.org/.../Myalgic...

https://pmc.ncbi.nlm.nih.gov/articles/PMC7466519/

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https://youtu.be/wuzmYJxM-r0?si=d4O-vHg6jfJwMlz7

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