# Review of the Glutathione Depletion—Methylation Cycle Block (GD-MCB) Hypothesis for CFS [1]

- 1. The person inherits a genetic predisposition (polymorphisms in several of certain genes) toward developing CFS. (This genetic factor is more important for the sporadic cases than for the cluster cases of CFS.)
- 2. The person then experiences some combination of a variety of possible stressors (physical, chemical, biological, psychological/emotional) that place demands on glutathione.
- 3. Glutathione levels drop, producing oxidative stress, removing protection from B12, allowing toxins to accumulate, and shifting the immune response to Th2.
- 4. Toxins react with B12, lowering the rate of formation of methylcobalamin.
- Lack of sufficient methylcobalamin inhibits methionine synthase, placing a partial block in the methylation cycle.
- 5. Sulfur metabolites drain through the transsulfuration pathway excessively, pass through sulfoxidation, and are excreted.
- 6. A vicious circle is established between the methylation cycle block and glutathione depletion, and the disorder becomes chronic.

Depletion of glutathione by Borrelia burgdorferi

- 1. Bb requires cysteine for its metabolism [2].
- 2. Cysteine diffuses passively into Bb from its host, i.e. there is no active transporter protein [2].
- 3. Bb uses cysteine in the synthesis of several of its essential enzymes: Osp A, Osp B, CoASH, a hemolysin, and others [2,3].
- 4. Bb does not use glutathione for its redox control. Instead, it uses reduced Coenzyme A (CoASH) [4].
- 5. Cysteine is the rate-limiting amino acid for the synthesis of glutathione in humans, so that depletion of cysteine will produce depletion of glutathione [5].
- 6. Bb lowers the cysteine and glutathione levels in its human host, and inhibits the activity of glutathione peroxidase [6].
- 7. Low glutathione and low activity of glutathione peroxidase allow a rise in hydrogen peroxide concentration and oxidative stress [7].
- 8. Elevation of hydrogen peroxide causes Bb to assume its cyst form [8], in which it is less vulnerable to antibiotics [9].

New hypothesis for a link between Lyme disease and chronic fatigue syndrome

- 1. Borrelia burgdorferi (Bb) deplete glutathione in the host.
- 2. For a person who is genetically susceptible to developing CFS, this provides a link to the GD-MCB hypothesis for CFS and is one of the possible routes into this disorder.

- 3. If Bb and its biotoxin were not eliminated, Lyme disease and CFS would coexist in the host, and this would constitute “chronic Lyme disease.”
- 4. If Bb and its biotoxin [10] were eliminated, but the methylation cycle block continued, the person would continue to be ill with CFS. This would constitute “post-Lyme disease syndrome,” which would be analogous to the other post-infective fatigue syndromes [11].
- 5. If Bb and its biotoxin were eliminated, and the methylation cycle block was lifted, I believe it is likely that the person would become well.

In addition,

- 6. Perhaps the Borrelia burgdorferi toxin is one of the toxins that will react with vitamin B12. Mold toxins have been implicated in such reactions, but no data were cited [12,13].

References


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