

Myalgic Encephalomyelitis (ME/CFS) Table of Biological Abnormalities, Clinical/Lab Tests and Drugs with Potential for Repurposing

* *A PATIENT-DRIVEN EFFORT* * *A WORK-IN-PROGRESS* *

FDA has determined that ME and CFS is a serious disease or set of diseases for which there are no approved drug treatments. The following table, compiled by patients, lists the clinical abnormalities found in ME/CFS patients, examples of clinical abnormalities (symptoms and abnormal test results) that an ME/CFS patient might experience, examples of the clinical/lab tests that patients have had to confirm the abnormalities (i.e. potential diagnostic biomarkers), and examples of the kinds of drugs that patients have been prescribed off-label by doctors or used in clinical trials for ME/CFS, and thus have potential for repurposing for ME/CFS patients.

BIOLOGICAL ABNORMALITIES¹	EXAMPLES²	CLINICAL/LAB TESTS³	DRUGS WITH POTENTIAL FOR REPURPOSING⁴
Neurological and cognitive impairment	Memory loss, processing speed, hyperacusis, vertigo, vestibular injuries, seizures, ataxia, expressive dysphasia, dyslexia, absence seizures, disorientation, visual disturbances (photophobia, diplopia, blurred vision), auditory processing dysfunction, tinnitus, parathesias, cranial nerve & sensory neuropathies, chronic cerebrospinal venous insufficiency	Spect scans, fMRI, Romberg test, CANTAB and other neurocognitive tests, Computerized Dynamic Posturography, qEEG, neurotransmitter levels	Deplin, Cerefolin-NAC, Cognex, anti-seizure medication, Adderall, Lamictal, selegiline, Neurontin, Snemet, Ceftriaxone IV, Ketamine IV, Cialis, Provigil, Aricept, piracetam, Klonopin
Autoimmunity	Autoreactive T and B cells, hyperactive B cells.	ANA, ACA, DS-DNA, cytokine profiles (inflammatory, anti-inflammatory), antibodies to retroviral Env & Gag proteins, B cell cytokine (IL7), CD20, flow cytometric immune profiles	Rituxan, Methotrexate, Alemtuzumab, ATGAM, Enbrel, Humira, Kineret, IVIG (gamma globulin)

BIOLOGICAL ABNORMALITIES¹	EXAMPLES²	CLINICAL/LAB TESTS³	DRUGS WITH POTENTIAL FOR REPURPOSING⁴
Immune dysfunction /deficiencies	Leukocyte deficiencies (NK cells, B cells, T cells, monocyte compartments), immunoglobulin subclass deficiencies, innate and adaptive immune disorders, Common variable immunodeficiency	MMP-9, C3a, C4a, TGF β 1, TNF α , IgA, IgG and IgM levels, IgA and IgG, CD56, CD57, ImmuKnow [®] , monocyte elastase, RNaseL, PKR, IFN α , Ig subclasses, NK cell function/lymphocyte enumeration, pre and post vaccination titers	Immune modulators including: GcMAF ⁵ , Enbrel, IVIG (gamma globulin), Alpha-1 antiprotinease, low dose naltrexone, Nexavir, Hepapressin ⁵ Isoprinosine, Equibrant ⁵ , IVIG
Chronic infections	<u>Viral</u> - EBV, CMV, HHV6A, shingles, enteroviruses, coxsackie B, parvovirus B19	IgG, IgM, viral titres and antibodies, cytokine profiles, enterovirus panels	Acyclovir, Valgancyclovir, Amantadine, Valacyclovir, Famvir, Cidofovir, Viread, Nexavir, Foscarnet, artemisinin, Interferon beta, Ampligen ⁶ , RAP-101 (formerly Peptide T) ⁶
	<u>Microbial and parasitic</u> - Borrelia (Lyme), Bartonella, Babesia, mycoplasma pneumonia, chlamydia pneumonia, Giardia	Microbial testing, cytokine profiles (e.g. IL8, TNF α , TGF β 1)	Various antibiotics, antimycotics, Bicillin, Ceftriaxone IV, Rifampin
	<u>Fungal</u> - Candida, mold	TGF β 1, MSH, MMP-9, C3a, C4a, vasoactive intestinal peptide (VIP), Leptin, VEGF	Diflucan, Nystatin, VIP, Cholestyramine, AmBisome
Autonomic dysfunction	Postural orthostatic tachycardia (POTS), neurally mediated hypotension (NMH), orthostatic intolerance (OI), loss of muscle tone	MSRI, echocardiogram, cerebral blood flow, heart rate, BP, tilt table	Florinef, Atenolol, Viagra, midodrine, saline ⁵
Sleep abnormalities	Primary and secondary insomnia, non-restorative sleep with alpha wave intrusion, lack stage-4 sleep	Polysomnogram	Xyrem, Suramin, Suvorexant ⁶ , Ambien, Oxytocin, Klonopin, Doxepin, Remerone, Trazadone
Energy production impairment, Post-exertional malaise (PEM) ⁷	Mitochondrial abnormalities, oxidative stress, exercise intolerance, abnormal anaerobic threshold, VO2max worse day 2	Muscle biopsy, mitochondrial function profile, cardiopulmonary exercise test with blood gases, Fitbit	Dichloroacetate (DCA) ⁶
Cardiovascular	Chronic venous insufficiency, hypercoagulation	CSSVI	Plavix

BIOLOGICAL ABNORMALITIES¹	EXAMPLES²	CLINICAL/LAB TESTS³	DRUGS WITH POTENTIAL FOR REPURPOSING⁴
Pain, peripheral neuropathy, vasculopathies, channelopathies	Joint and muscle pain, migraines, headaches behind eyes, numb hands/feet		Lyrica, Clonidine, Depakote, Aricept, prilocaine, lidocaine
GI abnormalities and infections	chronic diarrhea, constipation, SIBO (small intestinal bacterial overgrowth), leaky gut syndrome	LPS in blood, microbiome analysis/CDSA, secretory IgA, Lactulose Breath Test	Xifaxan, Flagyl, pre/probiotic treatment ⁵ , fecal microbiome transplant (FMT) ⁵
Hormonal abnormalities	Cortisol, progesterone, estrogen, testosterone, vitamin D, adrenalin, vasopressin, polyuria	Standard hormonal testing, urinalysis, fluid deprivation test, urine osmolality, serum anti diuretic hormone (ADH)	Cortisol, progesterone, estrogen, testosterone, DHEA, pregnenolone, human growth hormone, Metformin, Desmopressin
Epigenetic abnormalities	Methylation cycle defects		Deplin, Decitabine, hydroxocobalamin, methylcobalamin
Examples of Comorbidities, related tests and related treatments			
Fibromyalgia, chronic sinusitis, chronic allergies, interstitial cystitis, multiple chemical sensitivities, hypothyroidism Hashimoto's thyroiditis, carpal tunnel, Raynaud's, IBS, diabetes insipidus	Inflammatory cytokines (e.g. IL1 β , IL6, IL8), MIP1a/b, MCP1, MMP-9, C3a, C4a, TGF β 1, CD47, cystoscopy		Synthroid, Cytomel, Low dose naltrexone, Isoprinosine, Anatabloc, Lenalidomide, Ketotifen, Amantadine, antifungals, Nexavir, Hydroxyzine, antihistamines, Elmiron

DRAFT DOCUMENT -- This table is a patient-driven effort to show what tests and drugs they have been prescribed. It is a work-in-progress and should be viewed as a preliminary draft that will continue to be refined with additional input. It will be aligned with the clinical guidelines published by experts in the field (below). We are eager for feedback, suggestions and corrections from researchers, clinicians and patients. Please email MECFSACTION@YAHOO.COM using a subject line of "Biological abnormalities".

GUIDELINES -- For a drug to be included on this table, it must meet the following criteria:

- 1. Drugs: ME/CFS patients must have used the drugs listed to treat their ME/CFS. The drug was either prescribed off-label by their doctor or taken in the context of a ME/CFS drug trial. The drug is classified in RXlist.com as a drug. Currently the table uses a mix of brand names and generic names.*
- 2. Non-drug treatments: This list includes a few selected supplements, non-drug treatments or CAM (Complimentary and Alternative Medicine) that are widely used by this patient population. It is not intended to be an exhaustive list.*
- 3. Comorbidities: The most common comorbidities experienced by ME/CFS patients are listed at the end of the table.*

For Additional Information

Additional information on ME/CFS, its biological abnormalities, along with the tests and drugs used to diagnose and treat the disease, can be found in the following sources:

ME/CFS Case Definitions:

Canadian Consensus Criteria: <http://www.cfids-cab.org/MESA/ccpccd.pdf>

ME International Consensus Criteria: <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2011.02428.x/full>

Primers for Medical Practitioners:

IACFS/ME Primer for clinical practitioners: <http://guideline.gov/content.aspx?id=38316>

ME-ICC Primer for Medical Practitioners: http://www.hetalternatief.org/ICC_primer_2012.pdf

The most current version of this table can be found at: <http://bit.ly/15op5sE>

Footnotes:

¹ Biological Abnormalities: Biological and clinical abnormalities associated with ME/CFS.

² Examples: Examples of the clinical abnormalities (symptoms and abnormal test results) an ME/CFS patient might experience.

³ Clinical/Lab Tests: Used by some clinicians to assist diagnosis, and also to recommend and monitor treatments. Potential diagnostic biomarkers.

⁴ Drugs with Potential for Repurposing: These are prescription drugs that have been prescribed off-label by doctors to treat ME/CFS patients and are potential candidates for repurposing. These are examples only and not an exhaustive list.

⁵ Complementary or alternative medicine, supplements or non-drug therapies. Only a few are listed. See the Primers listed above for more information.

⁶ In development, studies in clinicaltrial.gov

⁷ PEM is also called Post-exertional neuroimmune exhaustion (PENE)