

Testimony

Joseph D. Landson

Note: Since I have testified previously, I have provided space for Dr. Thal of the CDOA.

Members of the committee, patients, caregivers, greetings. My name is Dr. Thal; I'm the public affairs director for the Cave Doctors of America (CDOA), an affiliate of International Cave Doctors (ICD), the oldest medical association on the planet. Thank you for this opportunity to address two points: namely, societal views on cave doctors and the medical community's views on ME/CFS.

In his testimony some months ago, a Mr. Landson opined that ME/CFS patients need a diagnostic test, and I quote, "so easy a cave-doctor can do it." Plus his use of the large duck, suggesting we are all quacks. Ha, ha, very funny.

Like so much other tiresome, uniformed commentary, the testimony of Mr. Landson ignores the clinical and research contributions of CDOA membership. For example, medical professionals everywhere are switching back to tablets, such as the iPad, for records access. Cave doctors pioneered the use of tablets, shortly after we discovered clay. Yet rather than acknowledging our contribution, commentators continue to demean and belittle us. As frustrating as this is, it does invoke some sympathy for the similar plight of ME/CFS patients, demeaned and belittled much as we are. I've addressed the slander of cave doctors in many forums and hope, perhaps foolishly, that this time will be the last.

This brings me to a suggestion for ME/CFS. For decades now, ME/CFS has been locked in a false dichotomy – yeah, that's right, we use big words – a false dichotomy between a psychogenic model and an infectious model. While there is some psychiatric involvement in ME/CFS – I venture that Mr. Landson is a clear example –

psychogenesis fails to explain many neuro-endocrine symptoms observed. Meanwhile the infectious model remains unproven, despite the many types of infectious agents investigated: Viruses; retroviruses; bacteria; mycoplasma; fungi. Perhaps we need to look more broadly, to other transmissible agents. One type of transmissible agent makes pretty good sense for ME/CFS. I speak of the prion, the conformational protein.

Yes, I readily concede that all known prion diseases cause pathology and death that we rarely see in ME/CFS. And yet mouse models show non-pathological prion infections in the lab. Specifically, by blanking the prion gene¹, or deleting the GPI prion anchor², researchers have created prion infections that cause none of the neuron damage we would otherwise expect. However, these synthetic prion infections do generate amyloid plaques, including, in one case, cardiac amyloidosis. This stiffens the walls of the heart, and hence is one potential explanation for orthostatic intolerance.

Setting aside pathology for a moment, think of the ways known prion diseases manifest: Sleep disturbance; emotional lability; cognitive dysfunction. Hello? If a cave doctor can see the parallels to ME/CFS, perhaps others can too.

Let's consider prions in light of the recent Rituximab study in Norway³. We've all heard how killing off and regenerating B-cells, the lymph-node-produced memory cells of the immune system, reduced or eliminated ME/CFS symptoms in two-thirds of subjects. Yet no one is quite sure why.

Here are some facts:

We know that prions target the lymphatic system, including the spleen⁴. We know that prions can infect the lymphatic system without prion protein expression in the B cell⁵.

What we don't know is how prions, as mere proteins without nucleic acids, convey information, beyond their shape. Could prions be exploiting information from the patients' own immune system, in true autoimmune fashion?

Look, I can't prove anything here: I'm just saying medicine needs to look at all the transmissible etiologies, not just the usual suspects. We at CDOA have known about prions since an unfortunate incident involving a chilled brain salad at an association picnic. We lost some good members, and learned the hard way about prions. So I hope against experience that you will consider this prion model seriously, rather than dismissing it, or using silly names, like "mad cave disease" or 'lymphomania', for instance.

Thank you all for allowing me to address you today. An oh, by the way, if any of you see Mr. Landson, tell him he has an appointment with Dr. Thal, in a dark alley, down by the river.

Neil Ander Thal, MD

1. Gadotti, V.M., Boniold, S.P & Zamponi, G.W. Depressive-like behaviour of mice lacking cellular prion protein. *Behavioral Brain Research* 1-5 (2011).doi:10.1016/j.bbr.2011.03.012.
2. Trifilo, M.J. Prion-Induced Amyloid Heart Disease with High Blood Infectivity in Transgenic Mice. *Science* **313**, 94-97 (2006).
3. Fluge,O. et al. Benefit from B-Lymphocyte Depletion Using the Anti-CD20 Antibody Rituximab in Chronic Fatigue Syndrome. A double-Blind and Placebo-Controlled Study. *PLoS ONE* **6**, e26358 (2011).
4. Aguzzi, A. & Weissmann, C. Studies on prion replication in spleen. *Developmental Immunology* (2001)
5. Hegyi, I., Zinkernagel, R. & Weissmann, C. PrP expression in B lymphocytes is not required for prion neuroinvasions. *Nature Medicine* (1998).