ME/CFS Treatment Resource Guide for Practitioners

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DISCLAIMER: The information contained in this document is meant for informational purposes only. The management of ME/CFS in any given patient must be approached on an individual basis using an Infectious Diseases' specialist's best judgment. This document is a culmination of over 20 years of ME/CFS practice and peer reviewed articles. This document is not a peer reviewed publication.

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Diagnostic Methodology

- **Initial patient visit:**

  Complete history, physical examination, chest X-ray, electrocardiogram, complete blood count, urinalysis, serum aspartate and aminotransferases (AST, ALT), glucose, thyroid stimulating hormone, sodium, potassium, uric acid, alkaline phosphatase and creatinine measurements performed.

- **ME/CFS analysis:**

  Energy Index Point Score® assessing physical functional capacity in activities of daily life documenting limitations. The EIPS® system defines the severity of patient fatigue, 0-10, through measurement of real-life situations including one's ability to sit, stand, be out of bed, work, perform housework, socialize, exercise. The EIPS® level is determined through discussion between the physician and patient. A change in EIPS® level of one is a significant change in health and lifestyle for the patient, as ME/CFS symptoms decrease when the EIPS® increases.

- **Cardiac testing:**
  - 24-hour Holter monitor - symptoms recorded (syncope, chest pain, palpitations, muscle aches)
  - Standard 12-lead resting electrocardiogram – if original ECG abnormal
  - Rest/stress myocardial perfusion study – if original ECG abnormal
  - Multigated (radionuclide) MUGA rest/stress ventriculographic examination – if original ECG abnormal
  - Monitor Blood Pressure (laying, sitting, standing)
  - Monitor Heart Rate (laying, sitting, standing)

Diagnostic Methodology Continued

- **Viral testing for EBV, HCMV, HHV6:**
  - EBV serum IgM viral capsid antibodies (VCA) - Diasorin, Inc., Stillwater, MN
  - EBV early antigen diffuse (EA) - Diasorin, Inc., Stillwater, MN
  - ELISA HCMV(V) IgG and IgM serum antibodies to viral capsid, strain 169 HCMV - Diasorin, Inc., Stillwater, MN
  - HHV6 IgM and IgG serum - Lab Corp, Dublin, OH

- **Co-infection testing:**
  - Western blot and ELISA to Borrelia burgdorferi (IgM and IgG) - Lab Corp, Dublin, OH
  - IgM and IgG of Babesia microti - Lab Corp, Dublin, OH
  - IgM and IgG of Anaplasma phagocytophila - Lab Corp, Dublin, OH
  - IgM and IgG of Mycoplasma pneumoniae - Lab Corp, Dublin, OH
  - Anti-streptolysin O (ASO) titer ≥400 units - Lab Corp, Dublin, OH

Note Lyme and Lyme co-infections can be elusive. Lyme disease can present clinically as ME/CFS. A significant portion of Lyme disease cases have negative Lyme serologic tests. We prefer Lab Corp for Lyme testing and use all 4 tests. The antigens used are those used by the CDC. An appropriate rural exposure, a tick bite, a bull's eye rash, can all add to the likelihood of Lyme disease. Due to the need for both clinical and diagnostic evaluation in Lyme disease, it is recommended to consider an Equivocal (not negative or positive) lab result, as positive and begin Lyme treatment.

Diagnostic Methodology Continued

- **Follow-up:**
  - Every 4-6 weeks - Complete blood counts, sodium, potassium, AST, ALT, alkaline phosphatase, creatinine and urinalysis.
  - Every 3 months – Serum assays for EBV VCA IgM, EBV EA, HCMV(V) IgM and IgG, HHV6 IgM and IgG and all co-infections which are positive originally

EIPS® - A Functional Capacity Measurement Tool For Chronic Fatigue Syndrome (CFS) Patients

- **To Physicians Caring for Patients with CFS**

  The Energy Index Point Score (EIPS) chart provides the severity of patient fatigue. A change in EIPS level of one is a large significant change. The EIPS level is determined by agreement of physician and patient with the EIPS chart easily available for viewing at out-patient visits. As the EIPS level increases, CFS symptoms lessen and disappear.

- How to use the EIPS system in four easy steps:
  1) Post the EIPS chart in examining room
  2) Ask patient to evaluate their level of activity based upon the prior two weeks
  3) Question the patient's EIPS evaluation
  4) Record and track the EIPS level. Report every 6-12 weeks.*

  * The EIPS is not assessed if the patient has an intercurrent infection (respiratory, gastroenteral, ...). At the same visit the following 4 symptoms are regularly categorized: 1) chest pain 2) palpitations 3) muscle aches 4) lightheadedness - noting whether absent or present. If present, when (beginning or end of day, how frequent), where, severity, etc. All of these factors are included in the EIPS assessment.

Energy Index Point Score®
Functional Capacity Criteria

0	Bed-ridden, up to bathroom only
1	30 minutes – 1 hour daily out-of-bed (sitting in chair, is out of bed)
2	Out of bed – over 30 min. to 2 hrs/day
3	Out of bed – 2 – 4 hrs/day
4	Out of bed – 4 – 6 hrs/day
5	Can work at sedentary job, 40 hrs/week with difficulty

Recovery

6	Daily naps in bed, may maintain a 40 hr. sedentary work week plus light, limited housekeeping and/or social activities
7	No naps in bed. Up 7:00 a.m. to 9:00 p.m. Able to work a sedentary job plus light housekeeping.
8	No naps. Able to manage full work (sedentary) plus manage a household.
9	May exercise at approximately 1/2 - 2/3 normal without excessive fatigue.
10	Normal

Reference: In Vivo 2008:22; 799-802

Antiviral Treatment of EBV

- **General Information**

  A diagnosis of Epstein-Barr virus(EBV) infection is made with a positive EBV EA antibody diffuse and/or a positive VCA IgM antibody.

- **Treatment**

  Valacyclovir (Valtrex) is remarkably effective and safe. The one concern is that valacyclovir is excreted by the glomerulus and secreted by the tubules and can cause acyclovir stones and obstructive uropathy. This will not occur if the patient drinks at least six 8-ounce glasses of water daily. Occasionally diarrhea may be caused by the valacyclovir. If the patient weighs 70 kg, the dosage is 1 gram four times daily, ideally every six hours; however safe to take four hours after the last dosage (it is not necessary to awake in the middle of the night for a dose). It is important that the patient take four doses for treatment. A higher dose of Valtrex may be necessary with patients who weigh more than 175 pounds and this must be done carefully. A patient who weighs more than 175 pounds may require 1.5 grams of Valtrex, valacyclovir four times daily. Please note valacyclovir is now available in generic form. While I have not had experience with all distributors of generic forms yet, I have had patients move to the generic form of valacyclovir by Teva and Mylan with no issue.

  Famvir at the same dosage can be substituted and although there is not the strong evidence that we have for valacyclovir, it likely is equally effective. One does not have the worries concerning renal calculi with Famvir and it has also been extraordinarily safe. It does not cause diarrhea.

Antiviral Treatment of EBV Continued

An initial worsening of symptoms with normal laboratory at a two-week special visit with worsening symptoms is a Jarisch Herxheimer reaction and predicts a good response. Initial benefit is usually not noted for the first six weeks' of therapy and then occurs thereafter. A minimum period of therapy is one year. Usually benefit is not opparent until after 3.5 months of therapy.

We have not seen thrombocytopenia with Valtrex, valacyclovir. However, an elevated mean corpuscular volume is seen. This is not a toxicity, and does not require one to stop medicines.

Antiviral Treatment of HCMV & HHV6

- **General Information**

  A diagnosis of cytomegalovirus(CMV) infection is made with an elevated CMV IgG titer. The IgM titer for CMV is inaccurate and insensitive. The higher the CMV IgG titer, the greater the viral load. Human herpes virus 6 infection is made with an elevated titer at least twice normal. The diagnosis of EBV, CMV, or HHV6 ME/CFS meets the Canadian consensus and Fukuda CFS criteria.

- **Treatment**

  The usual treatment for either/both is valganciclovir (Valcyte) one 450-mg capsule daily for three days, followed by two 450-mg capsules in the morning daily. Liver function tests are studied very carefully. If there is any abnormality, one alters the dosage. Given the patient's ability to safely tolerate two 450-mg capsules, dosing can be increased to two, 450-mg capsules in the morning and a one additional 450-mg capsule twelve hours later. Liver function tests, again, must be studied carefully and frequently.

  Both valacyclovir and valganciclovir are absorbed with a 20% increment if there is food in the stomach. The most common side effect of valganciclovir is hepatotoxicity. If this occurs, the drug is stopped, the dosage is decreased, and is again restarted. When monitoring reveals AST and ALT are normal, the monitoring can continue every four to six weeks, but more frequent with hepatotoxicity. The rule is no valganciclovir at all if there is any abnormality in liver function.

Antiviral Treatment of HCMV & HHV6

Continued

The duration of valganciclovir and therapy for CMV and/or HHV6 is aimed at one year to start with no improvement expected for the first four to six months. It is a general rule that the shorter the duration of ME/CFS, and the earlier appropriate therapy is started, the earlier recovery will occur. Recovery is a continuing, gradual process.

We have not seen thrombocytopenia with Valcyte, valganciclovir. An elevated mean corpuscular volume is seen. This is not a toxicity to stop medicines.

Antibiotic Treatment of Co-infections

- **Background**

  If the diagnosis of ME/CFS is made by the accepted criteria and there is no coinfection, one begins antiviral therapy promptly. However, if there is coinfection with a diagnosis of Lyme disease, Babesiosis, Ehrlichiosis, Mycoplasma pneumoniae, or adult rheumatic fever, these conditions are addressed first. After these conditions are addressed, ME/CFS is treated with antiviral therapy. Should one or more of these co-infections occur mid- antiviral treatment, do not stop but treat in parallel.

- **Treatment of Lyme Disease**

  The protocol for Lyme disease, serologically positive or epidemiologically positive and serologically negative, that I use is a six-week's course of intravenous therapy. Ceftriaxone is preferred. If there is a history of allergy to penicillins and it is not an immediate allergy, I routinely refer the patient to an allergist for cephalosporin testing. Under ordinary circumstances if this is negative, ceftriaxone is given; depending on the size of the individual 1-1.5 grams intravenously every 12 hours. The patient is seen weekly. They are asked not to travel further than 45 minutes from this office, because a PICC lines has been placed and infection of the PICC line site or side effects to the cephalosporin can occur; particularly biliary dyskinesia or abnormal liver function tests with ceftriaxone. Cefotaxime may be substituted for ceftriaxone in the case of biliary dyskinesia. If there is biliary dyskinesia, Unasyn, or ertapenem may be used. If diagnosis of Lyme occurs after antiviral treatment has commenced, and patient shows liver sensitivities with Valcyte dosing, Unasyn is recommended. Unasyn is given 2 grams IV piggyback every 12 hours. Ertapenem is given 2 grams IV piggyback every 24 hours. The same dosage of cefotaxime (as ceftriaxone) of 1-1.5 grams is used, but the administration of cefotaxime IV is every 8 hours, rather than every 12 hours, for ceftriaxone. Cefotaxime has no hepatotoxicity. Cefotaxime is excreted by the kidneys.

Antibiotic Treatment of Co-infections

Continued

The goal of Lyme therapy, of course, is a well patient, but particularly a negative serology. Oral suppressive therapy is continued for at least three months or until the Lyme serology is negative. Typical medicines used for Lyme suppression after the original six weeks are amoxicillin; in a 70-kg individual 750 mg before every meal and at bedtime. Doxycycline 100-150 mg twice daily after meals and with a full glass of water may be given in the place of amoxicillin for suppression.

- **Treatment of Mycoplasma Pneumonia**

  We use LabCorp less than 300 as a normal level. The patient is not considered to have persistent Mycoplasma pneumoniae infection unless the initial titer is 600 or more. Mycoplasma pneumoniae is treated intravenously with doxycycline 150 mg IV piggyback for six weeks followed by oral suppression with doxycycline 100-150 mg twice daily or moxifloxacin 400 mg once daily for three months. The goal of this therapy is a serum level which is less than twice the normal. The duration of time again is six weeks intravenously plus a minimum of three months oral suppression.

- **Treatment of Adult Rheumatic Fever**

  The diagnosis of adult rheumatic fever is made with an ASO titer of over 400. Echocardiograms are done in all patients with ME/CFS originally and any changes in the mitral valve, either thickening or mitral valve prolapse are additional supports for the diagnosis of adult rheumatic fever. A patient who meets the criteria for ME/CFS with an ASO titer of 400 or more is considered to have adult rheumatic fever and treated accordingly.

Antibiotic Treatment of Co-infections

Continued

Chest pain, joint pain, rash, life-altering fatigue are all common to ME/CFS and adult rheumatic fever. Patients are diagnosed with adult rheumatic fever with the following criteria:

(1) EIPS <5

(2) Diffuse, multi-joint pain

(3) Antistreptolysin O titer ≥ 400 (critical to diagnosis)

(4) Abnormal 24 hour Holter monitor with tachycardia and oscillating T-wave flattening, with or without T-wave inversions

(5) A thickened mitral valve at echocardiogram.

If there are symptoms of sinus disease, a CT of the sinuses is done to make certain there is no obstructive sinusitis which may need sinus surgery.

Patients are treated with intravenous Unasyn 3grams IV piggyback every 12 hours for 4-6 weeks, followed by 2.4 million units IM (1.2 million units each hip every 30 days) until ASO titer is ≤200.

Patient Management

- **Patient Visits and Testing**

  Check-ups with labwork should occur every 6 weeks in-person.

- **Diet and Exercise**

  A healthy, well balanced diet is a must. Minimize sugar intake. Minimize caffeine intake. Absolutely no alcohol allowed, as it may be a cardiac toxin for ME/CFS patients.

  No physical exertion or exercise until above a 7 Energy Index Point Score. Stretching regularly is recommended. Once the EIPS is 7, modest exercise can and should begin. The ultimate test is - Are you tired the next day after exercise? If you are, then the exercise that you have done is too much. Start out very slow. Just a few minutes, allowing for breaks and recovery time.

- **Lifestyle**

  10-12+ hours of sleep per day and daily naps until the EIPS is at least a 6. Avoid germs (think airplanes, libraries, churches). Stretch daily, minimize exertion, seek assistance with housework/chores/errands. Keep feet elevated, promote a network for assistance and ask for help. Daily energy envelope management is a must. Do not push until a crash. This is not productive. As much as possible, do not allow yourself to get overly tired. Healing is a slow process.

Publication Resources

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Publication Resources

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Patent Information

- A US patent (CFS LLC and The Ohio State University) is underway to be filed, February 2012, describing serum antibody to molecular markers EBV EA(D), EBV dUTPase and EBV DNA polymerase for diagnoses of EBV subset ME/CFS.

- CFS LLC has a US patent application pending entitled Methods for Diagnosis and Treatment of Chronic Fatigue Syndrome. Inventor Lerner, Albert Martin. Agents Barry, Thomas F. et al: Venable LLP, P.O. Box 3485 Washington, DC 20043-9998 (US). This patent differentiates Group A and Group B CFS.

- Further information concerning patents owned by CFS LLC can be found in US Pat Nos 5,872,123; 6,258,818; 6,399,622; 6,537,997 and 6,894,056.