Chronic Infectious Mononucleosis/EBV Management

Hypothesis

Continuous or intermittent Epstein-Barr virus (EBV) replication after primary EBV infection causes tissue damage resulting in a myriad of symptoms. Valacyclovir has been shown both in vitro and in vivo to reduce EBV replication [1, 2]. Reducing EBV replication by taking valacyclovir will reduce or eliminate symptoms of chronic infectious mononucleosis. In addition, a diet and the use of herbal therapies may enhance the immune system's ability to fight off EBV.

Definition of Chronic Infectious Mononucleosis/EBV

Patients have a severe case of acute infectious mononucleosis (Mono) due to a primary EBV infection. Then, there are 2 clinical patterns in patients who have responded to valacyclovir.

Pattern 1. Continuous illness for weeks, months or years after onset.

Pattern 2. Recovery from the acute illness but lingering or recurring symptoms for years.
### Symptoms

**Acute Mono.** These are listed in Table 1, which is based on prospective studies of University of Minnesota undergraduate students and a review of the literature [3].

| TABLE 1. Prevalence of signs, symptoms, and laboratory abnormalities in infectious mononucleosis
<table>
<thead>
<tr>
<th>Finding</th>
<th>Prevalence (%)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Signs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>100</td>
<td>Occasionally seen without sore throat</td>
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<tr>
<td>Cervical lymphadenopathy</td>
<td>95</td>
<td>Especially posterior cervical and postauricular</td>
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<tr>
<td>Fever</td>
<td>50</td>
<td>Often masked by antipyretics</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>25</td>
<td>Unusual in other acute illnesses</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>33</td>
<td>Unusual in other acute illnesses</td>
</tr>
<tr>
<td>Eyelid edema</td>
<td>10</td>
<td>Unusual in other acute illnesses</td>
</tr>
<tr>
<td>Rash</td>
<td>5</td>
<td>Virtually all patients given penicillin derivatives develop a rash</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sore throat</td>
<td>95</td>
<td>Many patients describe this as the “worst” they have ever had</td>
</tr>
<tr>
<td>Fatigue</td>
<td>90</td>
<td>Usually the last symptom to resolve</td>
</tr>
<tr>
<td>Headache</td>
<td>75</td>
<td>Common but underappreciated</td>
</tr>
<tr>
<td>Fever</td>
<td>70</td>
<td>Patients describe this as “like the flu”</td>
</tr>
<tr>
<td>Body aches</td>
<td>50</td>
<td>Due to mesenteric adenitis or hepatosplenomegaly</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td><strong>Laboratory abnormalities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>80</td>
<td>Five to 10% of patients are jaundiced</td>
</tr>
<tr>
<td>elevation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocystosis</td>
<td>40</td>
<td>Usually due to increase in CD8 cytotoxic lymphocytes</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>25</td>
<td>Thought to be autoimmune</td>
</tr>
<tr>
<td>Anemia</td>
<td>10</td>
<td>Thought to be autoimmune</td>
</tr>
</tbody>
</table>

* Based on a compilation of published series (54, 67, 84, 130, 167) and 116 subjects followed in natural history and treatment trials at the University of Minnesota (14–16).

* The median duration of illness is 16 days, and the mean duration is 19 days.
**Chronic Mono.** Table 2 is based on our experience and the information provided by many persons who contacted us in response to Jaye Watson's news story on 11alive Atlanta December 13, 2016 [4]. Here is a list of the more common symptoms.

Table 2. Clinical Abnormalities in Chronic Infectious Mononucleosis

<table>
<thead>
<tr>
<th>Finding</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>The most common symptom</td>
</tr>
<tr>
<td>Excessive sleepiness (Hypersomnia)</td>
<td></td>
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<tr>
<td>Weakness</td>
<td></td>
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<tr>
<td>Increased susceptibility to acute infections, especially sinusitis and</td>
<td>&quot;I get a cold from everyone who has one&quot;</td>
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<tr>
<td>tonsillitis</td>
<td></td>
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<td>Joint pain sometimes with redness and swelling</td>
<td></td>
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<tr>
<td>Allergies, especially to foods</td>
<td></td>
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<tr>
<td>Dizziness (Vertigo)</td>
<td></td>
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<tr>
<td>Swollen and often tender neck glands</td>
<td>Seen more often in Pattern 1 chronic mono</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
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<tr>
<td>Thyroid disorders</td>
<td></td>
</tr>
<tr>
<td>Abnormal sensations in hands and feet</td>
<td></td>
</tr>
<tr>
<td>Foggy thinking (Decreased cognition)</td>
<td>Affects school and work performance</td>
</tr>
</tbody>
</table>

**Laboratory Data**

Patients do not usually have EBV in the blood as measured by polymerase chain reaction (PCR).

The EBV-specific antibodies I pay attention to are called VCA IgM, VCA IgG, and EBNA-1 IgG. VCA stands for viral capsid antigen. EBNA stands for EBV nuclear antigen.

Patients with persistent acute Mono who respond to valacyclovir and the diet have positive VCA IgM, positive VCA IgG, and negative or low levels of EBNA-1 IgG.

Patients with chronic Mono who respond valacyclovir and the diet have negative VCA IgM, very high positive VCA IgG, and positive levels of EBNA-1 IgG but they usually are not as elevated as the VCA IgG levels.

I am not giving antibody indices or titers here because there are several testing platforms with different reference ranges.

**Antiviral Treatment**

Please note that not everyone will respond. Those who respond generally feel better by the first or second week of treatment and continue to improve. They may relapse if treatment is discontinued. There have been essentially 3 types of responses: a good response for several weeks but then relapse (most common); sustained response; no response.
**Persistent Acute Mono Pattern.** I have used valacyclovir, 1 gram 3 times daily, for at least a month. Some patients require 1 gram 4 times daily.

**Chronic Mono Pattern.** I have used valacyclovir, 1 gram 3 times daily, for 2 months or longer. Some patients will relapse when it is discontinued, but may respond again to subsequent courses.

**Diet**

A number of folks who have contacted me have reported that a version of the MS diet has relieved their symptoms.

Key items to avoid: sugar, gluten, dairy products, eggs.

The basic daily diet is 9 cups of vegetables and fruit. Meat and fish are allowed.

**Daily - Eat 9 Cups Vegetables/Fruit**

from: Food for Thought: Creating Health using the Wahls Protocol. For more information, please visit Dr. Terry Wahls’ website. [http://www.terrywahls.com/](http://www.terrywahls.com/)
Herbal Therapies

Contributed by Laurie Radovsky, M.D.

Given the fact that some patients initially respond to valacyclovir and then relapse, it is possible that EBV has developed resistance to the antiviral.¹ Herbs contain multiple compounds so development of resistance to their antiviral activity is unlikely. Also, herbs have synergistic properties that potentiate the effects of antibiotics and herbs, sometimes by sophisticated methods such as counteracting efflux pumps of drug-resistant bacteria.² This protocol can be used on its own or in conjunction with a pharmaceutical antiviral (valacyclovir). Use these herbs for a maximum of 2 months.

The herbs used have multiple functions, but their main ones are:

**Antiviral: Artemisia³ and/or Usnea⁴ (preferably both)**

**Immune support: Reishi⁵,⁶**

**Adaptogen: Licorice⁷,⁸ OR Eleuthero⁹ (Siberian Ginseng)**

Unlike pharmaceutical antibiotics, the effective dose for herbal antivirals varies from person to person. Start at a low dose (lower range of dose once a day) for a few days and work up to the maximum dose tolerated or until you are seeing a change in your symptoms. Start each component separately in this order, at least 3 days apart. This will allow you to identify any side effects from each component. Work up to your maximum dose with each one before moving on to the next one. Most herbs can be used as tinctures (liquid extracts) or in capsules. Both are effective and the decision of which to use should be based on personal preference.

1. Immune support: Reishi

Indications: A mushroom which is antibacterial, antifungal, antineoplastic, hepatoprotective, cardiotonic; active against plasmodial parasites. Strongly antiviral, especially against hepatitis viruses, herpes viruses, HIV and EBV. Profoundly immunostimulating, especially to the spleen. Activates immune effector cells including T cells, macrophages, and NK cells and stimulates the production of cytokines. Reishi has been used in China and Japan for 4,000 years for treatment

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of debility after a prolonged illness. It is a mushroom that can be eaten whole, but can be used medicinally as a powder or tincture.

Dose adult:
Tablets/powder: start with 1 gram once a day and work up to 1 gram 3 times a day.
Tincture: start with 1 tsp. once a day and work up to 2-4 tsp. up to 3 times a day.
Dose pregnant: probably safe.
Side effects/cautions: do not use in cases of obstructed bile duct. Do not use if you are on immunosuppressive therapy for organ transplant. May potentiate the effects of blood thinners such as warfarin or aspirin. May occasionally cause skin rash, diarrhea, dry mouth, sleepiness, bloating, frequent urination, sweating, nausea. Nausea may decrease when it is taken with food.
Brands:
Herb Pharm Reishi tincture costs $15.99 for one ounce in a 1:4 ratio (larger sizes available as dose increases).
Host Defense Reishi 500mg capsules cost $29.99 for 60 capsules.

2. Antiviral: Usnea
Common names: this is a lichen genus with multiple species and many names such as old man’s beard.
Indications: Antibacterial, antifungal, antiviral, antiparasitic, anti-inflammatory, antioxidant, Immunostimulant, inhibitor of biofilm formation, antineoplastic. Has activity against EBV and HSV.
Dose adult: the components to treat systemic illness must be extracted in alcohol, so only tinctures are recommended. Take 30-60 drops up to 4 times a day.
Dose pregnant: should not be used internally during pregnancy.
Side effects/cautions: may cause contact dermatitis.
Brands:
Usnea Herb Pharm tincture in a 1:4 ratio. 1 ounce costs $12.99 (larger sizes available as dose increases).

2. Antiviral: Artemisia annua
Common names: sweet Annie, sweet wormwood
Indications: Antibacterial, antifungal, antiviral, antimalarial, anti-protozoal, anti-inflammatory, antitumor, immune modulator, antineoplastic. Has activity against EBV. Not all constituents are systemic, which is why in vitro studies are not necessarily applicable to living organisms
Dose adult: Start with a low dose to see how you respond to it and work up. Divide dose into twice or 3 times a day for 30-40 days only. (If it has not cleared up in that time, it is not likely to be effective.) Take 30 minutes before meals.
Tincture: up to 40 drops in 2 oz. of water or juice, two to four times per day.
Capsules: 500 mg. total per day divided into 2-3 doses.
Dose pregnant: contraindicated at least in the first trimester.
Dose child: Should be avoided by young children.
Side effects/cautions: Decreased appetite, nausea, diarrhea at higher doses. At high doses, liver enzymes need to be checked periodically. Long-term use can cause neurotoxicity. May reduce N-Acetyl cysteine, vitamin E and possibly other antioxidants, increasing risk of hearing or neuropathy.
Brands:
Artemisinin 100 mg. capsules by Allergy Research Group, $75 for 90 capsules. 
Herb Pharm (tincture). 1:5 ratio : $12.99 for one ounce. (larger sizes available as dose increases).

3. **Adaptogen: Licorice (if you hate the taste of licorice or have high blood pressure, use Eleuthero instead)**

Indications: Antibacterial, antiviral, anti-inflammatory, antioxidant, immunomodulant and immunostimulant, antineoplastic. Accelerates the healing of gastric ulcers. Potent synergist (enhances effectiveness of other herbs and pharmaceuticals); in fact, it is preferable not to use it alone. It is effective against efflux mechanism of Gram negative organisms. Has activity against EBV.

Dose adult:
Powdered root: 5-15 grams a day
Solid licorice extract: 1/8 tsp. a day.
Dose pregnant: contraindicated.
Dose child: children should not use more than 4-5 grams a day.

Side effects/cautions: may increase blood pressure; avoid in patients with hypertension. Patients with normal blood pressure should check it after a week to make sure it is not being elevated. Prolonged use at high doses can cause edema, weakness, and headaches; it raises sodium and decreases potassium levels; have labs checked monthly. Do not use for more than 2 months. Should not be used with thiazide diuretics, potassium-sparing diuretics, digoxin or amiloride. May potentiate the effects of steroids such as prednisone and hydrocortisone. Has estrogenic effects.

Brands:
Wise Woman Herbals solid licorice extract; 2 oz. is $16.
Frontier Herbs bulk organic licorice root is $28/pound.

3. **Eleuthero (Siberian ginseng)**

Indications: Adaptogen. Particularly helpful for stressed, overworked patients. Eleutherococcus stimulates immune function, decreases fatigue, reduces brain fog, and reduces depression. Supports adrenal and thyroid function.

Dose adult:
Tincture: Start with 1 tsp. once a day and work up to 1 tsp. 3 times a day. Can increase or decrease based on weight/condition. Put the entire day's dose in a thermos of tea or water, & sip on it throughout the day.
Capsules: Start with 500 mg. a day and work up to 1 capsule 3 times a day.
Dose pregnant: safe in pregnancy; use the same dose as adult.

Side effects/contraindications: It can lead to insomnia if taken too late in the day. Transient diarrhea. May increase blood pressure though usually only temporarily. Can be photosensitizing.

Brands:
Tincture: HerbPharm; Herbalist & Alchemist.
Capsules: Nature’s Way.
Follow-Up

If you choose to treat patients, please send me a follow-up report. That's only way we all can learn if this regimen is clinically valuable. Right now, in all honesty, it is anecdotal.

Who We Are

We are a research program only. We do not provide clinical care and we do not have a referral network.

A Word About EBV Vaccine

Our research focus is development of an EBV vaccine. The one we are working on is for prevention of EBV infection. We will be testing it first in subjects who have never been infected by EBV. Our hope is to start clinical trials in 2018.

References


The Mono Project Website
http://z.umn.edu/ebvdiseases

Link to our Research Fund at the University of Minnesota Foundation
http://z.umn.edu/epsteinbarr

Henry H. Balfour, Jr. M.D.
email: balfo001@umn.edu