

Vaccines, depression, and neurodegeneration after age 50 years: another reason to avoid the recommended vaccines

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Abstract

There is growing evidence that a number of the psychiatric disorders are strongly related to glutamate excess. Likewise, recent studies have shown a connection between chronic inflammation and these same disorders. A compelling body of research links these two observations, glutamate excess (an excitotoxicity marker) and chronic inflammation (immune over-reactivity). It is known that systemic activation of the immune system also activates the brain's special immune system, which is regulated by the microglia. Based on results of studies of the sickness behavior response to natural infections, neuroscientists have deciphered much of the mechanism responsible for the behavioral effects associated with intense systemic immune activation, including social isolation, depression, anxiety, and a loss of appetite. Most of these symptoms are shared by the major depressive disorders. Other studies have linked neurodegeneration and a worsening of neurodegenerative diseases to systemic immune activation. This paper demonstrates the known links between: systemic immune activation, brain microglial activation, and both major depressive disorder and a worsening of neurodegenerative diseases. Because a number of vaccines are being recommended to adults, the risk of precipitating or worsening these disorders is quite real. The mechanism for this process is discussed.

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Six-million elderly Americans are estimated to suffer from major forms of depressive illness at an annual cost of US\$44 billion dollars. Onset of depression later in life tends to last longer and to be more severe than onset earlier in life. It is also associated with a high rate of suicide.

Previously, major depression was thought to be secondary to a deficiency in certain neurotransmitters in the brain, particularly the monoamines, which include serotonin, norepinephrine, and dopamine. While alterations in these important mood-related neurotransmitters are found with major depression, mounting evidence indicates that the primary culprit is low-grade, chronic brain inflammation [1-6]. In addition, it is now known that inflammatory cytokines can lower serotonin significantly and for long periods by a number of different mechanisms [7,8].

Researchers have also discovered that most people with major depressive disease (MDD) have higher levels of the neurotransmitter *glutamate* in their cerebrospinal fluid (CSF) and blood plasma [9-11]. This is the same glutamate found in some food additives, for example, MSG (monosodium glutamate), hydrolyzed proteins, calcium or sodium caseinate, soy protein isolate, and vegetable protein concentrate or isolate. Much of the free glutamate in the brain of depressed individuals comes from within—that is, it is secreted by specialized cells (typically identified as microglia, microglial cells, or astrocytes) within the brain itself. The free glutamate existing outside the neurons is very toxic to brain connections and the brain cells themselves—mainly by a process called excitotoxicity.

This connection between high brain glutamate levels and major depression was discovered quite by accident when researchers observed that the anesthetic drug Ketamine could relieve depression for a prolonged period. Ketamine is a powerful blocking drug for a class of glutamate receptors (the NMDA receptors).

For quite some time, depression has been known to be able to cause a loss of neurons in the hippocampus of the brain—the area most important for recent memory (declarative memory or working memory), the form of memory most affected in Alzheimer's disease [12,13]. This shrinkage of the brain usually occurred with long-term depression, yet it was shown, using sophisticated testing, that even without brain shrinkage, memory could be adversely affected. Some antidepressants have been shown to not only reverse the memory loss but also reverse the shrinkage as well.

The implications were that the elevated free glutamate levels in the brain, via excitotoxicity, were destroying brain connections and later killing brain cells in the hippocampus, and that the antidepressants were lowering the brain's glutamate levels. Subsequent studies have confirmed that drugs that block excitotoxicity, also reduce depression and that some antidepressants reduce brain glutamate levels [14-16].

The link between elevated brain glutamate and inflammation

Recent research has demonstrated the link between chronic low-level brain inflammation, elevated brain glutamate levels, and major depression [17,18]. We know that, as we age, the level of *inflammatory immune cytokines* (such as interleukin-1 β (IL-1), IL-6 and TNF- α) increase. Thus, the level of inflammation in our body increases with age, with high levels being seen at the extremes of life [19-22].

This progressive elevation in our body's inflammation increases our risk of a number of inflammation-linked diseases, such as cancer, arthritis, muscle weakness, fatigue, sleep disturbances, memory loss, and confusion. People with Alzheimer's and Parkinson's disease have even higher levels of these inflammatory cytokines [23,24].

When inflammatory cytokines are elevated in the brain, brain cells are more vulnerable to a number of toxins, many of which are found in the environment. One study demonstrated that if brain cells were exposed to low levels of a pesticide, there was little toxicity seen. Moreover, if these same brain cells were exposed to an immune stimulant alone, little damage occurred [25]. But if the brain cells were exposed first to the immune stimulant, the same low dose of pesticide destroyed a great number of brain cells.

The importance of this observation was that a vaccine caused the brain cells to be hypersensitive to the toxin so that even in concentrations that normally do not cause harm, the toxin was observed to destroy most of the neurons. One of the strongest connections between an environmental toxin (pesticides) and a neurological disorder is seen in *Parkinson's disease*. The reason this disease is more common in the elderly is that this cohort has the highest levels of inflammatory cytokines. This also explains the high incidence of *Alzheimer's disease*, which reaches incidences of 50% after age 80 years.

The link between the excitotoxicity and depression was also discovered by accident. Doctors using immune cytokines to treat patients with cancer or hepatitis found that one third of the patients developed major depressive illness within days of the treatment and that their depression only resolved when the treatment was terminated [26,27]. Other studies that measured inflammatory cytokine levels in patients with major depressive illness also found most patients exhibited high levels of these inflammatory mediators [28,29].

To their surprise, researchers found that many of the antidepressant medications commonly used, lowered inflammatory cytokine levels and that patients who failed to respond to these drugs had the highest level of cytokines.

So, how is this linked to excitotoxicity? Neuroscientists have known for some time that inflammatory cytokines cause the brain to release higher levels of glutamate—the more intense the inflammation, the higher the brain glutamate levels [30,31]. The highest cytokine levels are found in the *prefrontal lobes* and limbic system, the areas most related to mood control [32]. MSG consumption has also been shown to increase brain inflammation.

Vaccination and brain inflammation

A great number of animal studies have shown that, following vaccination, the body's inflammatory cytokines not only increase dramatically, but also so do the brain's inflammatory mediators [28,33–36]. The brain has its own immune system that is intimately connected to the body's immune system. One of the main immune cells in the brain is called a *microglial cell*, or *astrocyte*. The astrocyte, another type of glial cell which can also secrete immune cytokines, is controlled by the microglia. Normally, these brain cells are lying throughout the brain in a resting state (called ramified). Once activated, they can move around, traveling between brain cells like amoeba (called amoeboid microglia).

In the resting state, these immune cells release chemicals that support the growth and protection of brain cells and their connections (dendrites and synapses). But when activated, they secrete a number of very harmful chemicals, including inflam-

matory cytokines, chemokines, complement, free radicals, lipid peroxidation products, and two excitotoxins: *glutamate* and *quinolinic acid*.

In essence, since the body's immune system sent an emergency message that an invasion had occurred, these brain immune cells are out to kill invaders. With most infections, this phase of activation lasts no more than a few days to two weeks, during which time the immune system successfully kills off the invaders. Once that is accomplished, the immune system shuts down to allow time for things to return to normal and the brain to repair what damage was done by its own immune system.

During this period of activation, researchers know that individuals generally feel bad and what they experience closely resembles depression—a condition called “sickness behavior” [28]. Most of us have experienced these symptoms when suffering from a viral illness—such things as restlessness, irritability, a need to get away from people, trouble sleeping, fatigue, and difficulty thinking.

Studies have shown that there are two phases to this “sickness behavior”; one in which we have the flu-like symptoms and a later onset of depression-like symptoms that can last a while. All these symptoms are due to high levels of inflammatory cytokines in the brain which derive from activated microglia.

A number of studies have also shown that after age 50 years, individuals have exaggerated and prolonged “sickness behavior”, much more so than younger people [22]. This is one of the reasons why many elderly exhibit flu symptoms for months after exposure.

There is also another immune phenomenon that plays a major role in vaccine-related brain injury. Researchers discovered that when an animal is vaccinated, the brain microglia immune cells turn on partially (called priming), that is, they are in a state of high readiness. If the immune system is again activated (days, weeks to months) after this priming, these microglia explode into action, secreting levels of their destructive chemicals far higher than is normal. [38] This overreaction in humans can be very destructive and cause a feeling of depression.

Stimulating the immune system with a vaccine is far different than contracting an infectious illness naturally. Vaccines are made of multiple components—for example, the biological agent you wish to vaccinate against (e.g., the measles virus), preservative system, extraneous proteins, surfactant (e.g., Tween 80) and an immune system booster called an *immune adjuvant*. These adjuvants are typically things such as suspended, practically insoluble aluminum compounds as well as MSG, lipid compounds, and even Thimerosal and other mercury compounds. In general, these adjuvants are chosen to elicit intense generalized immune-system reactions that last for extended periods of time.

Studies have shown that, in some cases, the adjuvant from a single vaccination can cause localized macrophagic immune overactivation for as long as two years. Because this localized reaction can activate the brain's immune system, the brain's microglial cells can also be activated for this period, causing them to release increased levels of their destructive chemicals for some time. In fact, one study found that a single injection of an immune activating substance could cause the brain's immune system to remain in this activated state for more than a

year [39]. Obviously, this can be very destructive.

Flu vaccines and an expanding vaccine schedule for the elderly

Public health authorities and physician societies are in an all out campaign to have every elderly person vaccinated every year with the flu vaccine as well as a growing number of newer vaccines. When I was practicing neurosurgery, the hospitals had an automatic written order on all older patients' charts mandating a flu vaccine, unless it was countermanded by the physician, which I always did. Now, the flu shots are being administered in malls, tents, and every available site health authorities can muster. Often, propaganda from public health is not truthful and uses scare tactics to frighten the elderly into getting the shots (e.g., the bold lie that 36,000 elderly die from the flu every year—in the only large-scale published retrospective U.S. study [68], the reported annual numbers of flu-related deaths were in the range of 600 to 3,000 during the period from 1979 to 2000).

Moreover, studies have shown that the influenza vaccines are not effective in preventing those vaccinated from getting influenza [68,69].

As you age, your immune system, including that special immune system in your brain, releases significantly more inflammatory immune cytokines than when you were younger. This serves to prime the microglia, as discussed. So, when you receive your first flu shot, your microglia overreact and they do so for a very long period—perhaps years. In fact, many elderly report that the flu shot gave them the flu. Proponents of vaccine retort with a condescending laugh, "That it is impossible because the flu vaccine contains killed flu viruses." In truth, what these people are reporting is a prolonged, intense "sickness behavior" response to the vaccine. To the body, it is worse than getting the flu. Remember, no one is accurately recording adverse vaccine reactions, including the number of elderly who die after getting the flu shot—especially if death occurs months later, which is plausible with sickness behavior, especially if the individual had a preexisting chronic illness or was infirm.

Here is the shocking truth. With the elderly already having increased inflammatory cytokine levels both systemically and in their brain, stimulating these primed microglia so that a chronic overstimulation of the brain's immune system is triggered will not only increase their risk of developing one of the neurodegenerative diseases, but will also substantially increase their risk of developing major depression. This, in turn, also dramatically increases their risk of suicide and even homicide.

Anxiety is a major problem with depression, and vaccination(s) can greatly worsen the condition. In fact, vaccination, especially multiple vaccinations, will maintain the brain in a state of inflammation that will be self-perpetuating, because the excess release of glutamate in the brain as well as dietary glutamate serve to further enhance microglial activation and excitotoxicity [40,41].

Those prone to developing one of the neurodegenerative diseases, such as Alzheimer's disease or Parkinson's disease, will be at a drastically increased risk as we have seen experimentally in animals that developed neurologic worsening following exposure to subtoxic concentrations of environmental toxins and vaccination [25,43].

Studies have shown that the concentration of pesticides that are used in homes are sufficient to trigger Parkinson's disease in susceptible individuals. Vaccinations, as these studies have shown, greatly increase risk. Most doctors are completely unaware of this important research.

Keep in mind that "health authorities" urge the elderly to get the flu vaccine each and every year. This will keep the microglia in a *primed* and even *activated* state continuously. Recently, neurologists announced that the incidence of neurodegenerative disease had been grossly underestimated and that neurological diseases of the elderly were increasing at a frightening rate. They have no explanation. Over the last three decades the number of elderly receiving yearly flu vaccines has risen from 20% before 1980 to over 60% today.

If these statistics were not depressing enough, now the public health authorities and medical specialty societies are adding a whole new set of vaccines for those 50 years and older, including the pneumococcal and meningococcal vaccines. What is being completely ignored by the promoters of these vaccines is the effect of multiple doses of immune adjuvant that accompany each of these vaccines.

Let's say you see your doctor and he talks you into getting the flu vaccine, the pneumococcal, and meningococcal vaccines all during the same office visit. That way, he can save you the time and costs associated with extra office visits. What your doctor ignores is that he is giving you three doses of *powerful immune adjuvants* all in one sitting, which means that your body and brain are assaulted by a massive dose of powerful immune activators that have been proven to activate the brain's immune system to dangerous levels and do so for very long periods. This reaction can even occur when only a single vaccine dose is administered. Proof of this mechanism exists not only in animal studies, but in humans as well.

Mercury and aluminum

There are other ways that vaccines can reap havoc in the brain. Most vaccines contain aluminum compounds. A multitude of studies have shown that aluminum, especially if combined with fluoride, is a powerful brain toxin which accumulates in the brain [43]. With each vaccine injection, a dose of aluminum is given. These yearly inoculations with adjuvants containing aluminum compounds result in aluminum accumulating not only at the site of the injection, but traveling to the brain, where it enters neurons and glial cells (astrocytes and microglia). A number of studies have shown that aluminum can activate microglia and do so for long periods [44–47]. This means that the aluminum in your vaccination is priming your microglia to overreact. The next vaccine acts to trigger the enhanced inflammatory reaction and the release of the excitotoxins, glutamate, and quinolinic acid.

You must also appreciate that any infection, stroke, head injury, or other toxin exposure will also magnify this inflammatory brain reaction initially triggered by your vaccines. Studies have now indicated that the more one's immune system is activated, the more likely one will suffer from one of the neurodegenerative diseases [48].

Mercury is also a powerful activator of brain microglia and can do so in extremely low concentrations—in low nanomolar

amounts [49]. Because of its numerous reactions with sulfhydryl compounds in the body (which are ubiquitous), mercury can poison a number of enzymes both systemically and in the brain. Of special concern is the ability of mercury, especially ethylmercury (the kind found in Thimerosal, which is 50 weight-% mercury used as a preservative, or in “trace” amounts, in some vaccines) to inhibit the regulation of brain glutamate levels [50,51]. It accomplishes this dysregulation by inhibiting the glutamate transfer proteins that control the removal of glutamate from outside the neuron, where glutamate does its harm.

In essence, Thimerosal and its mercury-containing metabolites, in the concentrations being injected with vaccines, trigger excitotoxicity, increase brain free radicals and lipid peroxidation products, inhibit critical brain enzymes, inhibit antioxidant enzymes, and impair DNA repair capability. Even the “trace” (reduced) Thimerosal-containing flu vaccine doses contain sufficient quantities of mercury to do all of these things. Moreover, each flu vaccine injection adds to the mercury load supplied by previously administered vaccines, because some part (1% to 25%) of the mercury from Thimerosal progressively accumulates in your brain where its estimated half-life is about twenty years [70].

In addition, the aluminum adjuvants in some vaccines also prime microglia and, when combined with mercury poisoning of the brain’s immune system from, for example, a subsequent flu shot, can be more toxic to the brain than mercury by itself because of the aluminum adjuvant indirectly priming the brain’s immune system. Now, if this is not enough, we also have to consider the contamination of vaccines with foreign viruses and viral components. Studies have shown that this is not a rare occurrence, with up to 60% of vaccines being contaminated in one study of several major manufactured vaccines [52,53]. When confronted with this fact, vaccine proponents just shrug their shoulders and say, “We don’t think these things are harmful.”

Yet, the studies say otherwise. It has been found that insertion of *viral fragments*, not even the whole virus, is sufficient to trigger the brain’s microglial system and subsequent excitotoxicity, leading to progressive brain degeneration [54,55]. This is accepted to be the mechanism by which the HIV virus causes dementia in a great number of AIDS victims [56–58]. Fragments of the virus (gp140 and Tat) are engulfed by the microglia and this triggers chronic brain inflammation and excitotoxicity. The herpes virus and measles virus can do the same thing [59–61].

Danger of live virus vaccines

A number of studies have shown that live viruses used in vaccines can enter the brain and reside there for a lifetime. One such study, in which autopsied elderly were examined for the presence of the measles virus, found that 20% of the brains had live measles viruses and 45% of other organs were infected [62]. These viruses were highly mutated, indicating that they could be as potent, or even more virulent, than other natural measles virus strains. Worse yet, in most cases these persistent, chronic viruses cause a smoldering destruction of tissues without the obvious symptoms of infection.

Live virus vaccines are made using a process to attenuate (or weaken) the pathogenic or disease-causing virus by passing it through a series of cultures. The problem is that the reverse can also happen within the body. Studies have shown that when we produce free radicals in our body (and we produce substantial amounts of such radicals over a lifetime), these can mutate the viruses residing in our tissues. This was found in the autopsy study referred to above.

Likewise, these viruses can trigger brain inflammation and degeneration—that is, there exist a chronic degeneration of the brain over years or decades [63–65]. Because the resulting condition is so far separated from the time of administration of the original vaccine, physicians attribute the degeneration to old age or heredity—anything but the vaccines.

Virologists are also concerned that such mutated live viruses can also infect other people, leading to outbreaks of disease totally unsuspected by health authorities.

Conclusion

Current recommendations by the CDC for adult vaccinations include a total of 14 separate inoculations with infectious agents and powerful immune adjuvants [66]. To be fair, some of these are for special medical risks and conditions, such as high-risk behaviors, illegal drug use, and HIV infected individuals. If we eliminate these, women will be exposed to 10 inoculations and men 7, should they follow the CDC guidelines, for which many doctors advocate.

According to CDC recommendations, multiple vaccinations for a single disease are separated by no more than 4 weeks, which is sufficiently close together to produce priming and subsequent hyperactivation of brain microglia. We have seen that this can trigger a smoldering process of brain inflammation and excitotoxicity that may not only result in depression, anxiety, and high suicide rates, but can increase one’s risk of developing one of the neurodegenerative diseases as well.

We have also seen that in many cases a person will be injected with several vaccines during a single office visit and that this means their body is exposed to a very large dose of immune adjuvants. Compelling studies, using many animal species as well as humans, have shown that this overactivates the brain’s inflammatory mechanism, and this can last for years.

In addition, several additives to vaccines, such as mercury and aluminum compounds, are powerful brain toxins that are known to accumulate in the brain over decades and can trigger brain inflammatory/excitotoxic mechanisms. Vaccine contaminants, such as bacteria, mycoplasma, and viral fragments can also produce prolonged brain inflammation and neurodegeneration.

Because the elderly already have high levels of inflammatory cytokines, they are at a special risk. The very young (babies and small children) are at a high risk because their brains are undergoing the most rapid development at the very time they receive the greatest number of vaccinations—the first two years of life. In fact, they receive *24 vaccines during the first year of life*, one of which contains a full pediatric dose of mercury. Like adults, children receive many inoculations (up to 9 inoculations) during one office visit. This is insane and in my estimation, criminal.

Nasal flu vaccines are even worse because they introduce a live virus into the nasal passages which can then travel along the olfactory nerves, leading to the very portion or area of the brain first and most severely affected by Alzheimer's disease. A number of studies have shown that viruses and bacteria can pass along this route to the brain. In fact, in one study, scientists sprayed a bacterium into the nose of mice and observed a rapid development of Alzheimer's type plaques in the mouse's brain [66].

So, what should older people do?

First, studies have shown that the primary cause of immune deficiency in the elderly is purely dietary. The carotenoids, such as beta-carotene, alpha-carotene, canthaxanthin, lutein, and lycopene significantly enhance the immunity of the elderly. Zinc, magnesium and selenium are also essential. One should also avoid omega-6 oils (the vegetable oils: corn, safflower, sunflower, canola, soybean and peanut oils), since they greatly enhance inflammation and depress immunity. The EPA component of fish oils (omega-3 oils) is also a powerful immune suppressant. DHA is not. A healthy immune system means that you can fight infections efficiently and rapidly.

Regular exercise, such as brisk walking or weight exercises three to five times a week also boost immunity, while extreme exercise suppresses immunity. Exercise protects the brain from aging effects and from degeneration. Sugar and refined carbohydrates also suppress immunity and inflame the brain.

Adequate sleep is also vital to both brain health and good immune function. Public health officials and spokesmen for the major medical societies are not being truthful about vaccine safety. We now possess sufficient information from a great number of studies to halt this disastrous vaccine policy. We are facing a medial disaster in this country, which is already well on its way.

References

- [1] Dantzer R, Wollman E, Yirmiya R. Cytokines, stress and depression. *Adv Med Biol* 1999; 461:317–29.
- [2] Kent S, Bluthé R-M, Kelly KW, Danzer R. Sickness behavior as a new target for drug development. *Trends Pharmacol Sci* 1992;13:24–8.
- [3] Charlton BG. The malaise theory of depression: major depressive disorder in sickness behavior and antidepressants are analgesic. *Med Hypotheses* 2000;54:126–30.
- [4] Dantzer R. Cytokine-induced sickness behavior: where do we stand? *Brain Behav Immunol* 2001;15:331–87.
- [5] Larson SJ, Dunn AJ. Behavioral effects of cytokines. *Brain Behav Immunol* 2001;15:371–87.
- [6] Conner TJ, *et al.* Depression stress immunological activation: the role of cytokines in depressive disorders. *Life Sciences* 1998;62:583–606.
- [7] Zhu C-B, Blakely RD, Hewlett WA. The proinflammatory cytokines interleukin-1 β and tumor necrosis factor- α activate serotonin transporters. *Neuropsychopharmacology* 2006;31:2121–31.
- [8] Capuron L, Ravaud A, Neveu PJ, *et al.* Association between decreased serum tryptophan concentrations and depressive symptoms in cancer patients undergoing cytokine therapy. *Molecular Psychiatry* 2002;7:468–73.
- [9] Palucha A, Pilc A. The involvement of glutamate in the pathophysiology of depression. 2005;18:262–8.
- [10] Paul IA, Skolnick P. Glutamate and depression: clinical and preclinical studies. *Ann NY Acad Sci* 2003;1003:250–72.
- [11] Pittenger C, *et al.* The NMDA receptor as a therapeutic target in major depressive disorder. *CNS Neurol Disord Drug Targets* 2007;6:101–15.
- [12] Swab DF, Bao AM, Lucassen PJ. The stress system in the human brain in depression and neurodegeneration. *Aging Res Rev* 2005;4:141–94.
- [13] McQueen GM, Campbell S, McEwen BS, *et al.* Causes of illness, hippocampal function, and hippocampal volumes in major depression. *Proc Natl Acad Sci USA* 2003; 100: 1387–92.
- [14] Palucha A, Pilc A. On the role of metabotropic glutamate receptors in the mechanisms of action of antidepressants. *Pol J Pharmacol* 2002; 54: 581–86.
- [15] Paul IA, Skolnick P. Glutamate and depression: clinical and preclinical studies. *Ann NY Acad Sci* 2003; 1003:250–72.
- [16] Pittenger C, Sanacora G, Krystal JH. The NMDA receptor as a therapeutic target in major depressive disorder. *CNS Neurol Disord Drug Targets* 2007;6:101–15.
- [17] Shum FW, Wu LJ, Zhao MG, *et al.* Alteration of cingulate long-term plasticity and behavioral sensitization to inflammation by environmental enrichment. *Learn Mem* 2007;14:304–12.
- [18] Shanley LJ, Irving AJ, Harvey J. Leptin enhances NMDA receptor function and modulates hippocampal synaptic plasticity. *J Neuroscience* 2001;21:1–6.
- [19] Kiecolt-Glaser JK, Preacher KJ, MacCallum RC, *et al.* Chronic stress and age-related increases in the proinflammatory cytokine IL-6. *Proc Natl Acad Sci USA* 2003;100:9090–5.
- [20] Lue LF, Rydel R, Brigham EF, *et al.* Inflammatory repertoire of Alzheimer's disease and nondemented elderly microglia in vitro. *Glia* 2001;35:72–9.
- [21] Streit WJ, Sammons NW, Kuhns AJ, Sparks DL. Dystrophic microglia in the aging human brain. *Glia* 2004; 45:208–12.
- [22] Godbout JP, *et al.* Exaggerated neuroinflammation and sickness behavior in aged mice after activation of the peripheral innate immune system. *The FASEB J* 2005;19:1329–31.
- [23] Mrak RE, *et al.* Glial cytokines and Alzheimer's disease: Review and pathogenic implications. *Human Pathol* 1995;26:816–23.
- [24] Kim YS, Joh TH. Microglia, major players in the brain inflammation: their role in the pathogenesis of Parkinson's disease. *Exp Mol Medicine* 2006;38; 333–47.
- [25] Gao H-M *et al.* Synergistic dopaminergic neurotoxicity if the pesticide rotenone and inflammogen lipopolysacchride: relevance to the etiology of Parkinson's disease. *J Neurosciences* 2003;23:1228–36.
- [26] Renault PF, *et al.* Psychiatric complications of long-term interferon- α therapy. *Arch Internal Medicine* 1987;147:1577–80.
- [27] Adams F *et al.* Neuropsychiatric manifestations of human leukocyte interferon therapy in patients with cancer. *JAMA* 1984;252:938–41.
- [28] Danzer R, O'Connor JC, Freund GC, *et al.* From inflammation to sickness and depression: when the immune system subjugates the brain. *Nature Rev/Neuroscience* 2008;9:46–57.
- [29] Klatschmidt C, *et al.* Stimulation of ionotropic glutamate receptors activates transcription factor NF κ B in primary neurons. *Proc Nat Acad Sci USA* 1995;92:9618–22.
- [30] Tkenuchi H, Jin S, Wang J, *et al.* Tumor necrosis factor- α induces neurotoxicity via glutamate release from hemichannels of activated microglia in an autocrine manner. *J Biol Chem* 2006;281; 21362–8.
- [31] Pearson VL, Rothwell NJ, Toulmond S. Excitotoxic brain damage in the rat induces interleukin-1 β protein in microglia and astrocytes: correlation with the progression of cell death. *Glia* 1999;25:311–23.
- [32] Frenois F, Moreau M, O'Connor J, *et al.* Liposacchride induces delayed Fos/DeltaFosB immunostaining within the mouse extended amygdala, hippocampus and hypothalamus, that parallel the expression of depressive-like behavior. *Psychoneuroendocrinology* 2007;32:516–31.
- [33] van Dam AM, Browns M, Louise S, Berkenbosch F. Appearance of interleukin-1 in macrophages and in ramified microglia in the brain of endotoxin-treated rats: a pathway for the induction of non-specific symptoms of sickness? *Brain Res* 1992;588:291–6.
- [34] Quan N, Stern EL, Whiteside MB, Herkenham M. Induction of proinflammatory cytokine mRNAs in the brain after peripheral injection of sub-septic doses of lipopolysacchride in the rat. *J Neuroimmunol* 1999;93: 72–80.
- [35] Muller N, Schwarz MJ. The immune-mediated alteration of serotonin and glutamate towards an integrated view of depression. *Mol Psychiatry* 2007; 12:988–1000.
- [36] Comrinck MI, Perry VH, Cunningham C. Peripheral infection evokes exaggerated sickness behavior in preclinical murine prion disease. *Neuroscience* 2002;112:7–11.
- [37] Blaylock RL. Interaction of cytokines, excitotoxins, and reactive nitrogen and oxygen species in autism spectrum disorders. *JANA* 2003;6:21–35.
- [38] Kim W-G, Mohny RP, Wilson B, *et al.* Regional difference in susceptibility to lipopolysacchride-induced neurotoxicity in the rat brain.: role of microglia. *J Neuroscience* 2000;20:6309–16.
- [39] McGeer PL, Schwab C, Parent A, Doudet D. Presence of reactive micro-

- glia in monkey substantia nigra years after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine exposure. *Ann Neurol* 2003 Nov.;54:599–604.
- [40] Blaylock RL. Central role of excitotoxicity in autism. *JANA* 2003;6:7–19.
- [41] Blaylock RL. Food additive excitotoxins and degenerative brain disorders. *Medical Sentinel* 1999;4:212–5.
- [42] Dyatlov VA *et al.* neonatal lead exposure potentiates sickness behavior by *Listeria monocytogenes* infection in mice. *Brain Behav Immun* 2002; 16:477–92.
- [43] Fattoretti P, Bertoni-Freddari C, Biliotti M, *et al.* The effect of chronic aluminum (111) administration on the nervous system of aged rats: clues to understanding its suggested role in Alzheimer's disease. *J Alzheimer's Dis* 2003;5:437–44.
- [44] Campbell A. Inflammation, neurodegenerative diseases, and environmental exposures. *Ann NY Acad Sci* 2004; 1035: 117–32.
- [45] Campbell A, Becaria A, Lahiri DR, *et al.* Chronic exposure to aluminum in drinking water increases inflammatory parameters selectively in the brain. *J Neurosci Res* 2004;75:565–72.
- [46] Platt B, Fiddler G, Riedel G, Henderson Z. Aluminum toxicity in the rat brain: histochemical and immunocytochemical evidence. *Brain Res Bull* 2001;55:257–67.
- [47] Tsunoda M, Sharma RP. Modulation of tumor necrosis factor alpha expression in mouse brain after exposure to aluminum in drinking water. *Arch Toxicol* 1999;73:419–26.
- [48] Perry VH *et al.* The impact of infection on the progression of neurodegenerative disease. *Nature Rev Neuroscience* 2003;4:103–12.
- [49] Charleston JS, Body RL, Bolender RP, *et al.* Changes in the number of astrocytes and microglia in the thalamus of the monkey *Macaca fascicularis* following long-term subclinical methylmercury exposure. *Neurotoxicology* 1996;17:127–38.
- [50] Kim P, Choi BH. Selective inhibition of glutamate uptake by mercury in cultured mouse astrocytes. *Yonsei Med J* 1995;36:299–38.
- [51] Juarez BI, Martinez ML, Montante M, *et al.* Methylmercury increases glutamate extracellular levels in frontal cortex of awake rats. *Neurotoxicol Teratol* 2002;24:767–71.
- [52] Giaugaspero M, Vacirca G, Harasawa R, *et al.* Genotypes of pestivirus RNA detected in live virus vaccines for human use. *J Vet Med Sci* 2001; 63:723–33.
- [53] Harasawa R, Tomiyama T. Evidence of pestivirus RNA in human vaccines. *J Clin Microbiol* 1994;32:1604–5.
- [54] Brown DR, Schmidt B, Kretschmar HA. Role of microglia and host prion protein in neurotoxicity of a prion protein fragment. *Nature* 1996; 380:345–7.
- [55] Forioni G, *et al.* Neurotoxicity of a prion protein fragment. *Nature* 1993; 362:543–6.
- [56] Hult B, Chang G, Masliah E, Everall I. Neurobiology of HIV. In *Rev Psychiatry* 2008;20:3–13.
- [57] Erdmann N, Zhao J, Lopez AL, *et al.* Glutamate production by HIV-1 infected human macrophages is blocked by the inhibition of glutaminase. *J Neurochem* 2007;102:539–49.
- [58] Glass JD, Wesselingh SL. Microglia in HIV-associated neurological diseases. *Microsc Res Tech* 2001;54:95–105.
- [59] Eastman CL, *et al.* Increased brain quinolinic acid production in mice infected with a neurotropic measles virus. *Exp Neurol* 1994;125:119–24.
- [60] Anderson T *et al.* NMDA-receptor antagonist prevents measles virus-induced neurodegeneration. *Eur J Neurosci* 1991;3:66–71.
- [61] Dewey RA, Morrissey G, Cowsill CM, *et al.* Chronic brain inflammation and persistent herpes simplex virus 1 thymidine kinase expression in survivors of syngenic glioma treated by adenovirus-mediated gene therapy: implication for clinical trials. *Nat Med* 1999; 5: 1256–63.
- [62] Katayama Y, *et al.* Detection of measles virus nucleoprotein mRNA in autopsied brain tissues. *J General Virology* 1995;76:3201–4.
- [63] Nicolson GL *et al.* High frequency of systemic mycoplasma infections in Gulf War Veterans and civilians with amyotrophic lateral sclerosis. *J Clin Sci* 2002;9:525–9.
- [64] McGeer PL, McGeer EG. Local neuroinflammation and progression of Alzheimer's disease. *J Neurovirology* 2002;8:529–38.
- [65] Nakai Y, *et al.* Apoptosis and microglial activation in influenza encephalopathy. *Acta Neuropath (Berl)* 2003;105:233–9.
- [66] Vaccine Excepients and Media Summery Center for Disease Control and Prevention. (Also source for recommended vaccines for adults and children.)
- [67] Boelen E, Stassen FR, van der Ven AJ, *et al.* Detection of amyloid beta aggregates in the brain of BALB/c mice after Chlamydia pneumonia infection. *Acta Neuropathol* 2007;114:255–61.
- [68] Geier DA, King PG, Geier MR. Influenza Vaccine: Review of effectiveness of the U.S. immunization program, and policy considerations. *Journal of American Physicians and Surgeons* 2006 Fall;11(3):69–74.
- [69] Simonsen L, Reichert TA, Viboud C, *et al.* Impact of influenza vaccination on seasonal mortality in the U.S. elderly population. *Arch Intern Med* 2005; 165: 265–72.
- [70] Sugita M. The biological half-time of heavy metals. The existence of a third, “slowest” component. *Int Arch Occup Environ Health* 1978;41(1): 25–40.

Editorial Note

Vitamin D has been found to be highly protective against influenza. The need for extra vitamin D-3 is supported by two relatively new research papers:

Cannell JJ, Vieth R, Umhau JC, Holick MF, Grant WB, Madronich S, Garland CF, Giovannucci E. Epidemic influenza and vitamin D. *Epidemiol. Infect.* 2006 Dec;134(6):1129–40.

Travera-Mendoza LE, White JH. Cell defenses and the sunshine vitamin. *Scientific American* 2007 Nov.;2007:62–72.