

MUSCLE BREAKDOWN & MITOCHONDRIAL INJURY

◆ **High valine** → muscle damage. **High aspartate, low asparagine** → ammonia buildup. Ongoing oxidative stress and magnesium deficiency in muscle cells.

◆ **Glutathione, Taurine, Cysteine Deficiency** Oxidative stress and mitochondrial damage.

Neuroinflammation, neurodegeneration, and autoimmunity, poor detoxification (especially of heavy metals and drugs), Impaired immune defence, impaired energy metabolism, and redox imbalance.

◆ **Profound antioxidant depletion** → oxidative injury and immune dysregulation.

OTHER NOTABLE FINDINGS

◆ **Low Intracellular Magnesium** → Contributes to poor energy production, muscle cramping, and immune dysfunction.

◆ **Leaky Gut / IAG Elevation**
Peptide translocation to brain → neuroendocrine effects. Confirms **intestinal permeability** and links to **MCAS, autoimmunity**.

◆ **Low Blood Volume and Capillary Compliance**
Poor nutrient/oxygen delivery → **peripheral stasis, cognitive dysfunction, and fatigue**.

INJURIOUS METABOLIC AND IMMUNOLOGICAL CYCLES

◆ Glutamate ↔ low GABA ↔ neurotoxicity ↔ sympathetic overactivation

◆ Ammonia ↔ nitric oxide ↔ peroxynitrite ↔ mitochondrial damage ↔ inflammation

◆ Methionine and lysine ↔ no carnitine ↔ energy crash ↔ organ stress

◆ B6/B12 deficiency ↔ methylation block ↔ no neurotransmitters ↔ immune collapse

- ◆ Vitamin D receptor dysfunction ↔ immune tolerance loss ↔ autoimmunity escalation
- ◆ MCAS ↔ histamine/glutamate overload ↔ gut leakiness ↔ CNS irritation

LINKS TO AUTHORITATIVE SOURCES

Aim your phone's camera at the QR code and click the [bit.ly](https://bit.ly/biologyofME) link to automatically visit the website on your phone.

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: the biology of a neglected disease: bit.ly/biologyofME



NICE Guidelines for Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management, NICE guideline [NG206], published 29 October 2021.
bit.ly/ME-Guidelines



Deliberate misclassification as a psychological illness has served both financial and political interests *by reducing the burden on insurance companies and government welfare programs*. See Quotable Quotes at margaretwilliams.me.



COLOR KEY

RED = Most Serious and potentially life-threatening.

GREEN = Serious

PURPLE = Other Findings

ORANGE = Cycles of Harm

Information for Doctors Requisite Laboratory Assays for ME Diagnosis

BY JENNY WILSON

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Myalgic Encephalomyelitis (ME) is a complex, multi-system disease with significant dysfunction across the immune, neurological, cardiovascular, gastrointestinal, endocrine, and musculoskeletal systems. It is associated with substantial physiological impairment, often exceeding that observed in conditions such as multiple sclerosis, heart disease, lung cancer, and stroke (Hvidberg et al., 2015).

Mortality in ME is most frequently the result of medical neglect or mistreatment. These failures are rooted in the persistent adherence to an outdated, harmful, and scientifically discredited psychosomatic model, historically promoted by the Wessely School (Hansard, 1998). This paradigm has contributed to widespread diagnostic delays, therapeutic mismanagement, and under-provision of care.

Despite compelling evidence of serious pathophysiology, ME remains critically under-recognised within clinical practice.

The implications are serious. In a 2024 coroner's inquest, a consultant gastroenterologist acknowledged that a hospital declined to initiate enteral feeding for a severely ill ME patient, resulting in death from starvation. The rationale given was reluctance to 'medicalise' the patient's condition. The coroner issued a **Prevention of Future Deaths** report, yet subsequent deaths have since occurred under similar circumstances.

The standard battery of NHS blood tests returns mostly normal results, reinforcing the patient's GP's typical disbelieving attitude (Hng et al. 2021). Relevant testing is available to hospital consultants.

A patient with moderate to severe ME underwent an extensive battery of tests at leading UK laboratories, prompted by her involvement in a High Court case related to ME. The results were both revealing and alarming. While a wide range of variability exists—as with any disease—a highly experienced consultant noted that these findings likely represent other patients with moderate to severe ME. *However, advanced diagnostic testing must become widely accessible to replicate these findings.*

SUMMARY OF THE TEST RESULTS FROM A FEMALE WITH MODERATE TO SEVERE ME

The test results demonstrate that this patient has severe multisystem involvement with overlapping immune, neurological, endocrine, metabolic, gastrointestinal, and cardiovascular abnormalities. The presentation includes chronic infection, autoimmunity, mitochondrial dysfunction, and profound dysregulation of core metabolic cycles. Findings of biochemical deficits paint a picture of a patient with extensive multisystem failure and complex biochemical abnormalities, typically found in ME.

LIFE-THREATENING OR CRITICAL DYSFUNCTIONS

◆ Glutamate Toxicity (Neuro-metabolic Crisis)

Excessive glutamate → neuroinflammation, seizures, risk of stroke.

Low GABA → anxiety, insomnia, spasms, pain, gut dysmotility. **Blocks glycolysis**, triggers **gluconeogenesis**, breaks down tissue proteins.

Glucose toxicity and **hypoglycemia** → worsens glutamate accumulation. Depletes glutathione, increases oxidative stress and eosinophils.

◆ **Urea Cycle Dysfunction with Ammonia Toxicity**
Very low urea and **citrulline** and **ammonia accumulation** → neurotoxicity, risk of **autoimmune encephalitis**. Ammonia → Nitric Oxide → peroxynitrite → mitochondrial and cellular damage. This constellation of metabolic abnormalities—**urea cycle impairment, hyperammonemia, peroxynitrite formation**—is dangerous and could progress to **life-threatening encephalopathy** or **autoimmune brain injury**. It requires urgent **specialist-level medical intervention**.

◆ **Autoantibodies affecting CNS integrity and neurotransmission** → very serious and potentially life-threatening, depending on severity and progression, and systemic inflammation.

◆ **Severe Adrenal Insufficiency** → **Progressing toward Addison's disease**. Contributes to **labile BP swings (84/48 to 250/140)**, fatigue, and stress intolerance.

◆ Profound Immune Collapse

Extremely low NK cells, elevated T-helper cells (CD4), and **greatly reduced T-suppressor cells (CD8)**. **Grossly abnormal mast cells (MCAS)**. **IgG3 deficiency** → impaired immune complex clearance. **High histidine** → **high histamine** → MCAS, anaphylaxis risk. **Auto-immune** state resembling **SLE**. **Autoantibodies to reticulin** → gut and liver autoimmune issues.

◆ Chronic Enteroviral Infection (Coxsackie B)

Persistent viremia detected in blood. Triggers **autoimmunity, myocarditis risk**, and systemic **inflammation**.

◆ Liver Dysfunction

Enlarged liver, poor detoxification. **Impairs amino acid metabolism**, carnitine synthesis, and immune regulation.

◆ Pancreatic Insufficiency (19% function)

Leads to **malabsorption, malnutrition**, and metabolic collapse. Tied to **glucose instability** and energy failure.

◆ **Severe Mitochondrial Dysfunction/Energy Collapse**
Low ATP from both glycolysis and gluconeogenesis. Blocked **methionine and urea cycles**, excess metabolic waste. **Carnitine deficiency** due to blocked methionine/lysine reactions. Profound fatigue, breathlessness, muscle pain, and prolonged recovery. Carnitine loss → frequent urination (32 times per day), pulmonary strain, vision loss.

SEVERE SYSTEMIC FAILURES

◆ Vitamin B12 and D deficiencies

Critically low **vitamin D** due to a **non-functioning vitamin D receptor**. **Low B12** → impaired methylation, detox, red blood cell formation. Leads to **neuropathy, neuroinflammation, immune dysregulation**.

◆ B6 Deficiency

Affects neurotransmitter synthesis, immune function, and detox. Linked to **high aminoisobutyric acids**, poor antioxidant status.

◆ Endocrine Failure

Low T3 and T4 → **cellular hypothyroidism**. Loss of T4 → T3 conversion → tissue-level dysfunction, blood pressure instability.

◆ Structural Protein & Collagen Failure

Low proline, high hydroxylysine → tissue breakdown. **Impaired collagen synthesis** → weak connective tissue, vascular fragility, and joint pain. Indicates chronic infection and organ structure degradation. Disrupted neurotransmitter, immune, and detoxification pathways.

◆ Metabolic Pathway Collapse

Profound dysfunction in methionine, urea, and glutamate cycles; multiple amino acid imbalances (e.g., **high methionine, valine, histidine; low asparagine, citrulline**) → further disrupted neurotransmitter, immune, and detoxification pathways.