Lucija Tomljenovic, PhD
Neural Dynamics Research Group,
Dept. of Ophthalmology and Visual Sciences
University of British Columbia
828 W. 10th Ave, Vancouver, BC, V5Z 1L8
tel: 604-875-4111 (68375)

Regarding H.527

Distinguished Members of the Vermont House,

The argument of forcing a parent to vaccinate their child in the name of the "greater good argument" is flawed both scientifically and ethically. Firstly, all drugs are associated with some risks of adverse reactions. Because vaccines represent a special category of drugs which are by and large given to healthy individuals, and for prophylaxis against diseases to which an individual may never be exposed, the margin of tolerance for side effects is very narrow (in fact, the U.S. Food and Drug Administration (FDA) concurs with this point [1]) and careful assessment of risks versus benefits essential in deciding whether one should be vaccinated or not. Removing the "philosophical exemption" as a means to opt out from vaccination will put vulnerable but otherwise healthy individuals at risk of serious adverse reactions to vaccinations. Such an outcome should be of concern since cases of permanent neurodevelopmental disabilities and deaths following vaccination in children with underlying genetic and other susceptibilities have been firmly established in scientific literature [2-4]. Please consider carefully whether you wish to be responsible for such potential outcomes should you facilitate this legislation to come to pass.

Secondly, medical ethics demand that vaccination should be carried out with the participant's full and informed consent. This necessitates an objective disclosure of the known or foreseeable vaccination benefits and risks. The way in which pediatric vaccines are often promoted by various health authorities indicates that such disclosure is rarely given from the basis of best available knowledge but rather, largely unproven and/or untenable assumptions on both, vaccine safety and effectiveness. I shall herein elaborate on these arguments.

Is Vaccine Safety Evidence "Rock Solid"?

The statement by Dr Chen that "the science behind vaccination safety is rock solid" is factually inaccurate and contradicts a large body of scientific literature published on this subject [3-35]. As with any medication, vaccines can carry risks of adverse reactions (ADRs). However, in spite of the widespread notion that vaccines are largely safe and serious adverse complications are extremely rare, a close scrutiny of the scientific literature does not support this view [10-12]. For example, to date the clinical trials that could adequately address vaccine safety issues have not been conducted (i.e., comparing health outcomes in vaccinated versus non-vaccinated children). The lack of such controlled trials may be because historically, vaccines have been *assumed* safe [12]. There is also a view that conducting such trials would be extraordinarily difficult or unethical; the first is simply not correct, the second is not a scientific issue *per se*.

It is also often *assumed* that vaccines face a tougher safety standard than most pharmaceutical products. However, according to the U.S. FDA, "*Historically, the non-clinical safety assessment for preventive vaccines has often not included toxicity studies in animal models. This is because vaccines have not been viewed as inherently toxic"* [emphasis added] [1] This is a startling admission from an Agency which according to its own mission statement is *"responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs"*[36]. Essentially, what the FDA workshop [1] revealed is that not only are vaccines not adequately evaluated for toxicity but also, that the reason for such an oversight rested on a belief rather than scientific evidence. *S*cience is *not* a religion in which dogmatic statements of faith can replace adequately powered, controlled, longitudinal vaccine safety studies in animals and people. Furthermore, such assumptions of safety, in the absence of actual experimental data, are not only dangerous but have historically hampered serious scrutiny of potential vaccine harms.

To illustrate a recent example of grave consequences that resulted from pushing a poorly tested vaccine to young children, note that there have been a large numbers of major ADRs from seasonal influenza vaccines. Consequently, they have been suspended for use in children under five years of age in Australia. In a series of *Rapid Responses* addressing this issue, published in *British Medical Journal*, titled "*Adverse events following influenza vaccination in Australia-should we be surprised?"* Collignon (Director of Infectious Diseases & Microbiology at Australian National University) and colleagues from the Cochrane Collaboration review panel concluded: "*There is poor evidence on how well influenza vaccines prevent any influenza complications in children and other age groups. There is good evidence that influenza vaccines study reports cherry pick results and achieve spurious notoriety. Exposing human beings to uncertain effects is a risky business*" [25].The authors also noted that worldwide, the recommendations from public health authorities regarding influenza vaccination has been "misguided" [emphasis added] [26].

It important to note that even those in the scientific community who are strong proponents of vaccinations have come to question the scientific legitimacy of "one-size fits all" vaccination practices [37]. For example, Poland (Editor in Chief of the journal *Vaccine* and co-author of "*The age-old struggle against the antivaccinationists*" [38]) and colleagues rightly ask whether "*with the advances coming from the new biology of the 21st Century*", it is time to consider "*how might new genetic and molecular biology information inform vaccinology practices of the future?*" [37]. In light of this question Poland et al. conclude that "one-size fits all" approach for all vaccines and all persons should be abandoned. According to Poland, this conclusion applies to both vaccine efficacy, as well as safety [37]. Regarding the latter, the widely held view that serious vaccine-related ADRs are rare needs revision, as current worldwide vaccination policies indeed operate on "one-size fits all" *assumption*. This assumption persists despite the fact that historically, vaccine trials have routinely excluded vulnerable individuals with a variety of pre-existing conditions (i.e., premature birth, personal or family history of developmental delay or neurologic disorders including epilepsy/seizures, hypersensitivity to vaccine constituents etc. [39-43]). Because of such selection bias, the occurrence of serious ADRs resulting from vaccinations may be considerably underestimated. As mentioned previously, such an outcome should be of concern in view of documented evidence of permanent neurodevelopmental disabilities and deaths following vaccination in children with underlying genetic and other susceptibilities [2-4]. Poland et al.'s current data may thus have far broader implications for understanding vaccines, not only in terms of efficacy and the desired immune response, but also in terms of safety. Indeed, vulnerable populations will neither have the same antibody response nor the same level of tolerance to serious ADRs as non-vulnerable populations [37,44].

The Quality of Existing Vaccine Safety Data

A further obfuscation of the actual rate of serious vaccine-associated ADRs may also be due to methodological inadequacy of existing vaccine trials (i.e, the frequent exclusion of individuals with potential pre-existing susceptibilities to vaccine-associated ADRs) [12], and due the fact that the vast majority of such trials use an aluminum adjuvant-containing placebo or another aluminum-containing vaccine as the "control group" [45]. That aluminum is a demonstrated neurotoxin has been known for over 100 years [46] and in this context, it is becoming clear to a number of investigators that its use as a placebo control is scientifically untenable [45,47].

Furthermore, with regard to the studies which allegedly demonstrably show no link between autism and vaccines, it has to be emphasized that once such studies undergo proper expert scrutiny, the "evidence" against the link becomes rather flimsy. In reviewing the published literature on measles-mumps-rubella (MMR) vaccine (139 studies), the respected Cochrane Collaboration review panel concluded that, "*The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate"* [emphasis added] [48]. Moreover, none of the 31 studies that were included in the review met the Cochrane Collaboration's methodological criteria. More specifically, referring to the 2001 Fombonne and Chakrabarti study [49] which was widely regarded by medical health authorities as most *persuasive* in disproving the link between the MMR vaccine and autism, the Cochrane Collaboration commented the following: *"The number and possible impact of biases in this study was so high that interpretation of the results is impossible" [48].*

Although the Cochrane Review on the safety of MMR concluded that there was no credible link between MMR vaccination and autism and Crohn's disease, as pointed out earlier, the majority of the studies included in the evaluation were methodologically inadequate. The question thus is what "credible" or "rock solid" evidence can be derived from inadequate studies?

Demonstrated Toxicity of Vaccine Constituents

Vaccines contain known neurotoxins (i.e., mercury, aluminum, formaldehyde), potent adjuvants designed to hyperstimulate the immune system, as well as various antigenic compounds [10,50] albeit all in relatively small amounts. Thus a typical vaccine formulation contains all the necessary biochemical components to induce both autoimmune as well as neuoroimmune disorders. The question is not whether these compounds are in vaccines or if they are toxic, rather *if* in such concentrations alone or combined, they can harm the nervous and other systems. Experimental evidence indeed shows that some of these constituents (mercury and aluminum) can cause long-term neurological impairments in animal models when individually administered in vaccine-relevant human exposures [7,51-57].

Furthermore, data also demonstrate that over-stimulating the host's immune system by repeated immunization with immune antigens and/or adjuvants inevitably leads to autoimmunity even in genetically non-susceptible animals [58,59]. Specifically, simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity [59]. Yet in spite of these observations, according to the current U.S. immunization schedule by the time children are 4 to 6 years old, they will have received a total of 126 antigenic compounds along with high amounts of Al adjuvants [10].

Given the scarcity of evidence of safety of the combined pediatric schedule and the fact that administration of only a few vaccines in human adults can lead to brain dysfunction and a variety of autoimmune conditions [8,16,17,19], the concerns about the overall safety of current childhood vaccination programs are scientifically plausible and thus require urgent consideration [10].

The Biological Basis for Vaccine Toxicity

Despite the prevalent view that peripheral immune responses do not affect brain function, overwhelming research evidence clearly points to the contrary. Namely, it is now firmly established that there is a highly dynamic functional network of interactions between the brain and the immune system which plays crucial roles in immune regulation, brain function and maintenance of general homeostasis [60-68]. In turn, perturbations of this "immuno-neuroendocrine" network have been demonstrated in a variety of autoimmune/inflammatory conditions [69-78], as well as neurodevelopmental disorders, including autism [79]. It is also well established that immune molecules play integral roles in shaping of the developing central nervous system (CNS) [80-89]. Notably, the very same components of the immune system that regulate proper brain development and function [80-89] are also heavily targeted for impairment by a variety of immune stimuli including vaccines [10].

Altogether, these observations may explain why peripheral stimulation of the immune system by bacterial and viral mimetics during early development in animal models is sufficient to cause a variety of adverse developmental outcomes including long-term immune abnormalities as well as symptoms strikingly similar to autism spectrum disorders (ASD) [90-98]. In spite of this evidence, pediatric vaccinations which are clearly analogous in nature to the above cited examples of peripheral immune system stimulation, are routinely dismissed as a plausible cause of the growing burden of neurodevelopmental and immune abnormalities in children.

In addition, vaccines contain an array of known toxicants which may in their own right act as neuro-immune and endocrine disruptors (i.e., mercury, aluminum, polysorbate 80, phenol red, phenoxyethanol, formaldehyde, MSG, various antimicrobials, cell components of monkey tissues, calf skin and fetal aborted cell tissue, contaminant recombinant DNA, host-tissue infectious agents, etc). Although the significance of these potentially toxic vaccine constituents is frequently dismissed because they are only present in trace amounts [99,100], it is important to note that long-term adverse immune and neurological outcomes in animal models have been demonstrated following vaccine-relevant exposures to individual compounds such as aluminum [51-53] and mercury [7,54-57].

Although, several studies have examined the *in vivo* toxicity of individual vaccine constituents and individual vaccines, the entire combined U.S. pediatric schedule has never been thoroughly tested for toxicity in humans or animal models. The possible exception to the latter is the study by Hewitson et al. [6] which showed that rhesus macaque infants vaccinated according to the complete U.S. pediatric schedule failed to undergo normal maturational changes in amygdala volume that were otherwise observed in un-vaccinated animals [6]. The amygdala is a key centre in the brain responsible for emotional learning [101] and is frequently impaired in autistic individuals [102,103].
Currently, the absence of direct studies on the risks of cumulative vaccine exposure is a gap that has been filled with the experimentally unsupported assumption that the pediatric vaccine schedule is safe. In view of proven toxicity of individual vaccine constituents [7,51-57] such assumptions are disturbing and should be urgently re-evaluated.

Vaccines and Autism

The assertion that vaccine-autism concerns rest merely on spurious claims made by uneducated parents is in stark contrast with large body of scientific literature. As mentioned previously, extensive research data has underscored the tight connection between development of the immune system and that of the CNS, and thus the plausibility that disruption of critical events in immune development may play a role in neurobehavioral disorders including those of the autism spectrum [104-106]. Indeed, early-life immune challenges in critical windows of developmental vulnerability have been shown to produce long-lasting, highly abnormal cognitive and behavioral responses, including increased fear and anxiety, impaired social interactions, deficits in object recognition memory and sensorimotor gating deficits [55,56,94,96,107,108]. These symptoms are highly characteristic of autism.
It is thus indeed naive to assume that a manipulation of the immune system through an increasing number of vaccinations during sensitive periods of early development will not result in adverse neurological outcomes. Consistent with this, Shoenfeld and Cohen (world's leading experts in autoimmune diseases) noted that, ''vaccines have a predilection to affect the nervous system'' [emphasis added] [31]. Also, please refer to a number of publications we and others have authored on this subject (link between immune challenges and adverse neurological outcomes [10,91,92,94,109]). For specific publications on the links between vaccinations and autism, refer to the following citations [2,22,23,110-112].

Aluminum Adjuvants: What is Known About Their Safety?

With regard to the popular assertions that children obtain much more aluminum through regular diet than from routine vaccination and that therefore, vaccination does not represent a toxicological risk with respect to aluminum [99,100], although such opinions appear to be highly regarded, they contradict basic toxicological principles. For example, it should be obvious that the route of exposure which bypasses the protective barriers of the gastrointestinal tract and/or the skin will require a much lesser dose to produce a toxic outcome [47,112]. In the case of aluminum, research clearly shows that only ~0.25 % of dietary aluminum is absorbed into systemic circulation [113], while aluminum from vaccines may be absorbed at nearly 100% efficiency [114].
It is also not widely known that according to the World Health Organization (WHO) criteria, a large majority of children actually do exceed the safety standard for dietary aluminum [46]. Moreover, even regular dietary intake of aluminum can have long-term adverse consequences to the nervous system [46,115,116]. This is because aluminum is in fact highly toxic, and tends to selectively accumulate in specific areas of the brain [46]. In addition, according to the most recent toxicological report for aluminum prepared by the Agency for Toxic Substances and Disease Registry (ATSDR) [117], "There is a limited amount of information available on the toxicity of aluminum in children". The report also states that the effects of oral exposure to aluminum have not been "adequately investigated in healthy humans" [117]. Nonetheless, the ATSDR notes that, "there is a rather extensive database on the oral toxicity of aluminum in animals. These studies clearly identify the nervous system as the most sensitive target of aluminum toxicity" [117]. Of relevance, a recent study showed that autistic children have higher than normal levels of aluminum in the body (hair, blood and/or urine) [118].

Bottom line is that safety concerns regarding dietary aluminum in humans appear to have been prematurely dismissed, in the absence of relevant scientific evidence. Unfortunately, the same holds true for aluminum vaccine adjuvants [10,47,112]. For example, the consensus amongst the

participants of the *Aluminum in Vaccines* workshop (2002)[119] was that there existed "pervasive uncertainty", about what was still unknown concerning the use of aluminum in vaccines, such as"1) toxicology and pharmacokinetics, specifically the processing of aluminum by infants and children, 2) mechanisms by which aluminum adjuvants interact with the immune system and 3) the necessity of adjuvants in booster doses"[119]. In spite of these concerns, the workshop concluded that "the use of salts of aluminum as adjuvants in vaccines has proven to be safe and effective" [119]. Aluminum is neurotoxic [46,51,120,121] and inhibits prenatal and postnatal brain development in humans and experimental animals [122,123], and yet, to this date, the above items of "pervasive uncertainty" still remain largely unresolved [10,47,112].
Indeed, according to the statement of the WHO special Committee's report from 2005 on the Safety of Vaccine Adjuvants (http://www.who.int/wer/2005/wer8001.pdf):

"The Committee considered the safety of adjuvants used in vaccines. This hitherto neglected subject is becoming increasingly important given modern advances in vaccine development and manufacture." [emphasis added]

It is obvious from this publication that there was no good data in 2005 on this subject and the situation remains unchanged to this day, as evidenced from the lack of any updates on WHO website on the topic of vaccine adjuvants (http://www.who.int/vaccine_safety/topics/adjuvants/en/index.html).

The lack of good quality evidence on the safety of adjuvants is anything but reassuring, especially in the light of actual case studies which show serious adverse long-term, sequellae resulting from persistence of aluminum adjuvants in humans as well as animals. These include cognitive dysfunction [16], arthromyalgias, chronic fatigue and muscle weakness [15,124], demyelinating CNS disorders such as multiple sclerosis [13], peripheral neuropathies such as Guillain Barre [125], pseudolymphoma [30] etc. Since children receive much more aluminum from vaccines per kg of body weight than adults, they are at greater risk of aluminum-related neurotoxic effects. In summary, the widespread notion that aluminum adjuvants are safe is factually incorrect and at odds with experimental evidence.

In this regard, I would like to draw the attention to the latest special issue in the respectable journal *Lupus* dedicated to "ASIA" [Autoimmune/inflammatory syndrome induced by adjuvants], which was edited by one of the world's leading experts in autoimmunity Prof. Yehuda Shoenfeld. Prof Shoenfeld is the head of the Department of Medicine at the Tel Aviv University since 1984 (age 36). He has founded and is heading the Center for Autoimmune Diseases since 1985 - at the largest hospital in Israel- the Sheba Medical Center. He has authored more than 1500 papers in his career and is currently on the editorial board of 43 journals in the field of Rheumatology, and Autoimmunity. Much of the focus of his work has been on the toxic mechanisms by which vaccine adjuvants induce autoimmune diseases in humans. The contents of the special issue can be found here:

http://lup.sagepub.com/content/current

Prof. Christopher Shaw and I have authored a publication in this issue which specifically addresses the issue of aluminum adjuvant toxicity in pediatric populations [10].

Mercury (Thimerosal): Unresolved Safety Concerns

A significant association between exposure to thimerosal (49% ethylmercury-EtHg)-containing vaccines (TCVs) and neurodevelopmental disorders in children including autism, speech disorders, mental retardation, thinking abnormalities and personality disorders has been reported in some studies [22,23,126,127].

Alleged arguments for safety of EtHg which is present on thimerosal are primarily based on the notion that it has a shorter half-life in the human body than methyl-mercury (MetHg). In other words, EtHg is thought to be efficiently excreted from the body and therefore the *assumption* is that it does not represent a risk to the developing child, unlike MetHg which has been recognized as an important risk-factor for neurodevelopmental delays [128,129].

However, compelling experimental data from animal models unequivocally shows that low-dose exposure to thimerosal (in vaccine-relevant exposures) can harm the developing nervous system in a manner consistent with the pathology of autism [6,54-56]. Thus, despite claims to the contrary [99] the presence of thimerosal in vaccines should not be disregarded as a health risk for developing children [50].

Furthermore, in a landmark study comparing the toxicokinetics of EtHg and MetHg in infant macaques, Burbacher et al. [130] demonstrated that although EtHg indeed shows more efficient blood-clearance than MetHg, there was a much higher proportion of inorganic Hg in the brains of EtHg-exposed monkeys than in the brains of those exposed to MetHg (up to 71% vs. 10%). In addition, the average brain-to-blood concentration ratio was slightly higher for the EtHg-exposed monkeys. Notably, there was also a large difference in the blood Hg half-life compared with the brain half-life for the EtHg-exposed monkeys (6.9 days vs. 24 days), indicating that blood Hg may not be a good indicator of risk of adverse effects on the brain [130]. Overall, Burbacher et al.'s [130] data suggest that although the accumulation of mercury in the blood from TCV exposure is relatively small, accumulation in the brain from such exposures may still occur at potentially hazardous levels [50].

Herd Immunity: Can Infectious Diseases be Prevented by High-Vaccination Coverage?

The statement that high levels of vaccination prevent disease outbreaks is not accurate as infectious diseases do in fact occur even in fully vaccinated populations [131-133] as well as individuals [134] (see Table 1 for more examples). The likely reason for this is that vaccines primarily stimulate humoral immunity (antibody-based or Th2 responses) while they have little or no effect on cellular immunity (cytotoxic T-cells, Th1 responses), which is absolutely crucial for protection against viral as well as some bacterial pathogens [135,136]. This may be the reason why vaccine-induced immunities are transient, requiring booster shots, while naturally acquired immunity conferred by the cellular immune system in the absence of vaccination tends to be permanent. Taken together, these observations may explain why outbreaks of allegedly vaccine-preventable diseases do occur in fully vaccinated populations and why, immunity (or its absence) cannot be reliably determined on the basis of serologic determination (measure of antibody levels) [137], which is the most common measure of vaccine efficacy in clinical trials [40,42,138].

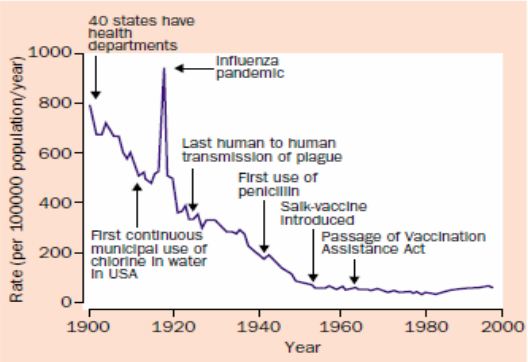
Table 1. Reports of infectious disease outbreaks despite high vaccination coverage.

From December 9, 1983, to January 13, 1984, 21 cases of measles occurred in Sangamon County, Illinois... The outbreak involved 16 high school students, all of whom had histories of measles vaccination after 15 months of age… The affected high school had 276 students and was in the same building as a junior high school with 135 students. A review of health records in the high school showed that all 411 students had documentation of measles vaccination on or after the first birthday, in accordance with Illinois law. This outbreak demonstrates that transmission of measles can occur within a school population with a documented immunization level of 100%.	*MMWR Morb Mortal Wkly Rep.* June 22, 1984; 33(24):349-51 [139]
During 2006, a total of 6584 confirmed and probable cases of mumps were reported to the Centers for Disease Control and Prevention...College campuses with mumps outbreaks included ones with 77% to 97% of students having had 2 doses of a mumps vaccine.	*Pediatr Infect Dis J.* 2008;27(10 Suppl):S75-9 [140]
The Czech republic has had a two dose MMR vaccination programme since 1987. The last outbreak of mumps was reported in 2002, but an increase in the number of mumps cases was observed in 2005, starting in October that year. In an 18 month period examined, 5,998 cases of mumps were notified, with a peak incidence in May of 2006. The highest incidence rate was observed in those in the age group of 15 to 19 years, in which 87% of the cases had received two doses of mumps vaccine.	*Euro Surveill.* 2008;13(16) [141]
Despite high levels of vaccination coverage against diphtheria, an ongoing outbreak of diphtheria has affected parts of the Russian Federation since 1990… an estimated 90% of children were fully vaccinated with four or more doses of	*MMWR Morb Mortal Wkly Rep.* Nov 5, 1993;42(43):840-841, 847 [133]

diphtheria toxoid by the time they entered school…The outbreak described in this report illustrates that, despite a high vaccination coverage rate among school-aged children, diphtheria can cause epidemic disease in developed countries.	
From January, 1988, to March, 1989, a widespread outbreak (118 cases) of poliomyelitis type 1 occurred in Oman. Incidence of paralytic disease was highest in children younger than 2 years (87/100,000) despite an immunisation programme that recently had raised coverage with 3 doses of oral poliovirus vaccine (OPV) among 12-month-old children from 67% to 87%.	*Lancet* 1991; 338 (8769): 715-720) [142]
Subclinical measles infection in vaccinated seropositive individuals in arctic Greenland. More than 90% of the total population was vaccinated and a 94-100% seroconversion was obtained.	*Vaccine;* 1998 7(4):345-8 [143]
"The rates of secondary immune response (SIR) and secondary vaccine failure (SVF) during a measles epidemic were evaluated…In conclusion, neither prior vaccination nor detectable SIR ensures protective immunity.	*J Clin Microbiol.* 1992; 30(7): 1778-1782 [144]
Results from two independent studies that both showed children faced a substantially increased rate of pertussis infection 4 or more years out from their fifth and final childhood vaccination... Recent surges in U.S. pertussis cases, which began in 2005, and then spiked even higher in 2010, implicated the acellular vaccine as the cause…It certainly caused the 2010 California epidemic, and it happened in Minnesota and Oregon, too. Waning immunity with acellular pertussis led to greater vulnerability in 7- to 10-year-olds...	*Internal Medicine News*. 22 Nov 2011 [145]

Vaccine- or Hygiene-Preventable Diseases?

The prevalent view that vaccines are the sole cause of the disappearance of infectious diseases requires intellectual caution because it has been clearly demonstrated that factors such as clean water and improved sanitation, as well as better nutrition, availability of antibiotics, greater access to health care, and technological advances in maternal and neonatal medicine) have also played a major impact on infectious disease incidence [146,147]. In fact, according to the U.S. Centers for Disease Control and Prevention(CDC), these measures accounted for 90% reduction in infant mortality and 99% reduction in maternal mortality since 1900 [146]. So clearly then, vaccines could not have played a major role in health as often claimed. This fact (of major reduction in mortality rates due to better sanitation measures prior introduction of vaccines) is also illustrated by a 2002 review in *Lancet Infectious Diseases* [147] which clearly shows that the crude death rate from infectious diseases in the U.S. in the 20th century has decreased to baseline levels prior wide-spread introduction of vaccination practices (see Figure below).



Crude death rate for infectious diseases, USA, 1900–1996. Adapted from: Achievement in public health, 1900–1999: control of infectious diseases. MMWR Morb Mortal Wkly Rep *1999; 48: 621–29; and Armstrong GL, Conn LA, Pinner RW. Trends in infectious disease mortality in the United States during the 20th century.* JAMA *1999; 281: 61–66.*

Figure 1. Source: Aiello and Larson [147].

Remarkably when one tries to find solid research data in support of the claim that vaccines are responsible for historical eradication of diseases such as smallpox, polio etc, none is found. For example, the 1999 report from the U.S. CDC [146] (recently quoted by Kata [148] as proof that vaccines are responsible for the dramatic declines in morbidity and mortality from infectious diseases), titled "Ten Great Public Health Achievements -United States, 1900–1999", lists the following Table:

TABLE 2. Baseline 20th century annual morbidity and 1998 provisional morbidity from nine diseases with vaccines recommended before 1990 for universal use in children — United States

Disease	Baseline 20th century annual morbidity	1998 Provisional morbidity	% Decrease
Smallpox	48,164*	0	100%
Diphtheria	175,885†	1	100%§
Pertussis	147,271¶	6,279	95.7%
Tetanus	1,314**	34	97.4%
Poliomyelitis (paralytic)	16,316††	0§§	100%
Measles	503,282¶¶	89	100%§
Mumps	152,209***	606	99.6%
Rubella	47,745†††	345	99.3%
Congenital rubella syndrome	*823§§§*	5	*99.4%*
Haemophilus influenzae type b	20,000¶¶¶	54****	99.7%

* Average annual number of cases during 1900–1904 (*1*).
† Average annual number of reported cases during 1920–1922, 3 years before vaccine development.
§ Rounded to nearest tenth.
¶ Average annual number of reported cases during 1922–1925, 4 years before vaccine development.
** Estimated number of cases based on reported number of deaths during 1922–1926 assuming a case-fatality rate of 90%.
†† Average annual number of reported cases during 1951–1954, 4 years before vaccine licensure.
§§ Excludes one cases of vaccine-associated polio reported in 1998.
¶¶ Average annual number of reported cases during 1958–1962, 5 years before vaccine licensure.
*** Number of reported cases in 1968, the first year reporting began and the first year after vaccine licensure.
††† Average annual number of reported cases during 1966–1968, 3 years before vaccine licensure.
§§§ Estimated number of cases based on seroprevalence data in the population and on the risk that women infected during a childbearing year would have a fetus with congenital rubella syndrome (*7*).
¶¶¶ Estimated number of cases from population-based surveillance studies before vaccine licensure in 1985 (*8*).
**** Excludes 71 cases of *Haemophilus influenzae* disease of unknown serotype.

This table only proves that the diseases listed decreased in incidence in the 20th century. It does not however prove that any of the vaccines were responsible for this decrease as there are other crucial factors which also changed during the course of the 20th century, such as improved hygiene, sanitation and nutrition. Remarkably, the U.S. CDC report lists these very factors (i.e., clean water and improved sanitation, as well as better nutrition, availability of antibiotics, greater access to health care, and technologic advances in maternal and neonatal medicine) among the top 10 achievements of the 20th century responsible for both control of infectious diseases and decreased infant mortality rates. Notably, these factors are listed separate from vaccines. Note also that like cholera and typhoid, polio is also a disease transmitted through contaminated water and is therefore a hygiene-preventable disease and not necessarily a vaccine-preventable disease.

Altogether these observations invalidate the claim that infectious diseases such as polio would return should vaccination rates fall.

Benefits from Naturally- versus Vaccine-Acquired Immunity

Scientific evidence has solidly established that naturally acquired childhood diseases provide long-term benefits to the immune system, including proper development of cellular (Th1) immunity which is crucial for long-term protection against infectious diseases, protection against asthma, allergies [149-151], neurodegenerative diseases [152] and even protection against the most common and most aggressive type of primary brain tumors in humans (glioblastoma multiforme [153]).

Several studies have explained that Th1 responses induced by microbial infections can counterbalance allergen-induced Th2 responses. For example, the work by Silverberg et al. demonstrates that wild type varicella zoster virus infection but not varicella vaccine, protects against asthma and atopic dermatitis (AD) in young children [149,150]. The reason why varicella vaccine was ineffective in eliciting this protection is that like most other vaccines, it induces primarily Th2 responses. Thus, contrary to some arguments, live vaccines do not have the same effect on the maturation of the immune system because they bypass the natural infection route (which is mucosal surfaces of the GI and respiratory tract). Thus, vaccines fail to stimulate cell-based (Th1) immune system which is present on these surfaces. Th1progenitor cells cannot mature in the absence of Th1 cytokines and Th2 responses inhibit Th1 responses (the two responses are mutually exclusive [135]). This means that continuous stimulation of Th2 immunity by vaccination is counterproductive to a balanced maturation of the immature immune system. Consistent with this notion, most recent work shows that annual vaccination against influenza hampers the development of virus-specific $CD8^+$T-cell immunity in children [154].
Studies continue to emphasize the importance of natural infections in helping a balanced development of a child's immune system. For example, research published in 2001 suggests that repeated viral infections early in life stimulate the immature immune system towards the Th1 phenotype, thereby reducing the risk for the development of asthma up to school age [151].

Taken together, these results are consistent with the hypothesis that early stimulation of cellular immunity (Th1) is necessary for proper development of the immune system, including the counterbalance of allergen-induced Th2 responses. It may also explain why in the last three decades, contemporary with introduction of more and more vaccines in routine vaccination schedules, there has been a dramatic increase in allergic diseases in children.

Personal statement and brief bio: I am a Research Associate at the University of British Columbia (in Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences). The key focus of my research is on the toxic impact of vaccines and vaccine adjuvants on neuronal development, particularly in regard to autism spectrum disorders (ASD). In the last year I have published extensively on the subject of vaccine safety. My publications have been featured in high-impact medical journals such as *Annals of Medicine, JAMA, Vaccine and Journal of Alzheimer's Disease* (see below, list of publications).

I serve as a peer reviewer of *Journal of Inorganic Biochemistry*, *Lupus, Surgical Neurology International* and *Human and Experimental Toxicology*. Last year, I co-organized the *Vaccine Safety-*

Evaluating the Science International Conference in Montego Bay, Jamaica 2011.
http://www.vaccinesafetyconference.com/index.html

This year I am a co-organizing a special lecture series on Vaccines, to be held at Green College at the University of British Columbia. I will also be speaking on the topic of vaccine safety at the 8th International Congress on Autoimmunity in Grenada, Spain (May 9-13, 2012) http://www2.kenes.com/autoimmunity/Pages/Home.aspx

Finally, early this year I have received an invite by Professor Victor Preedy (PhD DSc FRSPH FRCPath) from the Kings College London to contribute a chapter to *The Comprehensive Guide to Autism.* This new book aims to be the most comprehensive book on autism to date. It will be published by Springer, which is one of the world's leading academic book publisher (see www.springer.com). The Editors and Editorial Advisors are based at leading universities or institutions, including King's College London, University of Westminster and University of the West of Scotland. Together, the Editors have published over 40 books and volumes in the biomedical sciences including 7 multi-chapter works of 120 chapters or more. I have been asked to write a chapter on *Autism spectrum disorders and aluminium vaccine adjuvants*.
This invite shows that there is now a growing acceptance in the wider scientific community that vaccines may be a risk factor to autism and related neurodevelopmental disorders in children (attached is the list of chapters and contributors).

Selected recent Peer-reviewed Publications:

[1] Tomljenovic L, Shaw CA. Mechanisms of aluminum adjuvant toxicity in pediatric populations. *Lupus.* 2012; 21(2): 223-230.
[2] Tomljenovic L, Shaw CA. Do aluminum vaccine adjuvants contribute to the rising prevalence of autism? *J Inorg Biochem.* 2011; 105(11):1489-99.
[3] Tomljenovic L, Shaw CA. Aluminum Vaccine Adjuvants: Are they Safe? *Curr Med Chem.* 2011; 18(17): 2630-7.
[4] Tomljenovic L, Shaw CA. "One-size" fits all? *Vaccine.* 2012; 30(12):2040
[5] Tomljenovic L, Shaw CA. Human papillomavirus (HPV) vaccine policy and evidence-based medicine: are they at odds? *Annals Med.* 2011. doi: 10.3109/07853890.2011.645353
[6] Tomljenovic L, Shaw CA. Mandatory HPV vaccination. [Letter to Editor] *JAMA.* 2012; 307(3): 254; author reply 254-5.
[7] Tomljenovic L, Shaw CA. Microglia-mediated immunoexcitotoxicity, a key player in traumatic brain injury? [Commentary] *Surg Neuro Int.* 2011; 2(107).
[8] Tomljenovic L. Aluminum and Alzheimer's disease: after a century of controversy, is there a plausible link? *J Alzheimer's Dis.* 2011; 23(4): 567-598.

References cited

[1] Food and Drug Administration (FDA). Workshop on Non-clinical Safety Evaluation of Preventative Vaccines: Recent Advances and Regulatory Considerations. 2002. http://www.fda.gov/downloads/biologicsbloodvaccines/newsevents/workshopsmeetingsconferences/transcriptsminutes/ucm054459.pdf
[2] Poling, J.S., Frye, R.E., Shoffner, J. and Zimmerman, A.W. (2006) Developmental regression and mitochondrial dysfunction in a child with autism. J Child Neurol 21, 170-2.
[3] Yang, Y., Sujan, S., Sun, F., Zhang, Y., Jiang, Y., Song, J., Qin, J. and Wu, X. (2006) Acute metabolic crisis induced by vaccination in seven Chinese patients. Pediatr Neurol 35, 114-8.
[4] Ottaviani, G., Lavezzi, A.M. and Matturri, L. (2006) Sudden infant death syndrome (SIDS) shortly after hexavalent vaccination: another pathology in suspected SIDS? Virchows Arch 448, 100-4.
[5] Zinka, B., Rauch, E., Buettner, A., Rueff, F. and Penning, R. (2006) Unexplained cases of sudden infant death shortly after hexavalent vaccination. Vaccine 24, 5779-80.
[6] Hewitson, L., Lopresti, B.J., Stott, C., Mason, N.S. and Tomko, J. (2010) Influence of pediatric vaccines on amygdala growth and opioid ligand binding in rhesus macaque infants: A pilot study. Acta Neurobiol Exp (Wars) 70, 147-64.
[7] Hewitson, L., Houser, L.A., Stott, C., Sackett, G., Tomko, J.L., Atwood, D., Blue, L. and White, E.R. (2010) Delayed acquisition of neonatal reflexes in newborn primates receiving a

thimerosal-containing hepatitis B vaccine: influence of gestational age and birth weight. J Toxicol Environ Health A 73, 1298-313.
[8] Shoenfeld, Y. and Agmon-Levin, N. (2011) 'ASIA' - Autoimmune/inflammatory syndrome induced by adjuvants. J Autoimmun 36, 4-8.
[9] Agmon-Levin, N., Paz, Z., Israeli, E. and Shoenfeld, Y. (2009) Vaccines and autoimmunity. Nat Rev Rheumatol 5, 648-52.
[10] Tomljenovic, L. and Shaw, C.A. (2012) Mechanisms of aluminum adjuvant toxicity in pediatric populations. Lupus 21, 223-230.
[11] Tomljenovic, L. and Shaw, C.A. (2011) Human papillomavirus (HPV) vaccine policy and evidence-based medicine: Are they at odds? Ann Med. doi: 10.3109/07853890.2011.645353
[12] Tomljenovic, L. and Shaw, C.A. (2011) One-size fits all? Vaccine. 2012; 30(12):2040.
[13] Authier, F.J., Cherin, P., Creange, A., Bonnotte, B., Ferrer, X., Abdelmoumni, A., Ranoux, D., Pelletier, J., Figarella-Branger, D., Granel, B., Maisonobe, T., Coquet, M., Degos, J.D. and Gherardi, R.K. (2001) Central nervous system disease in patients with macrophagic myofasciitis. Brain 124, 974-83.
[14] Gherardi, R. and Authier, F. (2012) Macrophagic myofasciitis: characterization and pathophysiology. Lupus 21, 184-9.
[15] Exley, C., Swarbrick, L., Gherardi, R.K. and Authier, F.J. (2009) A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome. Med Hypotheses 72, 135-9.
[16] Couette, M., Boisse, M.F., Maison, P., Brugieres, P., Cesaro, P., Chevalier, X., Gherardi, R.K., Bachoud-Levi, A.C. and Authier, F.J. (2009) Long-term persistence of vaccine-derived aluminum hydroxide is associated with chronic cognitive dysfunction. J Inorg Biochem 103, 1571-8.
[17] Passeri, E., Villa, C., Couette, M., Itti, E., Brugieres, P., Cesaro, P., Gherardi, R.K., Bachoud-Levi, A.C. and Authier, F.J. (2011) Long-term follow-up of cognitive dysfunction in patients with aluminum hydroxide-induced macrophagic myofasciitis (MMF). J Inorg Biochem 105, 1457-63.
[18] Orbach, H., Agmon-Levin, N. and G., Z.-G. (2010) Vaccines and Autoimmune Diseases of the Adult. Discov Med 9, 90-97.
[19] Zafrir, Y., Agmon-Levin, N., Paz, Z., Shilton, T. and Shoenfeld, Y. (2012) Autoimmunity following Hepatitis B vaccine as part of the spectrum of 'Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants' (ASIA): analysis of 93 cases. Lupus 21, 146-52.
[20] Souayah, N., Nasar, A., Suri, M.F. and Qureshi, A.I. (2007) Guillain-Barre syndrome after vaccination in United States a report from the CDC/FDA Vaccine Adverse Event Reporting System. Vaccine 25, 5253-5.
[21] Sutton, I., Lahoria, R., Tan, I.L., Clouston, P. and Barnett, M.H. (2009) CNS demyelination and quadrivalent HPV vaccination. Multiple Sclerosis 15, 116–119.
[22] Gallagher, C.M. and Goodman, M.S. (2010) Hepatitis B vaccination of male neonates and autism diagnosis, NHIS 1997-2002. J Toxicol Environ Health A 73, 1665-77.
[23] Gallagher, C.M. and Goodman, M.S. (2008) Hepatitis B triple series vaccine and developmental disability in US children aged 1-9 years. Tox Env Chem. 90, 997-1008.
[24] Collignon, P., Doshi, P. and Jefferson, T. (2010) Child influenza vaccination. Ramifications of adverse events in children in Australia. BMJ 340, c2994.
[25] Collignon, P., Doshi, P. and Jefferson, T. Adverse events following influenza vaccination in Australia--should we be surprised? Rapid response to "Australia suspends seasonal flu vaccination of young children", BMJ 2010;340:c2419. http://www.bmj.com/content/340/bmj.c2419?tab=responses.
[26] Collignon, P., Doshi, P. and Jefferson, T. Re: Adverse events following influenza vaccination in Australia--should we be surprised? Rapid response to "Australia suspends seasonal flu vaccination of young children", BMJ 2010;340:c2419. http://www.bmj.com/content/340/bmj.c2419?tab=responses.
[27] Collignon, P. (2011) Influenza vaccination in young children. Lancet Infect Dis 11, 657; author reply 657-8.
[28] Pourcyrous, M., Korones, S.B., Arheart, K.L. and Bada, H.S. (2007) Primary immunization of premature infants with gestational age <35 weeks: cardiorespiratory complications and C-reactive protein responses associated with administration of single and multiple separate vaccines simultaneously. J Pediatr 151, 167-72.
[29] Fisher, M.A. and Eklund, S.A. (1999) Hepatitis B vaccine and liver problems in U.S. children less than 6 years old, 1993 and 1994. Epidemiology 10, 337-9.

[30] Hernandez, I., Sanmartin, O., Carda, C., Gome, S. and Alfaro, A. (2008) [B-cell pseudolymphoma caused by aluminium hydroxide following hyposensitization therapy]. Actas Dermosifiliogr 99, 213-6.
[31] Cohen, A.D. and Shoenfeld, Y. (1996) Vaccine-induced autoimmunity. J Autoimmun 9, 699-703.
[32] Friedrich, F. (1998) Neurologic complications associated with oral poliovirus vaccine and genomic variability of the vaccine strains after multiplication in humans. Acta Virol 42, 187-94.
[33] Girard, M. (2005) Autoimmune hazards of hepatitis B vaccine. Autoimmun Rev 4, 96-100.
[34] Centers for Disease Control and Prevention (CDC). Update: Guillain-Barré Syndrome Among Recipients of Menactra® Meningococcal Conjugate Vaccine - United States, June 2005--September 2006. Morb Mortal Wkly Rep (MMWR) 55, 1120-1124. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5541a2.htm.
[35] Centers for Disease Control and Prevention (CDC). Update: Recommendations from the Advisory Committee on Immunization Practices (ACIP) Regarding Administration of Combination MMRV Vaccine, March 14, 2008, MMWR 57(10);258-260.
[36] Food and Drug Administration (FDA). FDA Science and Mission at Risk, Report of the Subcommittee on Science and Technology (2007). http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf
[37] Poland, G.A., Ovsyannikova, I.G. and Jacobson, R.M. (2008) Vaccine immunogenetics: bedside to bench to population. Vaccine 26, 6183-8.
[38] Poland, G.A. and Jacobson, R.M. (2011) The age-old struggle against the antivaccinationists. N Engl J Med 364, 97-9.
[39] Kovel, A., Wald, E.R., Guerra, N., Serdy, C. and Meschievitz, C.K. (1992) Safety and immunogenicity of acellular diphtheria-tetanus-pertussis and Haemophilus conjugate vaccines given in combination or at separate injection sites. J Pediatr 120, 84-7.
[40] Kaplan, S.L., Lauer, B.A., Ward, M.A., Wiedermann, B.L., Boyer, K.M., Dukes, C.M., Schaffer, D.M., Paisley, J., Mendelson, R., Pedreira, F. and et al. (1994) Immunogenicity and safety of Haemophilus influenzae type b-tetanus protein conjugate vaccine alone or mixed with diphtheria-tetanus-pertussis vaccine in infants. J Pediatr 124, 323-7.
[41] Li, G., Zhang, H., Zhou, W., Ye, Q., Li, F., Wang, H., Hou, Q., Xu, Y., Ma, X., Tan, Y., Wang, L., Li, Y., Li, H., Meng, F., Liang, Q., Liu, A., Qin, C., Wei, W., Liu, J., Ruan, C., Tao, W., Zhang, S., Zheng, H. and Zhu, F. (2010) Safety and immunogenicity of a diphtheria, tetanus, acellular pertussis and Haemophilus influenzae Type b combination vaccine compared with separate administration of licensed equivalent vaccines in Chinese infants and toddlers for primary and booster immunization. Vaccine 28, 4215-23.
[42] Shinefield, H., Black, S., Digilio, L., Reisinger, K., Blatter, M., Gress, J.O., Brown, M.L., Eves, K.A., Klopfer, S.O., Schodel, F. and Kuter, B.J. (2005) Evaluation of a quadrivalent measles, mumps, rubella and varicella vaccine in healthy children. Pediatr Infect Dis J 24, 665-9.
[43] Velu, V., Nandakumar, S., Shanmugam, S., Shankar, E.M., Thangavel, S., Kulkarni, P.S. and Thyagarajan, S.P. (2007) Comparative efficacy of two dosages of recombinant hepatitis B vaccine in healthy adolescents in India. Pediatr Infect Dis J 26, 1038-41.
[44] Thomas, C. and Moridani, M. (2009) Interindividual variations in the efficacy and toxicity of vaccines. Toxicology 278, 204-10.
[45] Exley, C. (2011) Aluminium-based adjuvants should not be used as placebos in clinical trials. Vaccine 29, 9289.
[46] Tomljenovic, L. (2011) Aluminum and Alzheimer's disease: after a century of controversy, is there a plausible link? J Alzheimers Dis 23, 567-598.
[47] Tomljenovic, L. and Shaw, C.A. (2011) Aluminum Vaccine Adjuvants: Are they Safe? Current Medicinal Chemistry 18, 2630-2637.
[48] Demicheli, V., Jefferson, T., Rivetti, A. and Price, D. (2005) Vaccines for measles, mumps and rubella in children. Cochrane Database Syst Rev, CD004407.
[49] Fombonne, E. and Chakrabarti, S. (2001) No evidence for a new variant of measles-mumps-rubella-induced autism. Pediatrics 108, E58.
[50] Tomljenovic, L. Dorea, J.G. and Shaw, A.C. (2012) Commentary: A Link Between Mercury Exposure, Autism Spectrum Disorder and Other Neurodevelopmental Disorders? Implications for Thimerosal-Containing Vaccines. Journal on Developmental Disabilities 17(2), 29-37.
[51] Shaw, C.A. and Petrik, M.S. (2009) Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration. J Inorg Biochem 103, 1555-62.

[52] Petrik, M.S., Wong, M.C., Tabata, R.C., Garry, R.F. and Shaw, C.A. (2007) Aluminum adjuvant linked to Gulf War illness induces motor neuron death in mice. Neuromolecular Med 9, 83-100.
[53] Authier, F.J., Sauvat, S., Christov, C., Chariot, P., Raisbeck, G., Poron, M.F., Yiou, F. and Gherardi, R. (2006) AlOH3-adjuvanted vaccine-induced macrophagic myofasciitis in rats is influenced by the genetic background. Neuromuscul Disord 16, 347-52.
[54] Olczak, M., Duszczyk, M., Mierzejewski, P., Wierzba-Bobrowicz, T. and Majewska, M.D. (2011) Lasting neuropathological changes in rat brain after intermittent neonatal administration of thimerosal. Folia Neuropathol 48, 258-69.
[55] Olczak, M., Duszczyk, M., Mierzejewski, P., Meyza, K. and Majewska, M.D. (2011) Persistent behavioral impairments and alterations of brain dopamine system after early postnatal administration of thimerosal in rats. Behav Brain Res 223, 107-18.
[56] Hornig, M., Chian, D. and Lipkin, W.I. (2004) Neurotoxic effects of postnatal thimerosal are mouse strain dependent. Mol Psychiatry 9, 833-45.
[57] Dorea, J.G. (2011) Integrating experimental (in vitro and in vivo) neurotoxicity studies of low-dose thimerosal relevant to vaccines. Neurochem Res 36, 927-38.
[58] Tsumiyama, K., Miyazaki, Y. and Shiozawa, S. (2009) Self-organized criticality theory of autoimmunity. PLoS One 4, e8382.
[59] Rose, N.R. (2010) Autoimmunity, infection and adjuvants. Lupus 19, 354-8.
[60] Besedovsky, H.O. and del Rey, A. (2010) Central and peripheral cytokines mediate immune-brain connectivity. Neurochem Res 36, 1-6.
[61] Besedovsky HO, Rey A. Brain Cytokines as Integrators of the Immune–Neuroendocrine Network. In: Lajtha A, Besedovsky HO, Galoyan A (eds). Handbook of Neurochemistry and Molecular Neurobiology. Springer. 2008; p. 3-17.
[62] Elenkov, I.J., Wilder, R.L., Chrousos, G.P. and Vizi, E.S. (2000) The sympathetic nerve--an integrative interface between two supersystems: the brain and the immune system. Pharmacol Rev 52, 595-638.
[63] Eskandari, F., Webster, J.I. and Sternberg, E.M. (2003) Neural immune pathways and their connection to inflammatory diseases. Arthritis Res Ther 5, 251-65.
[64] Rivest, S. (2010) Interactions between the immune and neuroendocrine systems. Prog Brain Res 181, 43-53.
[65] Turrin, N.P. and Rivest, S. (2004) Unraveling the molecular details involved in the intimate link between the immune and neuroendocrine systems. Exp Biol Med (Maywood) 229, 996-1006.
[66] del Rey, A., Roggero, E., Randolf, A., Mahuad, C., McCann, S., Rettori, V. and Besedovsky, H.O. (2006) IL-1 resets glucose homeostasis at central levels. Proc Natl Acad Sci U S A 103, 16039-44.
[67] del Rey, A., Wolff, C., Wildmann, J., Randolf, A., Hahnel, A., Besedovsky, H.O. and Straub, R.H. (2008) Disrupted brain-immune system-joint communication during experimental arthritis. Arthritis Rheum 58, 3090-9.
[68] Wilder, R.L. (1995) Neuroendocrine-immune system interactions and autoimmunity. Annu Rev Immunol 13, 307-38.
[69] Demitrack, M.A. and Crofford, L.J. (1998) Evidence for and pathophysiologic implications of hypothalamic-pituitary-adrenal axis dysregulation in fibromyalgia and chronic fatigue syndrome. Ann N Y Acad Sci 840, 684-97.
[70] Neeck, G. and Crofford, L.J. (2000) Neuroendocrine perturbations in fibromyalgia and chronic fatigue syndrome. Rheum Dis Clin North Am 26, 989-1002.
[71] Demitrack, M.A., Dale, J.K., Straus, S.E., Laue, L., Listwak, S.J., Kruesi, M.J., Chrousos, G.P. and Gold, P.W. (1991) Evidence for impaired activation of the hypothalamic-pituitary-adrenal axis in patients with chronic fatigue syndrome. J Clin Endocrinol Metab 73, 1224-34.
[72] Gutierrez, M.A., Garcia, M.E., Rodriguez, J.A., Rivero, S. and Jacobelli, S. (1998) Hypothalamic-pituitary-adrenal axis function and prolactin secretion in systemic lupus erythematosus. Lupus 7, 404-8.
[73] Straub, R.H. and Cutolo, M. (2001) Involvement of the hypothalamic--pituitary--adrenal/gonadal axis and the peripheral nervous system in rheumatoid arthritis: viewpoint based on a systemic pathogenetic role. Arthritis Rheum 44, 493-507.
[74] Eijsbouts, A.M. and Murphy, E.P. (1999) The role of the hypothalamic-pituitary-adrenal axis in rheumatoid arthritis. Baillieres Best Pract Res Clin Rheumatol 13, 599-613.
[75] Chikanza, I.C., Petrou, P., Kingsley, G., Chrousos, G. and Panayi, G.S. (1992) Defective hypothalamic response to immune and inflammatory stimuli in patients with rheumatoid arthritis. Arthritis Rheum 35, 1281-8.

[76] Gutierrez, M.A., Garcia, M.E., Rodriguez, J.A., Mardonez, G., Jacobelli, S. and Rivero, S. (1999) Hypothalamic-pituitary-adrenal axis function in patients with active rheumatoid arthritis: a controlled study using insulin hypoglycemia stress test and prolactin stimulation. J Rheumatol 26, 277-81.
[77] Michelson, D., Stone, L., Galliven, E., Magiakou, M.A., Chrousos, G.P., Sternberg, E.M. and Gold, P.W. (1994) Multiple sclerosis is associated with alterations in hypothalamic-pituitary-adrenal axis function. J Clin Endocrinol Metab 79, 848-53.
[78] Wei, T. and Lightman, S.L. (1997) The neuroendocrine axis in patients with multiple sclerosis. Brain 120 (Pt 6), 1067-76.
[79] Porges, S.W. (2005) The vagus: a mediator of behavioral and physiologic features associated with autism. In: The neurobiology of autism (Bauman, M.L. and Kemper, T.L., eds.), pp. 65-78, The Johns Hopkins University Press, Baltimore, Maryland.
[80] Garay, P.A. and McAllister, A.K. (2010) Novel roles for immune molecules in neural development: implications for neurodevelopmental disorders. Front Synaptic Neurosci 2, 136.
[81] Stevens, B., Allen, N.J., Vazquez, L.E., Howell, G.R., Christopherson, K.S., Nouri, N., Micheva, K.D., Mehalow, A.K., Huberman, A.D., Stafford, B., Sher, A., Litke, A.M., Lambris, J.D., Smith, S.J., John, S.W. and Barres, B.A. (2007) The classical complement cascade mediates CNS synapse elimination. Cell 131, 1164-78.
[82] Boulanger, L.M. (2004) MHC class I in activity-dependent structural and functional plasticity. Neuron Glia Biol 1, 283-9.
[83] Shatz, C.J. (2009) MHC class I: an unexpected role in neuronal plasticity. Neuron 64, 40-5.
[84] Goddard, C.A., Butts, D.A. and Shatz, C.J. (2007) Regulation of CNS synapses by neuronal MHC class I. Proc Natl Acad Sci U S A 104, 6828-33.
[85] Huh, G.S., Boulanger, L.M., Du, H., Riquelme, P.A., Brotz, T.M. and Shatz, C.J. (2000) Functional requirement for class I MHC in CNS development and plasticity. Science 290, 2155-9.
[86] Corriveau, R.A., Huh, G.S. and Shatz, C.J. (1998) Regulation of class I MHC gene expression in the developing and mature CNS by neural activity. Neuron 21, 505-20.
[87] Schafer, D.P. and Stevens, B. (2010) Synapse elimination during development and disease: immune molecules take centre stage. Biochem Soc Trans 38, 476-81.
[88] Boulanger, L.M. (2009) Immune proteins in brain development and synaptic plasticity. Neuron 64, 93-109.
[89] Fourgeaud, L. and Boulanger, L.M. (2010) Role of immune molecules in the establishment and plasticity of glutamatergic synapses. Eur J Neurosci 32, 207-17.
[90] Hodgson, D.M. and Knott, B. (2002) Potentiation of tumor metastasis in adulthood by neonatal endotoxin exposure: sex differences. Psychoneuroendocrinology 27, 791-804.
[91] Spencer, S.J., Hyland, N.P., Sharkey, K.A. and Pittman, Q.J. (2007) Neonatal immune challenge exacerbates experimental colitis in adult rats: potential role for TNF-alpha. Am J Physiol Regul Integr Comp Physiol 292, R308-15.
[92] Galic, M.A., Riazi, K., Heida, J.G., Mouihate, A., Fournier, N.M., Spencer, S.J., Kalynchuk, L.E., Teskey, G.C. and Pittman, Q.J. (2008) Postnatal inflammation increases seizure susceptibility in adult rats. J Neurosci 28, 6904-13.
[93] Bilbo, S.D., Biedenkapp, J.C., Der-Avakian, A., Watkins, L.R., Rudy, J.W. and Maier, S.F. (2005) Neonatal infection-induced memory impairment after lipopolysaccharide in adulthood is prevented via caspase-1 inhibition. J Neurosci 25, 8000-9.
[94] Konat, G.W., Lally, B.E., Toth, A.A. and Salm, A.K. (2011) Peripheral immune challenge with viral mimic during early postnatal period robustly enhances anxiety-like behavior in young adult rats. Metab Brain Dis 26, 237-240.
[95] Spencer, S.J., Auer, R.N. and Pittman, Q.J. (2006) Rat neonatal immune challenge alters adult responses to cerebral ischaemia. J Cereb Blood Flow Metab 26, 456-67.
[96] Shi, L., Fatemi, S.H., Sidwell, R.W. and Patterson, P.H. (2003) Maternal influenza infection causes marked behavioral and pharmacological changes in the offspring. J Neurosci 23, 297-302.
[97] Fatemi, S.H., Reutiman, T.J., Folsom, T.D., Huang, H., Oishi, K., Mori, S., Smee, D.F., Pearce, D.A., Winter, C., Sohr, R. and Juckel, G. (2008) Maternal infection leads to abnormal gene regulation and brain atrophy in mouse offspring: implications for genesis of neurodevelopmental disorders. Schizophr Res 99, 56-70.
[98] Shi, L., Smith, S.E., Malkova, N., Tse, D., Su, Y. and Patterson, P.H. (2009) Activation of the maternal immune system alters cerebellar development in the offspring. Brain Behav Immun 23, 116-23.

[99] Offit, P.A. and Jew, R.K. (2003) Addressing parents' concerns: do vaccines contain harmful preservatives, adjuvants, additives, or residuals? Pediatrics 112, 1394-7.
[100] Eldred, B.E., Dean, A.J., McGuire, T.M. and Nash, A.L. (2006) Vaccine components and constituents: responding to consumer concerns. Med J Aust 184, 170-5.
[101] Rhawn, J. (1996) Normal and abnormal amygdala development. In: Neuropsychiatry, Neuropsychology, and Clinical Neuroscience,3rd Ed. Lippincott Williams & Wilkins. http://brainmind.com/EmotionalBrainDevelopment4.html
[102] Munson, J., Dawson, G., Abbott, R., Faja, S., Webb, S.J., Friedman, S.D., Shaw, D., Artru, A. and Dager, S.R. (2006) Amygdalar volume and behavioral development in autism. Arch Gen Psychiatry 63, 686-93.
[103] Baron-Cohen, S., Ring, H.A., Bullmore, E.T., Wheelwright, S., Ashwin, C. and Williams, S.C. (2000) The amygdala theory of autism. Neurosci Biobehav Rev 24, 355-64.
[104] Hertz-Picciotto, I., Park, H.Y., Dostal, M., Kocan, A., Trnovec, T. and Sram, R. (2008) Prenatal exposures to persistent and non-persistent organic compounds and effects on immune system development. Basic Clin Pharmacol Toxicol 102, 146-54.
[105] Dietert, R.R. and Dietert, J.M. (2008) Potential for early-life immune insult including developmental immunotoxicity in autism and autism spectrum disorders: focus on critical windows of immune vulnerability. J Toxicol Environ Health B Crit Rev 11, 660-80.
[106] Belmonte, M.K., Allen, G., Beckel-Mitchener, A., Boulanger, L.M., Carper, R.A. and Webb, S.J. (2004) Autism and abnormal development of brain connectivity. J Neurosci 24, 9228-31.
[107] Ibi, D., Nagai, T., Kitahara, Y., Mizoguchi, H., Koike, H., Shiraki, A., Takuma, K., Kamei, H., Noda, Y., Nitta, A., Nabeshima, T., Yoneda, Y. and Yamada, K. (2009) Neonatal polyI:C treatment in mice results in schizophrenia-like behavioral and neurochemical abnormalities in adulthood. Neurosci Res 64, 297-305.
[108] Spencer, S.J., Heida, J.G. and Pittman, Q.J. (2005) Early life immune challenge--effects on behavioural indices of adult rat fear and anxiety. Behav Brain Res 164, 231-8.
[109] Galic, M.A., Riazi, K., Henderson, A.K., Tsutsui, S. and Pittman, Q.J. (2009) Viral-like brain inflammation during development causes increased seizure susceptibility in adult rats. Neurobiol Dis 36, 343-51.
[110] Ratajczak, H.V. (2011) Theoretical aspects of autism: causes--a review. J Immunotoxicol 8, 68-79.
[111] Delong, G. (2011) A Positive Association found between Autism Prevalence and Childhood Vaccination uptake across the U.S. Population. J Toxicol Environ Health A 74, 903-16.
[112] Tomljenovic, L. and Shaw, C.A. (2011) Do aluminum vaccine adjuvants contribute to the rising prevalence of autism? J Inorg Biochem 105, 1489-1499.
[113] Yokel, R.A., Hicks, C.L. and Florence, R.L. (2008) Aluminum bioavailability from basic sodium aluminum phosphate, an approved food additive emulsifying agent, incorporated in cheese. Food Chem Toxicol 46, 2261-6.
[114] Yokel, R.A. and McNamara, P.J. (2001) Aluminium toxicokinetics: an updated minireview. Pharmacol Toxicol 88, 159-67.
[115] Walton, J.R. (2007) A longitudinal study of rats chronically exposed to aluminum at human dietary levels. Neurosci Lett 412, 29-33.
[116] Walton, J.R. (2009) Functional impairment in aged rats chronically exposed to human range dietary aluminum equivalents. Neurotoxicology 30, 182-93.
[117] Agency for toxic substances, disease registry (ATSDR), Toxicological profile for aluminum. Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp22.html
[118] Lopes, M.M. and Caldas, L.Q.A. (2011) Young children with austim spectrum disorders: Can aluminium bodyburden cause metabolism disruption? Toxicology Letters 205S, S60-S179.
[119] Eickhoff, T.C. and Myers, M. (2002) Workshop summary. Aluminum in vaccines. Vaccine 20 Suppl 3, S1-4.
[120] Walton, J.R. (2007) An aluminum-based rat model for Alzheimer's disease exhibits oxidative damage, inhibition of PP2A activity, hyperphosphorylated tau, and granulovacuolar degeneration. J Inorg Biochem 101, 1275-84.
[121] Exley, C. (2006) Aluminium and iron, but neither copper nor zinc, are key to the precipitation of beta-sheets of Abeta_{42} in senile plaque cores in Alzheimer's disease. J Alzheimers Dis 10, 173-7.
[122] Yumoto, S., Nagai, H., Matsuzaki, H., Matsumura, H., Tada, W., Nagatsuma, E. and Kobayashi, K. (2001) Aluminium incorporation into the brain of rat fetuses and sucklings. Brain Res Bull 55, 229-34.

[123] Bishop, N.J., Morley, R., Day, J.P. and Lucas, A. (1997) Aluminum neurotoxicity in preterm infants receiving intravenous-feeding solutions. N Engl J Med 336, 1557-61.
[124] Gherardi, R.K., Coquet, M., Cherin, P., Belec, L., Moretto, P., Dreyfus, P.A., Pellissier, J.F., Chariot, P. and Authier, F.J. (2001) Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. Brain 124, 1821-31.
[125] Quiroz-Rothe, E., Ginel, P.J., Pérez, J., Lucena, R. and Rivero, J.L.L. (2005) Vaccine-associated acute polyneuropathy resembling Guillain-Barré syndrome in a dog. EJCAP 15.
[126] Geier, D.A. and Geier, M.R. (2006) A meta-analysis epidemiological assessment of neurodevelopmental disorders following vaccines administered from 1994 through 2000 in the United States. Neuro Endocrinol Lett 27, 401-13.
[127] Young, H.A., Geier, D.A. and Geier, M.R. (2008) Thimerosal exposure in infants and neurodevelopmental disorders: an assessment of computerized medical records in the Vaccine Safety Datalink. J Neurol Sci 271, 110-8.
[128] Corbett, S.J. and Poon, C.C. (2008) Toxic levels of mercury in Chinese infants eating fish congee. Med J Aust 188, 59-60.
[129] Freire, C., Ramos, R., Lopez-Espinosa, M.J., Diez, S., Vioque, J., Ballester, F. and Fernandez, M.F. (2009) Hair mercury levels, fish consumption, and cognitive development in preschool children from Granada, Spain. Environ Res 110, 96-104.
[130] Burbacher, T.M., Shen, D.D., Liberato, N., Grant, K.S., Cernichiari, E. and Clarkson, T. (2005) Comparison of blood and brain mercury levels in infant monkeys exposed to methylmercury or vaccines containing thimerosal. Environ Health Perspect 113, 1015-21.
[131] Polk, B.F., White, J.A., DeGirolami, P.C. and Modlin, J.F. (1980) An outbreak of rubella among hospital personnel. N Engl J Med 303, 541-5.
[132] Gustafson, T.L., Lievens, A.W., Brunell, P.A., Moellenberg, R.G., Buttery, C.M. and Sehulster, L.M. (1987) Measles outbreak in a fully immunized secondary-school population. N Engl J Med 316, 771-4.
[133] Centers for Disease Control and Prevention (CDC). (1993) Diphtheria outbreak--Russian Federation, 1990-1993. MMWR Morb Mortal Wkly Rep 42, 840-1, 847.
[134] Kim, H.W., Canchola, J.G., Brandt, C.D., Pyles, G., Chanock, R.M., Jensen, K. and Parrott, R.H. (1969) Respiratory syncytial virus disease in infants despite prior administration of antigenic inactivated vaccine. Am J Epidemiol 89, 422-34.
[135] Deenick, E.K. and Tangye, S.G. (2007) Autoimmunity: IL-21: a new player in Th17-cell differentiation. Immunol Cell Biol 85, 503-5.
[136] Romagnani, S. (1995) Biology of human TH1 and TH2 cells. J Clin Immunol 15, 121-9.
[137] Zweerink, H.J. and Stanton, L.W. (1981) Immune response to herpes simplex virus infections: virus-specific antibodies in sera from patients with recurrent facial infections. Infect Immun 31, 624-30.
[138] Miller, E., Andrews, N., Waight, P., Findlow, H., Ashton, L., England, A., Stanford, E., Matheson, M., Southern, J., Sheasby, E., Goldblatt, D. and Borrow, R. (2011) Safety and immunogenicity of co-administering a combined meningococcal serogroup C and Haemophilus influenzae type b conjugate vaccine with 7-valent pneumococcal conjugate vaccine and measles, mumps and rubella vaccine at 12 months of age. Clin Vaccine Immunol 18, 367–372.
[139] Centers for Disease Control and Prevention (CDC). (1984) Measles outbreak among vaccinated high school students--Illinois. Morb Mortal Wkly Rep (MMWR) Jun 22;33(24):349-51. http://www.cdc.gov/mmwr/preview/mmwrhtml/00000359.htm.
[140] Anderson, L.J. and Seward, J.F. (2008) Mumps epidemiology and immunity: the anatomy of a modern epidemic. Pediatr Infect Dis J 27, S75-9.
[141] Boxall, N., Kubinyiova, M., Prikazsky, V., Benes, C. and Castkova, J. (2008) An increase in the number of mumps cases in the Czech Republic, 2005-2006. Euro Surveill 13.
[142] Sutter, R.W., Patriarca, P.A., Brogan, S., Malankar, P.G., Pallansch, M.A., Kew, O.M., Bass, A.G., Cochi, S.L., Alexander, J.P., Hall, D.B. and et al. (1991) Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children. Lancet 338, 715-20.
[143] Pedersen, I.R., Mordhorst, C.H., Glikmann, G. and von Magnus, H. (1989) Subclinical measles infection in vaccinated seropositive individuals in arctic Greenland. Vaccine 7, 345-8.
[144] Ozanne, G. and d'Halewyn, M.A. (1992) Secondary immune response in a vaccinated population during a large measles epidemic. J Clin Microbiol 30, 1778-82.
[145] Internal Medicine News. 22 Nov 2011. Infectious Diseases Society of America Conference. Acellular Pertussis Vaccine's Waning Immunity Caused California Epidemic.

http://www.internalmedicinenews.com/news/conference-news/infectious-diseases-society-of-america-conference/single-article/acellular-pertussis-vaccine-s-waning-immunity-caused-california-epidemic/71de9826f4.html.
[146] Centers for Disease Control and Prevention (CDC). (1999) Ten great public health achievements--United States, 1900-1999. MMWR Morb Mortal Wkly Rep 48, 241-3.
[147] Aiello, A.E. and Larson, E.L. (2002) What is the evidence for a causal link between hygiene and infections? Lancet Infect Dis 2, 103-10.
[148] Kata, A. (2011) Anti-vaccine activists, Web 2.0, and the postmodern paradigm - An overview of tactics and tropes used online by the anti-vaccination movement. Vaccine.
[149] Silverberg, J.I., Norowitz, K.B., Kleiman, E., Silverberg, N.B., Durkin, H.G., Joks, R. and Smith-Norowitz, T.A. (2010) Association between varicella zoster virus infection and atopic dermatitis in early and late childhood: a case-control study. J Allergy Clin Immunol 126, 300-5.
[150] Silverberg, J.I., Norowitz, K.B., Kleiman, E., Durkin, H.G. and Smith-Norowitz, T.A. (2009) Varicella zoster virus (wild-type) infection, but not varicella vaccine, in late childhood is associated with delayed asthma onset, milder symptoms, and decreased atopy. Pediatr Asthma Allergy Immunol 22, 15-20.
[151] Illi, S., von Mutius, E., Lau, S., Bergmann, R., Niggemann, B., Sommerfeld, C. and Wahn, U. (2001) Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. BMJ 322, 390-5.
[152] Sasco, A.J. and Paffenbarger, R.S., Jr. (1985) Measles infection and Parkinson's disease. Am J Epidemiol 122, 1017-31.
[153] Wrensch, M., Weinberg, A., Wiencke, J., Miike, R., Sison, J., Wiemels, J., Barger, G., DeLorenze, G., Aldape, K. and Kelsey, K. (2005) History of chickenpox and shingles and prevalence of antibodies to varicella-zoster virus and three other herpesviruses among adults with glioma and controls. Am J Epidemiol 161, 929-38.
[154] Bodewes, R., Fraaij, P.L., Geelhoed-Mieras, M.M., van Baalen, C.A., Tiddens, H.A., van Rossum, A.M., van der Klis, F.R., Fouchier, R.A., Osterhaus, A.D. and Rimmelzwaan, G.F. (2011) Annual vaccination against influenza virus hampers development of virus-specific CD8 T cell immunity in children. J Virol 85, 11995-2000.