

Paradigm Change Blog #12

“The Depression Response”

By Erik Johnson and Lisa Petrisson

From Lisa:

It's long been observed that the illness that the U.S. government historically has chosen to call Chronic Fatigue Syndrome (properly referred to and defined as Myalgic Encephalomyelitis) and depression are often co-morbid conditions. Depending on the specific population being studied and the definitions being used, between 30 and 70% of patients with “CFS” (the name used in the medical literature and thus used in this discussion of that literature) also qualify for a diagnosis of major depression. (1)

The literature makes it clear that “CFS” and depression are not the same thing. “CFS” is a much more complex condition than depression, with more than 400 peer-reviewed studies demonstrating a very wide variety of physiological medical abnormalities. (2) Treating the depressive component of the illness (e.g. with talking therapy or drugs) never has resulted in more than a slight improvement in overall “CFS” symptoms in any studies, making it seem unlikely that depression is an important cause of the overall illness. (1)

Frequently, the stresses of having “CFS” (such as inability to work, financial problems, relationship difficulties and challenges with regard to getting good medical care) have been cited as possibly being responsible for the depression. (1)

However, a new stream of literature has suggested a more integral connection between “CFS” and depression. Depression now appears to be associated with specific physiological abnormalities, including elevations in the cytokines IL-1b, IL-6 and TNF-alpha; dysregulation of NF-k-B; oxidative stress; and mitochondrial dysfunction. (3) All of these appear to be issues in “CFS” as well. (4) According to researcher Michael Maes and colleagues (2012):

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“The co-occurrence between depression and ME/CFS is explained by partially overlapping aberrations in inflammatory, oxidative and nitrosative (IO&NS) pathways. Both disorders are accompanied by systemic inflammation, characterized by increased levels of proinflammatory cytokines and increased levels of acute phase reactants; diminished levels of antioxidants, including zinc and coenzyme Q10 and antioxidant enzymes; O&NS damage to fatty acids, proteins and DNA; dysfunctional mitochondria; a lowered ω -3/ ω -9 polyunsaturated fatty acid ratio; increased translocation of gram-negative bacteria, and aberrations in intracellular signal transduction and apoptosis pathways.” (5)



*A self-portrait by Vincent van Gogh, whose depressions and mood swings **may have been prompted by the toxic substances in the paints he used.** While living in Arles, Van Gogh stored his many paintings before they dried in his poorly ventilated sleeping room and also was said to be in the habit of licking his paintbrushes.*



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Although the pattern of abnormalities is the same in both groups, levels of oxidative stress tend to be “more severely and/or persistently” elevated in “CFS” than in depression, they note. (5)

Considering that a large number of studies have revealed cardiac problems to be fundamental in “CFS” (2), it is interesting to note that cardiac patients without “CFS” have been found to have the same pattern of cytokine dysfunctions as those observed in “CFS” and depression (6).

The reason that these cytokines are abnormally elevated in individuals suffering from these illnesses is as yet unclear in the literature. For instance, with regard to “CFS,” Maes suggests a whole grab bag of possible triggers, none of which seems sufficient to distinguish sufferers from non-sufferers:

“The emerging view that CFS is a medical syndrome caused by a peripheral and central activation of IO&NS pathways, which are secondary to a number of trigger factors. The latter include psychological stress, sustained strenuous exercise, viral infections, bacterial infections and any other condition which is accompanied by IO&NS, for example autoimmune disorders, cancers, radiation therapy, and so on. The above mentioned trigger factors may activate NFkb, whereby NFkb functions as a ‘smoke sensor’ that detects the above mentioned threats and acts as a switch to turn inflammation and O&NS on and off.” (7)

Another factor brought up by Maes and others is the biotoxin LPS (also known as endotoxin), which is made by certain types of pathogenic bacteria. The presence of these bacteria in a suboptimal gut may trigger inflammation, these researchers speculate. (8)

One factor that appears to be yet to be examined in this stream of literature is the possibility that one or more environmental toxins might be playing a role. As a start, we thus will consider the possible role of a toxin that we believe to be specifically associated with “CFS”: the trichothecene mycotoxins made by the toxic “black mold” *Stachybotrys chartarum*.

A recent paper by Dr. Joseph Brewer and colleagues revealed that 93% of a group of “CFS” patients had mycotoxins in their urine compared to 0% of a group of controls without a history of exposure to moldy buildings (9), and the possible connection



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between Sick Building Syndrome and “CFS” has been brought up in the academic literature in the past (10). Researchers from Brown University were surprised to find that living in a damp or moldy house led to an elevated risk of depression that couldn’t be explained away by other factors (11), and other papers have suggested that depression is a common symptom presenting in mold illness patients (12). And at least in animal studies, certain trichothecenes seem to have the potential to lead to cardiac abnormalities. (13)

Anecdotally, *Stachybotrys* seems to be the toxic mold that is most associated with “CFS”. Like other trichothecenes, the mycotoxins made by *Stachybotrys* create massive amounts of oxidative stress that are especially damaging to the mitochondria. (14)

Pei & Gunsch (2013) investigated cytokine reactions in the human monocytic THP-2 cell line exposed to *Stachybotrys* and found substantial elevations in IL-1b, IL-8 and TNF-alpha. Cytokine mRNA expression was generally upregulated 2-10 times following a 24 hour exposure to the fungal extracts. (15)

Another study showed that NF-kappa-beta played a role in the toxicity of the trichothecene nivalenol in human cells. (16)

In addition, a number of studies have shown that *Stachybotrys* is much more toxic at low levels and produces a wider range of cytokine abnormalities (including with IL-6 and NF-kappa-beta) when it is administered in conjunction with LPS. (17)

Interestingly, LPS is also made by certain bacteria (such as *Streptomyces californicus*) that have been found in water-damaged buildings, meaning that people exposed to problematic buildings may not even need to have gut dysbiosis to be affected by it. (17) It also may be that the effects of mycotoxins in the gut make it more likely that toxin-producing bacteria will establish residence there — more on that in a future blog essay.

The effects of trichothecenes on the immune system are well-established in the agricultural literature, with pigs (animals that are fairly close to humans in terms of their immune systems) being especially susceptible to the toxin. For instance, Seeboth and her co-authors (2012) found with the toxin T-2 the same IL-1b and TNF-alpha abnormalities that we see with the other trichothecenes. They write:

“Our results suggest that ingestion of low concentrations of T-2 toxin affects the TLR activation by decreasing pattern recognition of pathogens and thus interferes with initiation of inflammatory immune response against bacteria and viruses. Consequently,



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mycotoxins could increase the susceptibility of humans and animals to infectious diseases. Then, mycotoxins, especially T-2 toxin, could play a determining role in lowering the immune response of pigs to these bacterial and viral infections.” (18)

So to summarize: these studies seem to suggest that even alone but especially in combination with the LPS produced by certain gut bugs or environmental bacteria, trichothecene toxins found in water-damaged buildings have the potential of creating the cytokine effects that have been observed by researchers such as Maes to be associated with “CFS,” cardiac disease and depression.

IL-1b: Increased in depression/”CFS.” Increased with Trichothecenes.

IL-6: Increased in depression/”CFS.” Increased with Trichothecenes + LPS

TNF-alpha: Increased in depression/”CFS.” Increased with Trichothecenes.

NfKb: Dysregulated in depression/”CFS.” Problematic with Trichothecenes.

Oxidative Stress: High in depression/”CFS.” High with Trichothecenes.

Mitochondrial Dysfunction: High in depression/”CFS.” High with Trichothecenes.

IL-8: Increased with Trichothecenes.

Note that these are ALL of the cytokine abnormalities reported by Maes and co-authors in their papers looking at “CFS” and depression, and also ALL of the cytokine abnormalities that I was able to find associated with trichothecenes. The abnormalities are very specific and consistent — suggesting that it is possible that the mycotoxins are at least in part responsible for the disease states.

This leads to the question of how these conditions might be related to one another in the context of a toxic exposure — a topic that Erik has been contemplating for decades. Here is his hypothesis, formulated in the mid 1990’s.

From Erik:

I believe that depression is not an illness.

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It is a warning.

It is the sixth sense – a perceptual interface with immune response.

Depression is to toxic exposures as pain is to a hot stove.

Depression is just the signal that tells the brain about the inflammatory response. It is not an illness in and of itself.

It is a desirable response designed by nature to convey a sense of immunological dysregulation.



Erik hikes to the top of Mt. Judah near Lake Tahoe, feeling happy and energetic in the clean air.

If nature wanted to induce an animal to change its location or eating habits to avoid toxic exposures, what “emotions” would serve better than anxiety and depression?



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My own experience is that depression and grief are only connected inasmuch as they can coexist and layer onto each other and feel similar enough to appear to be the same phenomenon.

I have grieved deeply for my lost life and the profound expressions of my grief correspond to the profound nature of this illness.

Depression never correlated to any emotional stimulus.

I could have bouts of depression that were layered onto my grief and make it seem like my emotional state had driven me into a supremely suicidal state, but it struck me as really odd that I could have sudden-onset depression when nothing in my life had changed that should have induced an emotional change.

At least it struck me as odd until I found that my depression had a perfect correlation to cytokine storm from exposure to my MCS irritants.

I discovered that my primary chemical trigger was *Stachybotrys mycotoxins*.

If I am exposed to Stachy, I still suffer from overwhelming depression that I cannot mentally control even though I know it is just a symptom of chemical sensitivity.

I can eliminate the depression response through avoidance and decontamination. And I can do it quickly!

I turned my “weakness” into a strength by employing the strategy of using depression as an indicator of toxic exposure.

Avoidance is something that should come naturally to any animal in the kingdom. It should be the normal organic response to such a sensation.

One would expect that any “dumb” animal would wish to evacuate areas of discomfort and would appropriately act upon that impulse. It is only humans that would even attempt to overpower their discomfort by using mind over matter.

From Lisa:

More of Erik’s writings on this topic are [here](#).



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If Erik's theory is correct and depression indeed is nature's warning that people are being exposed to toxins that will eventually cause them physical harm (e.g. immune dysfunction, cardiac problems, "CFS"), then the increased prevalence of depression in the population overall should be ringing a lot of warning bells for us as a society.

Just as the appropriate response to the smoke detector going off in the middle of the night is to first evacuate and then call for help in putting out the fire, perhaps the appropriate response to depression is also evacuation and then cautious remediation of the environmental hazard. Antidepressant drugs or psychotherapy, on the other hand, may be the equivalent of removing the batteries from the smoke alarm to get it to shut up and then going back to bed — not necessarily a smart strategy.

The topic of seeking out "feel-good" places where the depression response goes into hiding is the focus of the [Locations Effect Facebook page](#) that Paul Beith and I started a few months ago. Here's a description:

"Is being in a good location the next frontier in healthy living? We think so! This page reports on places where people have enjoyed enhanced feelings of health or experienced improvement in chronic health conditions. Please share your photos and stories here."

The [Locations Effect website](#) (another project initiated by Paul and me) provides a location for mold avoiders and others sensitive to their environments to share their experiences in different places.

[A Kindle book summarizing Erik's experiences](#) learning about the role of toxic mold in his illness also is available.

For a list of references cited in this blog, [click here](#).

The original blog is here:

<http://paradigmchange.me/wp/?p=440>

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