



# BRAIN ON FIRE

How Biotoxins  
Cause Brain  
Inflammation

# INFLAMMATION and DEPRESSION

- \* A very recent study out of Denmark of 3 million people showed that a diagnosis of **autoimmune disease** increased the risk of a subsequent mood disorder diagnosis by **45%**. Any history of hospitalization **for infection** increased the risk of later mood disorders by **62%**. The 2 risk factors interacted synergistically and increased the risk of subsequent mood disorders more than 2 fold (2.35 fold)

- \* **Autoimmune Diseases and Severe Infections as Risk Factors for Mood Disorders: A Nationwide Study**

- \* Michael E. Benros, MD<sup>1,2</sup>; Berit L. Waltoft, MSc<sup>1</sup>; Merete Nordentoft, DrMedSc<sup>3,4</sup>; Søren D. Østergaard, MD<sup>3</sup>; William W. Eaton, PhD<sup>5</sup>; Jesper Krogh, MD<sup>2</sup>; Preben B. Mortensen, DrMedSc<sup>1,4</sup>

- \* *JAMA Psychiatry*. 2013;70(8):812-820. doi:10.1001/jamapsychiatry.2013.1111.

# INFECTIOUS and TOXIC AGENTS ASSOCIATED WITH PSYCHIATRIC ILLNESS

- \* MOLD
- \* NEUROLYME and coinfections
- \* STREPTOCOCCUS OCD (PANDAS)
- \* ENCEPHALOPATHIES – VIRAL
- \* TOXOPLASMOSIS (suicide and schizophrenia)

# Neural Injury Mechanisms

- \* Cytokines (MMP-9, TGF beta)
- \* Vasculitis
- \* Microglial activation
- \* Autoimmune
- \* Excitotoxicity

# MOLD and DEPRESSION

- \* About 40% of the residents lived in visibly damp, moldy households, **and overall their risk for depression averaged 34–44% higher** than that for residents of mold-free dwellings (from a study of almost 6000 European adults)
- \* Dampness and mold in the home and depression: an examination of mold-related illness and perceived control of one's home as possible depression pathways.
- \* [Shenassa ED, Daskalakis C, Liebhaber A, Braubach M, Brown M. Am J Public Health.](#) 2007 Oct;97(10):1893-9. Epub 2007 Aug 29.

# Depression or Sickness Behavior?

- \* Sickness behavior is cytokine based
- \* Guilt, worthlessness, hopelessness (MDD) vs fatigue and anhedonia (biotxin illness, chronic fatigue)
- \* [J Affect Disord.](#) 2012 Dec 10;141(2-3):130-42. doi: 10.1016/j.jad.2012.04.004. Epub 2012 May 11.
- \* **Inflammatory fatigue and sickness behaviour - lessons for the diagnosis and management of chronic fatigue syndrome.**
- \* [Arnett SV](#), [Clark IA](#).

# Cytokines and Depression

- \* Gardner A, Boles RG. **Beyond the serotonin hypothesis: mitochondria, inflammation and neurodegeneration in major depression and affective spectrum disorders.** *Progress in Neuro-Psychopharmacology and Biological Psychiatry.* 2011;35:730–743
- \* **A metaanalysis of cytokines in major depression including 24 studies reports significantly higher concentrations of the proinflammatory cytokines TN alpha and IL6 in depressed subjects compared with control subjects**
- \* Dowlati Y, Herrmann N, Swardfager W, et al. A metaanalysis of cytokines in major depression. *Biol Psychiatry* 2010; 67: 44657.

# Cytokines and SSRI's

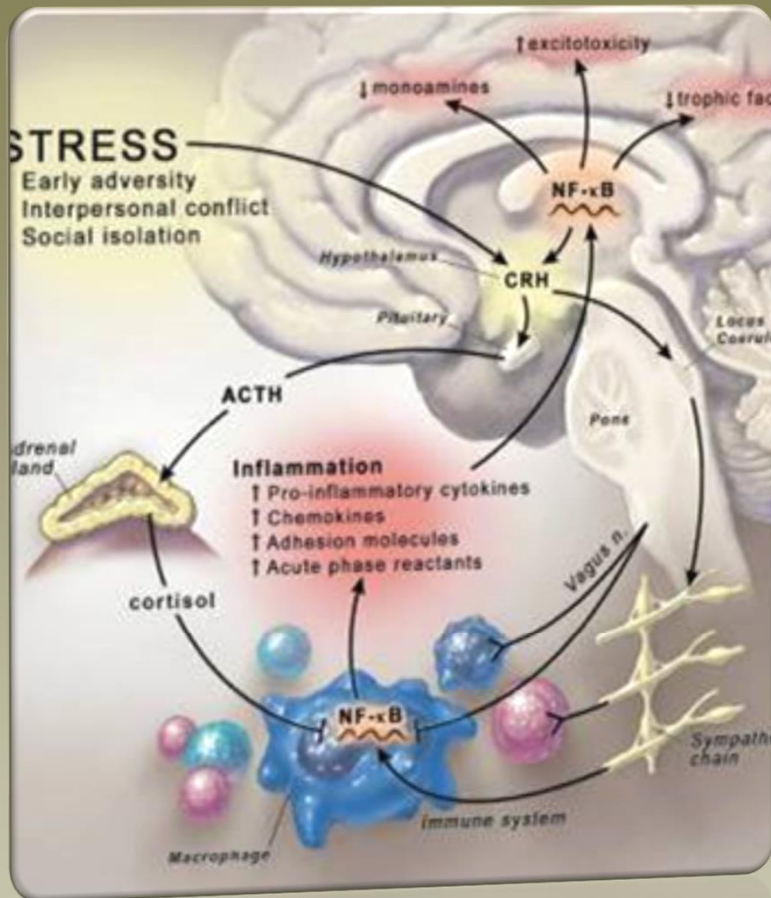
- \* Cytokines can reduce the expression and function of serotonin transporters that conventional antidepressants inhibit, thereby sabotaging their efficacy.
- \* **Not only are patients with TRD more likely to exhibit increased levels of inflammatory markers, but also increased levels of inflammatory markers before treatment have also been found to be associated with a lower likelihood of response.**<sup>12,14-16</sup>
- \* **12.** Miller AH, Maletic V, Raison CL. Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. *Biol Psychiatry*. 2009;65:732-741.



# Depression and Immune Function

- \* A randomized cohort study of 92 adults older than 59 years showed that those with MDD who were not being treated with antidepressants had lower CMI to the VZV up to 2 years after vaccination compared with both healthy peers and patients with MDD who were treated with SSRI's
- \* **Supports hypothesis that depression lowers immune function**

\* Untreated Depression and Response to Shingles Vaccination in Older Adults  
\* (*Clin Infect Dis.* Published online February 13, 2013. [Abstract](#))

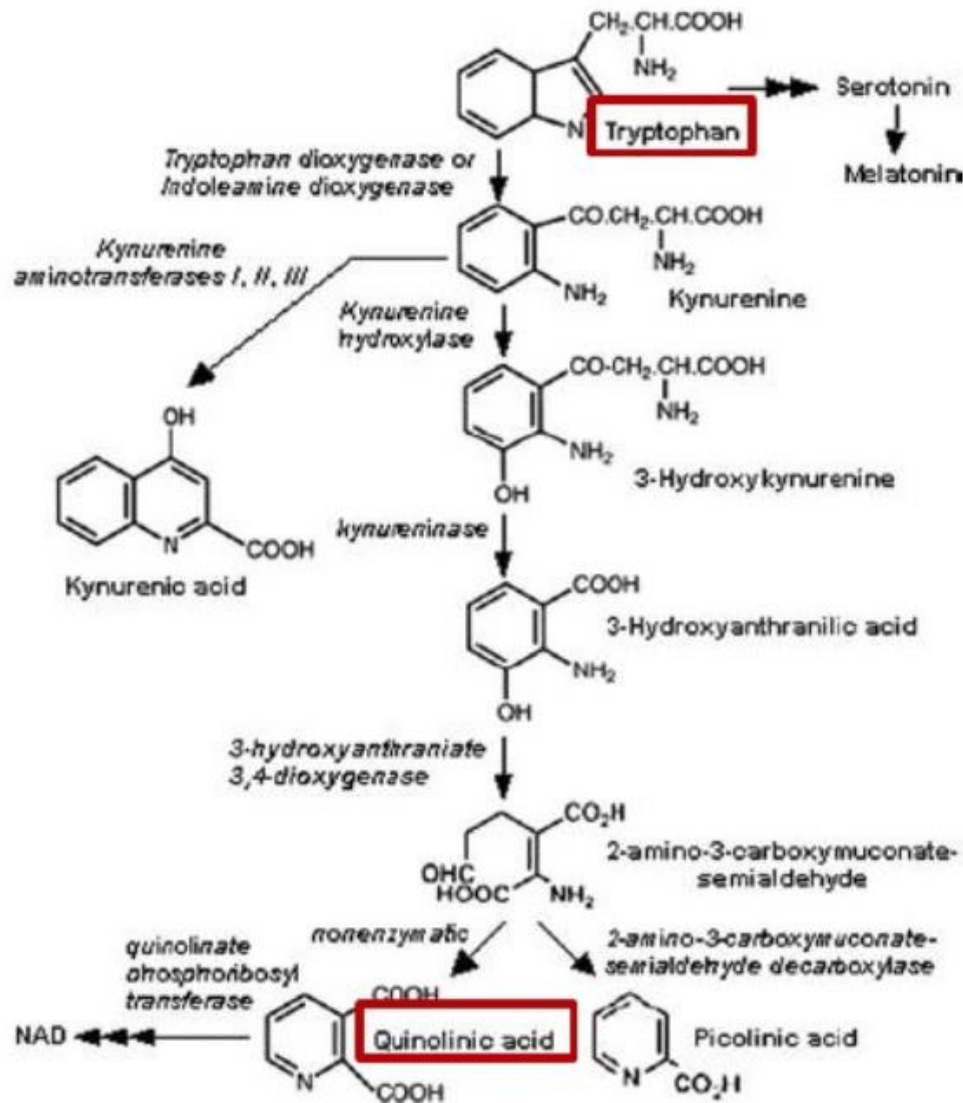


# STRESS and NEURO INFLAMMATION

Stress from early childhood adversity as well as social isolation and interpersonal conflict increase's the brain's excitotoxicity

## KYNURENINE PATHWAY

Tryptophan is degraded into Quinolinic acid which is involved in Alzheimer's, Huntington's, AIDS dementia and Parkinson's



# Quinolinic Acid and Suicide

- \* New Study Links Suicide Attempts to Amount of Quinolinic Acid in CSF
- \* [Neuropsychopharmacology](#). 2013 Apr;38(5):743-52. doi: 10.1038/npp.2012.248. Epub 2012 Dec 3.
- \* **Connecting inflammation with glutamate agonism in suicidality.**
- \* [Erhardt S](#), [Lim CK](#), [Linderholm KR](#), [Janelidze S](#), [Lindqvist D](#), [Samuelsson M](#), [Lundberg K](#), [Postolache TT](#), [Träskman-Bendz L](#), [Guillemin GJ](#), [Brundin L](#).

# Brain Inflammation(Leaky Brain)

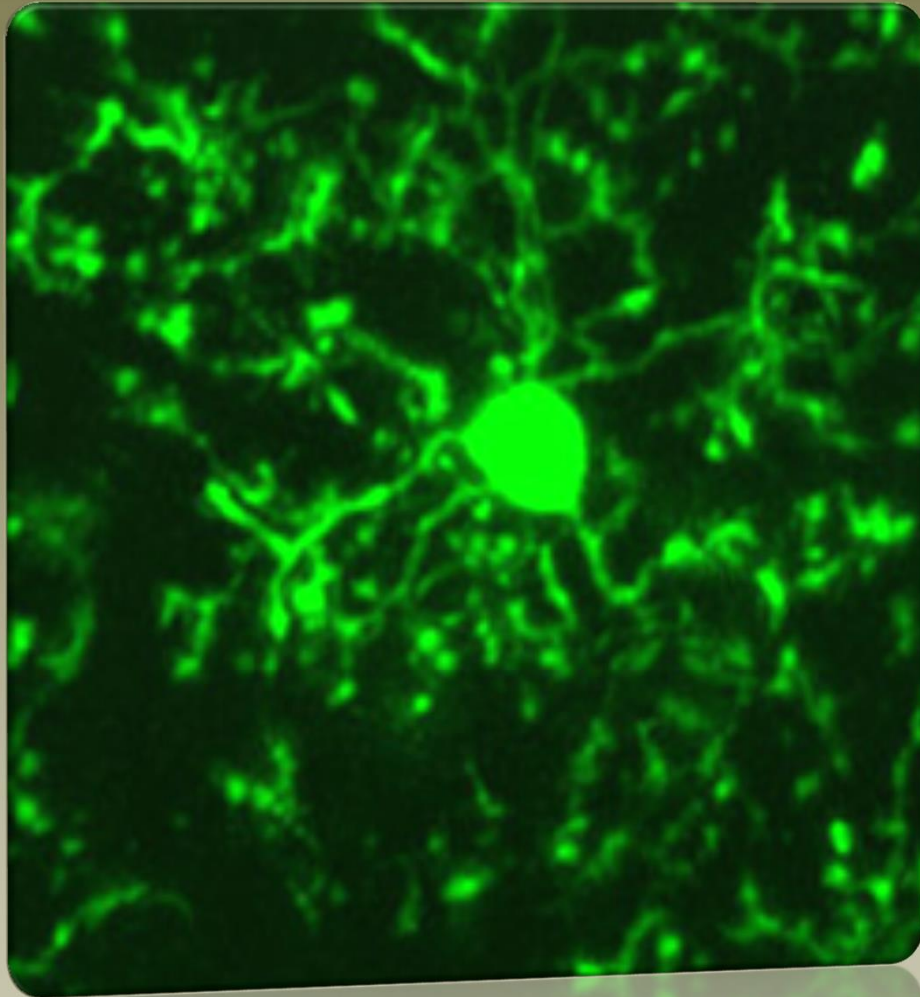


- \* Inflammatory cytokines like IL-1, IL-6 and TNF as well as bacterial toxins produce symptoms of depression and anxiety
- \* Cytokines increase the permeability of the BB barrier
- \* Cytokines activate the stress response in the HP axis
- \* Cytokines decrease the amount of serotonin in the brain by breaking down tryptophan
- \* Cytokines decrease conversion of T4 to T3

# Psychosis and Inflammation

- \* Tatiana Falcone T, Carlton E, Franco K, Janigro D. **Inflammation, psychosis, and the brain.** Psychiatr Times 2009; 26.





## MICROGLIA

Primary immune component of brain. Cause inflammation, can be activated by head injury. Persistent activation can lead to neurodegeneration such as Alzheimer's

# Bipolar Disorder and Cytokines

- \* **Microglial activation in bipolar patients**
- \* Stertz L, Magalhães PV, Kapczinski F. **Is bipolar disorder an inflammatory condition? The relevance of microglial activation.** *Curr Opin Psychiatry.* 2013;26:19-26.



# *Schizophrenia and Immune Function*

- \* In the recent CATIE trial 23.% of those with schizophrenia had IgA anti-AGA antibodies (anti-gliadin) compared to 3.1% of a comparison group, and 5.4% had high levels of tTG antibodies compared to 0.8% of the comparison group.

# COGNITIVE IMPAIRMENT and MOLD

- \* ***“My brain doesn’t work the way it used to !”***
- \* Several studies have validated that the cognitive impairment many CIRS patients complain of is real.
  
- \* [Arch Environ Health.](#) 2003 Aug;58(8):452-63.
- \* **Psychological, neuropsychological, and electrocortical effects of mixed mold exposure.**
- \* [Crago BR, Gray MR, Nelson LA, Davis M, Arnold L, Thrasher JD.](#)
  
- \* [Appl Neuropsychol.](#) 2004;11(2):65-74.
- \* **Cognitive impairment associated with toxigenic fungal exposure: a replication and extension of previous findings.**
- \* [Gordon WA, Cantor JB, Johanning E, Charatz HJ, Ashman TA, Breeze JL, Haddad L, Abramowitz S.](#)

# Mechanisms of Mycotoxin Neurotoxicity

- \* Tricothecenes (stachy) kills olfactory neurons (MCS?)
- \* T-2 (fusarium) kills neuronal brain cells, adult and fetal
- \* Ochratoxin (OTA, asperg) depletes striatal dopamine including substantia nigra, striatum and hippocampus (mood and movement disorders?)
- \* Fumonisin (fusarium, corn) induces neuronal degeneration in the cerebral cortex
- \* [Int J Mol Sci.](#) 2011;12(8):5213-37. doi: 10.3390/ijms12085213. Epub 2011 Aug 15.
- \* **Mechanisms of Mycotoxin-Induced Neurotoxicity through Oxidative Stress-Associated Pathways.**
- \* [Doi K, Uetsuka K.](#)

# Cognitive Decline in 6 year olds

277 Polish children living in homes with visible mold infestation showed significant decline in IQ scores, with longer exposure increasing the decline to almost 10 points

- \* [Physiol Behav.](#) 2011 Oct 24;104(5):989-95. doi: 10.1016/j.physbeh.2011.06.019. Epub 2011 Jul 8.
- \* **Cognitive function of 6-year old children exposed to mold-contaminated homes in early postnatal period. Prospective birth cohort study in Poland.**
- \* [Jedrychowski W](#), [Maugeri U](#), [Perera F](#), [Stigter L](#), [Jankowski J](#), [Butscher M](#), [Mroz E](#), [Flak E](#), [Skarupa A](#), [Sowa A](#)

# ALZHEIMER'S and INFLAMMATION

- \* ALZHEIMER'S A meta analysis of cytokines in AD which reviewed 86 studies found that AD is accompanied by an inflammatory response with particularly higher peripheral concentrations of IL6, TNF, IL1, **transforming growth factor**, IL12 and IL18 and higher CSF concentrations of **transforming growth factor**
- \* Swardfager W, Lanctôt K, Rothenburg L, Wong A, Cappell J, Herrmann N. A metaanalysis of cytokines in Alzheimer's disease. Biol Psychiatry 2010; 68: 93041

# Neuroinflammation and Mold

- \* CYTOKINES (TGF beta, MMP-9)
- \* Swelling of frontal lobes, hippocampus and cerebellum
- \* Shrinkage of caudate (involved in movement and dopamine rich)
- \* <http://www.survivingmold.com/diagnosis/neuroquant>

# DIAGNOSIS MOST IMPORTANT

- \* All treatment starts first with diagnosis
- \* Neuroinflammation is rarely, if ever, considered in the diagnosis of what looks primarily like a psychiatric presentation

## **CLUES**

1. No family history (a big red flag)
- \* 2. Unusual age of presentation, such as bipolar starting at age 50
  - \* 3. Known exposure to mold or lyme – always ask!
  - \* 4. Unusual reactions to medications – small doses increasing anxiety through the roof is typical, or meds completely ineffective. Patient may be labeled histrionic or hypochondriacal

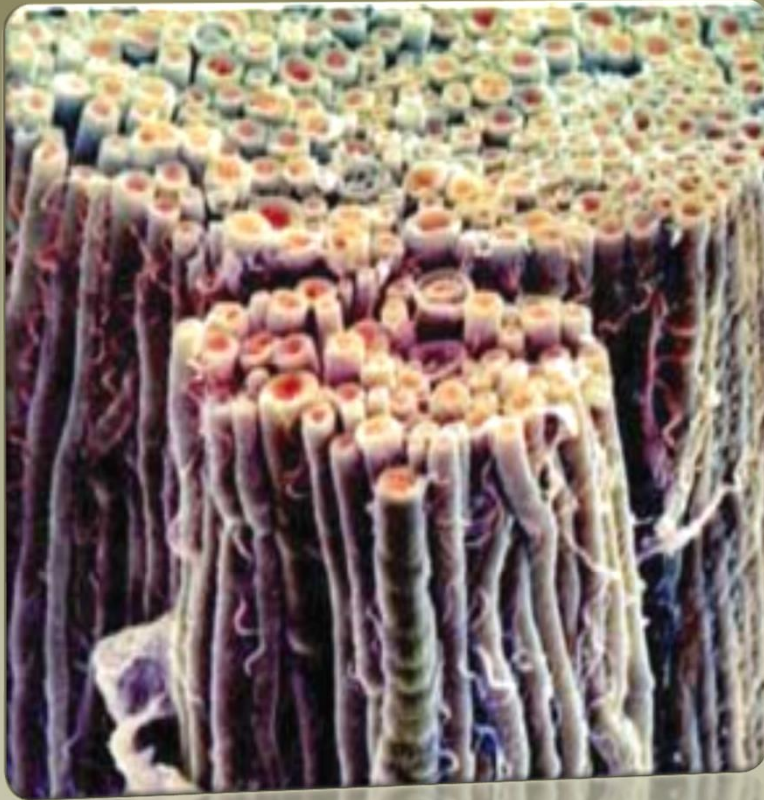
# TREATMENT

- \* Biotoxin Protocol
- \* EPA/DHA Fish Oil 4 to 8 gms biotoxin or bipolar
- \* DIET (reduce sugar and insulin spikes – amylose free, ketogenic, paleo)
- \* Mag Citrate 200 to 400 gms for constipation and much more
- \* Vit D 2000 to 5000 IU
- \* Tumeric 1200 to 2400 gms
- \* EmPowerPlus or Equilib
- \* Allopathic meds if indicated



# Fish oil supplements prevent psychotic mental illness'

- \* A three-month course of fish oil appeared to be as effective as drugs, cutting the rate of psychotic illness like schizophrenia by a quarter. Omega-3 fatty acids found in the supplements may alter brain signalling in the brain with beneficial effects
- \* Archives of General Psychiatry Feb 2010



Better  
Electrical  
Signal  
”  
Conduction  
Myelin Sheath  
Insulation for  
Nerve “Wires”

# OMEGA 3 FATTY ACIDS

- “ Increases ability of serotonin and dopamine to bind to receptors
- “ Down regulates cortisol
- “ Down regulates inflammatory cytokines
- “ Increases thyroid hormone transfer to the brain

# Anti Inflammatory DIET

- \* Reducing sugar – amylose free, ketogenic, paleo
- \* Eliminating food sensitivities – gluten, dairy, autoimmune paleo
- \* Schizophrenia – almost 25% have anti gliadin antibodies
- \* Bipolar – ketogenic (antiepileptic) diet
  
- \* Rejuvenation Res. 2012 Apr;15(2):217-21. doi: 10.1089/rej.2011.1289.
- \* **Can Alzheimer disease be a form of type 3 diabetes?**
- \* Accardi G, Caruso C, Colonna-Romano G, Camarda C, Monastero R, Candore G.
  
- \* <http://mypassion4health.blogspot.com/2013/09/ketogenic-diet-resources.html>

# Magnesium

- \* 68% of Americans do not consume the recommended daily intake of magnesium.
- \* According to NIH the early signs of magnesium deficiency are depression, anxiety, insomnia and muscle twitching
- \* Decreases glutamate excitability in brain. Glutamate excitability is highly associated with anxiety

# Magnesium

- \* Best forms citrate or glycinate
- \* Dosage between 400 to 800 mg daily
- \* A number of cases have been documented showing rapid recovery from depression when magnesium was supplemented. The authors of that study also raised the possibility that magnesium deficiency *is the cause of most major depression and related mental health problems* including IQ loss and addiction
- \* *Med Hyp* 2006

# Turmeric As Effective as Prozac

A new study from India found that 1000mg of turmeric a day was as effective as 20mg of Prozac in a six week trial.

Curcumin is known to inhibit inflammatory cytokines and TNF alpha. Due to its lipophilicity, curcumin can easily cross the BBB

In addition turmeric can reduce the neurotoxicity of quinolenic acid

△ Braidy N, Grant R, Adams S, Guillemin GJ (January 2010). "Neuroprotective effects of naturally occurring polyphenols on quinolinic acid-induced excitotoxicity in human neurons". *FEBS J.* 277 (2): 368–82. [doi:10.1111/j.1742-4658.2009.07487.x](https://doi.org/10.1111/j.1742-4658.2009.07487.x). PMID 20015232.



# Probiotics

- \* **MSH receptors** in gut lining mediate tight junctions between cells (leaky gut?)
  - \* Strong connection between pathogenic gut bacteria and anxiety
  - \* **Probiotics shown to improve anxiety and depression symptoms** in volunteers in one month of treatment
- \* (2) Messaoudi, M. et al. (2011) Beneficial psychological effects of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in healthy human volunteers. *Gut Microbes* 2, 256–261
- (3) Benton, D. et al. (2007) Impact of consuming a milk drink containing a probiotic on mood and cognition. *Eur. J. Clin. Nutr.* 61, 355–361



# Vitamin D Benefits

- \* Cardiovascular
- \* Immune System
- \* Cancer protective
- \* Diabetes
- \* Osteoporosis
- \* Depression
- \* Autoimmune

# Vitamin D and Depression

- \* *Those with Vitamin D levels above 40 scored significantly lower on depression ratings.*
- \* *In the group given Vitamin D for one year there was significant improvement in depression ratings*
- \* *J Intern Med 2008*

# HAPPINESS and INFLAMMATION

- \* People who had high levels of happiness derived from having a strong sense of purpose and meaning in life – also known as eudaimonic – also showed a very favorable immune system profile *at the genetic level*. People whose happiness was derived more from self gratification, also known as hedonic happiness, showed a much more unfavorable profile.
- \* **A functional genomic perspective on human well-being**
- \* PROC NATL ACAD SCI USA 2013 Aug 13;110(33):13684-9. doi: 10.1073/pnas.1305419110. Epub 2013 Jul 29.
- \* .

# INFLAMMATORY MARKERS

- \* More specifically the eudaimonic, or “noble purpose” group actually had decreased the expression of genes responsible for producing the proinflammatory cytokines such as IL1B, IL6, IL8, and TNF, and had increased the expression of genes responsible for killing viruses and bacteria, such as type I IFN antiviral responses and IgG1 antibody synthesis . The hedonic group showed the opposite profile

# Meditation and Neuroplasticity

- \* **Other nonpharmacological treatments may include mindfulness meditation – encouraging parasympathetic output and new neural pathways**
- \* **40.** Pace TW, Negi LT, Adame DD, et al. Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. *Psychoneuroendocrinology*. 2009;34:87-98

# Results

- \* About 60 percent of the biotoxin patients I see find the depression, insomnia and anxiety gradually resolve over 2 to 4 months as they reduce exposure and start the protocol. It just becomes a nonissue, and some even forget it was a problem
- \* About 30 percent may need more intensive supplemental or allopathic intervention such as benzodiazepines.
- \* Therapy or support can be helpful
- \* Ten percent have intense psychiatric process occurring with severe agitation, depression and psychosis requiring antipsychotics, trans cranial stimulation or ECT