Peer-Reviewed Reports Raise Various Vaccine Safety Issues – as of 2017:

> "*We identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.. Onset of behavioural symptoms was associated, by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another."(Wakefield et al. The Lancet, 1998)*

The same year, 1998, a serology study in the journal, *Clinical Immunology Immunopathology*, by Dr. Vikesh Singh, a gastroenterologist (University of Michigan) found an association between virus serology and brain autoantibody in autism. The study supported the hypothesis that an autoimmune response to the live measles virus in MMR vaccine "*may play a causal role in autism.*"

Those tentative findings have subsequently been confirmed, and amplified by others. But their work – if it ever reached public notice – has been effectively marginalized, disparaged or suppressed. In November 2011 Fiona Godlee, Editor in Chief, *BMJ* responded to the numerous readers who objected to a slanderous series of articles in the *BMJ,* and to her injudicious defamatory editorial in which she accused Dr. Andrew Wakefield of outright "scientific and ethical fraud," and characterized his *Lancet* report as "an elaborate fraud." Dr. Godlee asserted:

"*We are unaware of any peer reviewed paper replicating Andrew Wakefield's research or confirming his claims to have identified a new syndrome of regressive autism and inflammatory bowel disease associated with MMR vaccination…The existence of a gastrointestinal disturbance specific to persons with ASD (eg 'autistic enterocolitis')has not been established."*

That assertion is astonishing! And her clarion call to "close the door" on research that the BMJ business partnership deemed a "damaging vaccine scare" is irresponsible. Either the editor of the BMJ was completely ignorant about a body of peer-reviewed research reports; or she simply dismisses them all out of hand, as if that entire body of vaccine research is beyond the pale.

Dr. Lucija Tomljenovic responded by posting several references to published studies validating a link between autism and inflammatory intestinal disease on the *BMJ* website.

[1] "Panenteric IBD-Like Disease in a Patient with Regressive Autism Shown for the First Time by the Wireless Capsule Enteroscopy: Another Piece in the Jigsaw of this Gut-Brain Syndrome?" *The American Journal of Gastroenterology* (2005)

[2] "Autism and the Gastrointestinal Tract," Editorial by E Quigley and D Hurley, ***The American Journal of Gastroenterology*** (2000) *"Wakefield et al. are to be congratulated on opening yet another window onto the ever-broadening spectrum of gut-brain interactions. Their findings raise many challenging questions that should provoke further much-needed research in this area, research that may provide true grounds for optimism for affected patients and their families.*"

[3] "The Intestinal Lesion of Autistic Spectrum Disorder," Editorial by J Jass, ***European Journal of Gastroenterology & Hepatology*** (2005)

"There is good evidence linking autism with a specific form of chronic ileocolitis that differs from other forms of idiopathic inflammatory bowel disease. Nevertheless, the association of chronic LNH with autism is not widely known nor has it been incorporated into standard texts. Are the intestinal and cognitive manifestations merely different components of a syndrome complex of unknown pathogenesis or could they be causally related?

***These possibilities deserve further investigation and should not be lost in the fog of the controversy regarding the role of measles/mumps/rubella vaccination in the aetiology of autistic spectrum disorder**."*[highlight added]

[4] "Evaluation, Diagnosis, and Treatment of Gastrointestinal Disorders in Individuals with ASD: A Consensus Report**,"** ***Pediatrics***, 2010

"Gastrointestinal problems in individuals with ASDs can be challenging to evaluate. Clinical practice guidelines exist for the evaluation and management of ASDs by primary care and other physicians responsible for the care of individuals with ASDs but do not include routine consideration of potential gastrointestinal and other medical problems… Evidence-based algorithms for the assessment of abdominal pain, constipation, chronic diarrhea, and gastroesophageal reflux disease (GERD) should be developed."

The tentative reported clinical observational findings reported in the *Lancet (1998)* of a connection between gastrointestinal disease and autism in children spurred a surge of research that validated and amplified those "controversial" reported findings in the Lancet.
In fact, the link between gastrointestinal disorders and autism spectrum is widely accepted globally in mainstream published medical scientific reports – even as their existence is denied by the BMJ and the institutions that are dependent on pharmaceutical industry funding.

The relationship neurological brain dysfunction in autism spectrum and gastrointestinal disease is explored in hundreds of published studies: 655 listed on PubMed.

- Between 1998 and 2010, when the *Lancet* article was retracted; 184 scientific reports listed in PubMed linked autism and gastroinstestinal disorders;
- Since 2010, there have been 571 reports;
- 87 studies were published in 2017;
- 146 were published in 2016;
- 185 in 2015; 154 in 2014; 133 in 2013… The bibliography is posted here.

During this period, scientists have also been documenting and analyzing the toxic ingredients and cumulative, synergistic toxic effects of individual vaccines and raising questions about the safey of the CDC- recommended Childhood Vaccination Schedule that subjects infants to clusters of multiple vaccines simultaneously.

We have compiled the following additional annotated list of peer-reviewed reports

These reveal a wide range of research: some seek to identify possible genetic markers that might identify populations predisposed ("at risk") for autism (ASD); some examine links between autism, mitochondrial disorder, gastrointestinal disease, and pervasive developmental regression. Some researchers focus on vaccines and vaccine ingredients – e.g., mercury (thimerosal), live and attenuated viruses; and vaccine adjuvants such as aluminum – and the propensity of these toxins to trigger neurological disorders including autoimmunity. Some research reports confirm an association between measles virus, regressive autism and inflammatory bowel disease (some call it a syndrome). And some researchers are raising questions about the safety of the US Childhood Vaccination Schedule – the selection, timing, and cluster of multiple vaccines administered simultaneously: the children's vaccination schedule has not ever undergone proper safety tests.

The most recent peer-reviewed reports are listed first:

[1] "New Quality-Control Investigations on Vaccines: Micro- and Nanocontamination," Dr. Antonietta M. Gatti, Stefano Montanari, *International Journal of Vaccines and Vaccination*, January 2017 [National Council of Research , Institute for Science and Technology, Italy]

Scientists found contaminants in all vaccines; yet, they are not disclosed on their label.
Summary: An electron-microscopy investigation method was applied to the study of vaccines, aimed at verifying the presence of solid contaminants by means of an Environmental Scanning Electron Microscope equipped with an X-ray microprobe. Forty-four vaccines from Italy and France were analyzed. The results show the presence of micro- and nanosized particulate matter composed of inorganic elements in vaccine samples which are not declared among the components; their presence is, for the time being, inexplicable. A considerable part of those particulate contaminants have already been reported in literature as non-biodegradable and non-biocompatible. The evidence collected is suggestive of some hypotheses correlated to diseases."

"Given the contaminations we observed in all samples of human-use vaccines, adverse effects after the injection of those vaccines are possible and credible and have the character of randomness, since they depend on where the contaminants are carried by the blood circulation. It is only obvious that similar quantities of these foreign bodies can have a more serious impact on very small organisms like those of children."

Vaccines contain components that could themselves be the cause of adverse effects. It is a well-known fact in toxicology is that contaminants exert a mutual, synergic effect, and as the number of contaminants increases, the effects grow less and less predictable. The more so when some substances are unknown – they should not be present in any injectable medicament, let alone in vaccines – especially those injected into infants.

The episodic evidence of adverse side-effects reported by people allegedly damaged by vaccines is twofold: some say the damage occurred and became visible within a few hours from administration, and some maintain that it was a matter of some weeks.

"The analyses carried out show that in all samples checked vaccines contain non biocompatible and bio-persistent foreign bodies which are not declared by the Producers, against which the body reacts in any case. This new investigation represents a new quality control that can be adopted to assess the safety of a vaccine. Our hypothesis is that this contamination is unintentional, since it is probably due to polluted components or procedures of industrial processes (e.g. filtrations) used to produce vaccines, not investigated and not detected by the Producers. If our hypothesis is actually the case, a close inspection of the working places and the full knowledge of the whole procedure of vaccine preparation would probably allow to eliminate the problem."

What is one to make of their finding that: "Feligen, the only veterinary vaccine tested, proved to be the only sample free from inorganic contamination."

[2] "Non-Linear Dose-Response Of Aluminium Hydroxide Adjuvant Particles: Selective Low Dose Neurotoxicity," Crépeaux G, Eidi H, David MO, Baba-Amer Y, Tzavara E, Giros B, Authier FJ, Exley C, Shaw CA, Cadusseau J, Gherardi RK. *Toxicology*, 2017.
[Study by French, British & Canadian scientists]

Summary: "Aluminium (Al) oxyhydroxide (Alhydrogel®), the main adjuvant licensed for human and animal vaccines, consists of primary nanoparticles that spontaneously agglomerate. Concerns about its safety emerged following recognition of its unexpectedly long-lasting biopersistence within immune cells in some individuals, and reports of chronic fatigue syndrome, cognitive dysfunction, myalgia, dysautonomia and autoimmune/inflammatory features temporally linked to multiple Al-containing vaccine administrations.

Mouse experiments have documented its capture and slow transportation by monocyte-lineage cells from the injected muscle to lymphoid organs and eventually the brain. The present study aimed at evaluating mouse brain function and Al concentration 180days after injection of various doses of Alhydrogel in in adult female CD1 mice. Cognitive and motor performances were assessed by 8 validated tests… An unusual neuro-toxicological pattern limited to a low dose of Alhydrogel® was observed. Neurobehavioural changes, including decreased activity levels and altered anxiety-like behaviour, were observed compared to controls… Consistently, microglial number appeared increased in the ventral forebrain of the [low dose] 200µg Al/kg group. Cerebral Al levels were selectively increased in animals exposed to the lowest dose.

We conclude that Alhydrogel® injected at low dose in mouse muscle may selectively induce long-term Al cerebral accumulation and neurotoxic effects. To explain this unexpected result, an avenue that could be explored in the future relates to the adjuvant size since the injected suspensions corresponding to the lowest dose, but not to the highest doses."

[3] "Severe Manifestations Of Autoimmune Syndrome Induced By Adjuvants (Shoenfeld's Syndrome)" Jara LJ, García-Collinot G, Medina G, Cruz-Dominguez MDP, Vera-Lastra O, Carranza-Muleiro RA, Saavedra MA. *Immunological Research*, 2017 [Mexican study]

Abstract Summary: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) encompassing conditions linked to previous exposure to an adjuvant substance. The clinical picture is very heterogeneous, from mild to severe manifestations, including death. The aim of this study was to systematically review the literature on severe ASIA cases. A systematic review of the literature was performed investigating severe ASIA cases. All publications were identified through PubMed, EMBASE, MEDLINE and Cochrane, and were published from 2011 to 2016.

Severe ASIA was arbitrarily defined as follows: major organ involvement, life-threatening conditions, intensive treatment, disability, hospitalization and outcome (survival and death). Cases described before 2011 were excluded. From 2011 to 2016, we identified 4479 ASIA cases, of them 305 fulfilled arbitrary criteria of severe ASIA including our case presentation and 11 deaths. The majority of severe ASIA cases were related to HPV vaccine, silicone, influenza vaccine. The interval from exposition to severe manifestation was from 2 days to 23 years. This is the first study that analyzes all cases published on ASIA with severe manifestations. Efforts should be made to discover the connection between adjuvants, autoimmunity and autoimmune diseases, because there is an increase in cases severe and life-threatening of ASIA.

[4] "The Pilot Comparative Study On The Health Of Vaccinated And Unvaccinated 6- To 12-Year Old U.S. Children," Anthony R Mawson, Brian D Ray, Azad R Bhuiyan, Binu Jacob, *The Journal of Translational Science*, 2017. [Removed without explanation—as was report [2] However, both papers are posted: here, also here]

"This study aimed 1) to compare vaccinated and unvaccinated children on a broad range of health outcomes, and 2) to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors…NDD, a derived diagnostic measure, was defined as having one or more of the following three closely-related diagnoses: a learning disability, Attention Deficient Hyperactivity Disorder, and Autism Spectrum Disorder."

The study included 666 children homeschooled in Florida, Louisiana, Mississippi and Oregon of who 261 were unvaccinated. "The vaccinated were less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but more likely to have been diagnosed with pneumonia, otitis media, allergies and NDD."

"In conclusion, vaccinated homeschool children were found to have a higher rate of allergies and NDD than unvaccinated homeschool children. While vaccination remained significantly associated with NDD after controlling for other factors, preterm birth coupled with vaccination

was associated with an apparent synergistic increase in the odds of NDD. Further research involving larger, independent samples and stronger research designs is needed to verify and understand these unexpected findings in order to optimize the impact of vaccines on children's health. Vaccination also remained significantly associated with NDD after controlling for other factors, whereas preterm birth, long considered a major risk factor for NDD, was not associated with NDD after controlling for the interaction between preterm birth and vaccination. In addition, preterm birth coupled with vaccination was associated with an apparent synergistic increase in the odds of NDD above that of vaccination alone."**

[5] "Preterm Birth, Vaccination And Neurodevelopmental Disorders: A Cross-Sectional Study Of 6- To 12-Year-Old Vaccinated And Unvaccinated Children," Anthony R Mawson, Azad Bhuiyan, Binu Jacob, Brian D Ray, Journal of Translational Science, 2017 [Removed without explanation]**

"No association was found between preterm birth and NDD in the absence of vaccination, but vaccination was significantly associated with NDD in children born at term (OR 2.7, 95% CI: 1.2, 6.0). However, vaccination coupled with preterm birth was associated with increasing odds of NDD, ranging from 5.4 compared to vaccinated but non-preterm children, to 14.5 compared to children who were neither preterm nor vaccinated. The results of this pilot study suggest clues to the epidemiology and causation of NDD but question the safety of current vaccination practices for preterm infants. Further research is needed to validate and investigate these associations in order to optimize the impact of vaccines on children's health."

** We were informed that this study has been peer reviewed and accepted for publication on no fewer than 4 occasions. It was pulled twice at the last minute--with no explanation and no second chance of publication. On the third occasion the abstract was published online in advance of the full paper (as is the journal's standard practice). It generated immediate hostility which resulted, once again in successful censorship. In this fourth time around, two papers by the authors were published – and then, without a word of explanation, the links went dead. AHRP posted the Mawson papers because we believe in the open, honest exchange of scientific information – a fast disappearing commodity in this era of corporate-government control of information. [Both papers are here, also here

[6] "Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome) - An update," Watad A, Quaresma M, Brown S, Cohen Tervaert JW, Rodríguez-Pint I, Cervera R, Perricone C, Shoenfeld Y, *Lupus*, 2017
[International team of researchers from Israel, the Netherlands, Italy, Spain]

Abstract: "Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been widely described in many studies conducted thus far. The syndrome incorporates five immune-mediated conditions, all associated with previous exposure to various agents such as vaccines, silicone implants and several others.

The emergence of ASIA syndrome is associated with individual genetic predisposition, for instance those carrying HLA-DRB1*01 or HLA-DRB4 and results from exposure to external or endogenous factors triggering autoimmunity. Such factors have been demonstrated as able to induce autoimmunity in both animal models and humans via a variety of proposed mechanisms. In recent years, physicians have become more aware of the existence of ASIA syndrome and the relationship between adjuvants exposure and autoimmunity and more cases are being reported.

Accordingly, we have created a registry that includes at present more than 300 ASIA syndrome cases that have been reported by different physicians worldwide, describing various autoimmune conditions induced by diverse adjuvants. In this review, we have summarized the updated literature on ASIA syndrome and the knowledge accumulated since 2013 in order to elucidate the association between the exposure to various adjuvant agents and its possible clinical manifestations. Furthermore, we especially referred to the relationship between ASIA syndrome and systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS)."

[7] "Autoimmune/Inflammatory Syndrome Induced by Adjuvants and Thyroid Autoimmunity." Watad A, David P, Brown S, Shoenfeld Y, Front Endocrinology (Lausanne) 2017

Abstract: "The autoimmune/inflammatory syndrome induced by adjuvants (ASIA), presented by Shoenfeld and Agmon-Levin in 2011, is an entity that incorporates diverse autoimmune conditions induced by the exposure to various adjuvants. Adjuvants are agents that entail the capability to induce immune reactions. Adjuvants are found in many vaccines and used mainly to increase the response to vaccination in the general population. Silicone has also been reported to be able to induce diverse immune reactions.

Clinical cases and series of heterogeneous autoimmune conditions including systemic sclerosis, systemic lupus erythematosus, and rheumatoid arthritis have been reported to be induced by several adjuvants. However, only a small number of cases of autoimmune thyroid disorder have been included under the umbrella of ASIA syndrome. Indeed, clinical cases of Hashimoto's thyroiditis and/or subacute thyroiditis were observed after the exposure to vaccines as well as silicone implantation. In our review, we aimed to summarize the current knowledge on ASIA syndrome presented as endocrinopathies, focusing on autoimmune thyroid disorders associated with the various adjuvants."

[8] "Temporal Association Of Certain Neuropsychiatric Disorders Following Vaccination Of Children And Adolescents: A Pilot Case-Control Study." Leslie DL, Robert. Richmand BJ, Aktan Guloksuz S & Leckman JF, *Frontiers in Psychiatry* (2017).
[Pennsylvania State University College of Medicine and Yale Child Study Center, Yale University School of Medicine] [Open access]

ABSTRACT:
"…the onset of certain brain-related autoimmune and inflammatory disorders has been found to be temporally associated with the antecedent administration of various vaccines. This study examines whether antecedent vaccinations are associated with increased incidence of obsessive–compulsive disorder (OCD), anorexia nervosa (AN), anxiety disorder, chronic tic disorder,

attention deficit hyperactivity disorder, major depressive disorder, and bipolar disorder in a national sample of privately insured children.

R**esults:** Subjects with newly diagnosed AN were more likely than controls to have had any vaccination in the previous 3 months [hazard ratio (HR) 1.80, 95% confidence interval 1.21–2.68]. Influenza vaccinations during the prior 3, 6, and 12 months were also associated with incident diagnoses of AN, OCD, and an anxiety disorder. Several other associations were also significant with HRs greater than 1.40 (hepatitis A with OCD and AN; hepatitis B with AN; and meningitis with AN and chronic tic disorder).

C**onclusion:** This pilot epidemiologic analysis implies that the onset of some neuro-psychiatric disorders may be temporally related to prior vaccinations in a subset of individuals."

[9] "The Introduction Of Diptheria-Tetanus-Pertussis And Oral Polio Vaccine Among Young Infants In An Urban African Community: A Natural Experiment." Søren Wengel Mogensen, Andreas Andersen, Amabelia Rodrigues, Christine S Benn, Peter Aaby. *EBioMedicine, 2017* [Open access Full Text] [Funded by the Danish International Development Agency]

Highlights

- When DTP and OPV[polio] were introduced in Guinea-Bissau in 1981, allocation by birthday resulted in a natural experiment of being vaccinated early or late.
- Between 3 and 5 months of age, children who received DTP and OPV early had 5-fold higher mortality than still unvaccinated children.
- In the only two studies of the introduction of DTP and OPV, co-administration of OPV with DTP may have reduced the negative effects of DTP.

5 Conclusions: DTP was associated with 5-fold higher mortality than being unvaccinated. No prospective study has shown beneficial survival effects of DTP. Unfortunately, DTP is the most widely used vaccine, and the proportion who receives DTP3 is used globally as an indicator of the performance of national vaccination programs. **It should be of concern that the effect of routine vaccinations on all cause mortality was not tested in randomized trials.** All currently available evidence suggests that DTP vaccine may kill more children from other causes than it saves from diphtheria, tetanus or pertussis. Though a vaccine protects children against the target disease it may simultaneously increase susceptibility to unrelated infections.

The recently published SAGE review called for randomized trials of DTP (Higgins et al., 2014). However, at the same time the IVIR-AC committee to which SAGE delegated the follow-up studies of the NSEs of vaccines has indicated that it will not be possible to examine the effect of DTP in an unbiased way. If that decision by IVIR-AC remains unchallenged, the present study may remain the closest we will ever come to a RCT of the NSEs of DTP.

There is only one other study of the introduction of DTP. In rural Guinea-Bissau, DTP (±OPV) was associated with 2-fold higher mortality (Aaby et al., 2004a). All studies that documented vaccination status and followed children prospectively indicate that DTP has negative effects; a

meta-analysis of the eight studies found 2-fold higher mortality for DTP-vaccinated compared with DTP-unvaccinated, mostly BCG-vaccinated controls (Aaby et al., 2016) (Appendix A).

[10] "Behavioral Abnormalities In Female Mice Following Administration Of Aluminum Adjuvants And The Human Papillomavirus (HPV) Vaccine Gardasil," Rotem Inbar, Ronen Weiss, Lucija Tomljenovic, Maria-Teresa Arango, Yael Deri, Christopher A, Shaw, Joab Chapman, Miri Blank, Yehuda Shoenfeld, *Immunological Research*, Feb 2017
[Israeli study]

Summary: "Vaccine adjuvants and vaccines may induce autoimmune and inflammatory manifestations in susceptible individuals. To date most human vaccine trials utilize aluminum (Al) adjuvants as placebos despite much evidence showing that Al in vaccine-relevant exposures can be toxic to humans and animals…It appears that Gardasil via its Al adjuvant and HPV antigens has the ability to trigger neuroinflammation and autoimmune reactions, further leading to behavioral changes…In light of these findings, this study highlights the necessity of proceeding with caution with respect to further mass-immunization practices with a vaccine of yet unproven long-term clinical benefit in cervical cancer prevention "

[11]"Epidemiologic and Molecular Relationship Between Vaccine Manufacture and Autism Spectrum Disorder Prevalence**,"** Deisher TA, Doan NV, Koyama K, Bwabye S, ***Issues in Law & Medicine***, 2015

*"*A worldwide autism epidemic is copiously established by the number of peer reviewed articles on the subject, including the observations from numerous institutions that de novo genetic insertions and mutations are excessive in children with autism…Vaccines manufactured in human fetal cell lines contain unacceptably high levels of fetal DNA fragment contaminants. The human genome naturally contains regions that are susceptible to double strand break formation and DNA insertional mutagenesis."

The authors note that MMR vaccination rate in the UK, Norway and Sweden, fell below 90% after Dr. Wakefield's 1998 publication, then recovered slowly after 2001 until reaching over 90% coverage again by 2004. During the same time period, the average autism spectrum disorder prevalence in those three countries dropped substantially after birth year 1998 and gradually increased again after birth year 2000. The authors hypothesize that: *"The Wakefield Scare" created a natural experiment that may provide evidence supporting a causal relationship between fetal cell-line manufactured vaccines and ASD prevalence."*

[12] "Insight Into The Cellular Fate And Toxicity Of Aluminium Adjuvants Used In Clinically Approved Human Vaccinations," Matthew Mold, Emma Shardlow & Christopher Exley, *Nature Scientific Reports*, 2016

Compares the reactivity and fate of aluminum adjuvants commonly used in vaccines. Aluminum-containing adjuvants have been known to be associated with adverse reactions after vaccinations. There are no sound scientific studies or controlled clinical trials to understand adjuvant effect and toxicity of aluminum-containing adjuvant.

Summary: Aluminum based adjuvants (ABA) remain the most widely used and effective adjuvants in vaccination and immunotherapy. ABA are included in human vaccinations to boost or potentiate the immune response to the injected antigen. It has become increasingly recognized that activation of the innate immune response is crucial for increased antibody titres. "The continued and widespread use of ABA has followed the emergence of recombinantly expressed protein antigens of high purity as a safer alternative to inactivated or attenuated pathogens. Owing to the homogeneity and generally weak immunogenicity of recombinant antigens, the inclusion of adjuvants is often necessary for the induction of robust immune responses and effective immunization."

Noting that few studies have employed direct comparative assessments of the physicochemical properties of clinically used ABA formulations with their resultant cellular uptake, the research team at Keele University investigated the relationship between the physico-chemical properties of aluminum adjuvants and the immune response. They compared the physical properties and toxicity of two adjuvants used in vaccines: aluminum oxyhydroxide (Alhydrogel) and aluminum hydroxyphosphate (Adju-Phos).

By comparing the biological reactivity and potential toxicities -- both at the injection site and throughout the body – they found that the high loading Alhydrogel, which is more easily loaded into immune reactive cells – is more easily transported throughout the body. Professor Exley and his Keele research team note that this loading of aluminum into viable cells offers a mechanism whereby significant amounts of aluminum – a known neurotoxin – might be translocated throughout the body and even across the blood brain barrier and into the central nervous system.

However, the use of adjuvants in human vaccinations has been linked to adverse effects often classified under Autoimmune (or autoinflammatory) syndrome induced by adjuvants (ASIA). Combined with the relatively low cost of hydrated colloidal aluminium salts and their ease of inclusion as effective adjuvants within clinically approved vaccine formulations, the continued use of ABA in human vaccinations is likely to continue.

[The findings are at odds with the Code of Federal Regulations Title 21 requiring satisfactory evidence of safety: "an adjuvant shall not be introduced into a product unless there is satisfactory evidence that it does not affect adversely the safety or potency of the product.." (21 CFR 610.15)

In 2013, Professor Exley wrote:

"The immunopotency of aluminium has been known for at least 100 years and still today forms the basis for the use of aluminium salts as adjuvants in vaccinations and allergy therapies. What is then surprising is the uncertainty regarding their mechanism of action and burgeoning evidence of their toxicity in potentially susceptible individuals."

There is [sic] a perception that aluminium is a 'safe' metal with few if any signicant implications for human health. This is a view which though seemingly convenient for the aluminium industry is neither supported by observation; for example, aluminium is the cause of dialysis encephalopathy, nor by decades of animal experimentation demonstrating intoxication. It is truly an anomaly that the perceived innocuousness of aluminium in humans has persisted

through to the present day and to the extent that there is no legislation whatsoever limiting human's exposure to aluminium. (Human Exposure to Aluminum, *Environmental Science Processes & Impacts*, 2013)

[13] "Autoimmune/Inflammatory Syndrome Induced by Adjuvants and Sjögren's Syndrome," Serena Colafrancesco, Carlo Perricone, Yehuda Shoenfeld, IMAJ • Vol 18, March-April 2016 [Israeli and Italian scientists]

Summary: "Several case reports have suggested that both vaccines and silicone may trigger the development of SS [Sjögren's syndrome, a chronic systemic autoimmune inflammatory condition involving the exocrine glands]. Aluminum is one of the principal adjuvants used in vaccine formulation and may be responsible for the development of ASIA syndrome. It seems that its ability to behave as an adjuvant might be related to evidence that aluminum salts seem to both induce the activation of dendritic cells and complement components and increase the level of chemokine secretion at the injection site… other vaccines including Bacillus Calmette Guérin (BCG), hepatitis A and/or B and human papillomavirus, should be avoided or considered only in selected patients… There is considerable evidence raising the possibility of vaccine-triggered autoimmunit

[14] "Combining Childhood Vaccines at One Visit Is Not Safe," Neil Z. Miller *Journal of American Physicians and Surgeons*, Summer 2016 [Open Access]

Summary "Our study showed that infants who receive several vaccines concurrently, as recommended by CDC, are significantly more likely to be hospitalized or die when compared with infants who receive fewer vaccines simultaneously. It also showed that reported adverse effects were more likely to lead to hospitalization or death in younger infants. The safety of CDC's childhood vaccination schedule was never affirmed in clinical studies. Vaccines are administered to millions of infants every year, yet health authorities have no scientific data from synergistic toxicity studies on all combinations of vaccines that infants are likely to receive. National vaccination campaigns must be supported by scientific evidence."

[15] "Aluminum in Childhood Vaccines Is Unsafe," Neil Z. Miller *Journal of American Physicians and Surgeons*, Winter 2016

Summary: When the US phased out mercury from vaccines in 2002, CDC added two doses of mercury-containing influenza vaccines to the CDC schedule for babies aged 6 to 23 months. And CDC added new vaccines high in aluminum content to the childhood vaccination schedule.

"Prior to the mercury phase-out (pre-2000), babies received 3,925 micrograms (mcg) of aluminum in their first year-and-a-half of life. After pneumococcal and hepatitis A vaccines were added to the immunization schedule, babies began receiving 4,925 mcg of aluminum during the same age period—a 25% increase."

"Numerous studies provide compelling evidence that injected aluminum can be detrimental to health. Aluminum is capable of remaining in cells long after vaccination and may cause neurologic and autoimmune disorders. During early development, the child's brain is more

susceptible to toxins and the kidneys are less able to eliminate them. Thus, children have a greater risk than adults of adverse reactions to aluminum in vaccines. Millions of children every year are injected with vaccines containing mercury and aluminum despite well-established experimental evidence of the potential for additive or synergistic toxicity when an organism is exposed to two or more toxic metals."

Toxic metals such as aluminum do not belong in prophylactic medications administered to children, teenagers, or adults.

[16] "Evidence that Food Proteins in Vaccines Cause the Development of Food Allergies and Its Implications for Vaccine Policy," Vinu Arumugham, *Journal of Developing Drugs*, 2015 [Open Access]

Summary: An estimated 15 million Americans suffer life-threatening food allergies. According to CDC website, food allergies in U.S. children from birth to age17 increased by 50% from 1997 to 2011. In the UK hospital admissions for anaphylaxis among children increased 700% and admissions for food allergy increased 500% since 1990. Whereas most food allergy studies avoid vaccines, this article addresses the controversial question.

Allergen content and quantities in vaccines are unregulated. The FDA confirmed that: *No safe level or limits have ever been established or enforced for the allergens contained in vaccines*. The Institute of Medicine acknowledges that food proteins in vaccines "*occasionally induce…sensitization…and subsequent hypersensitivity reactions, including anaphylaxis.*" (Report, 2012)

"*The vaccine schedule has increased the number of vaccine shots to 30–40 and up to five vaccines are simultaneously administered to children. Vaccines contain food proteins, adjuvants such as aluminum compounds and pertussis toxin that also increase the immunogenicity of injected food proteins. This combination of atopic children and food protein injection along with adjuvants, contributes to millions developing life-threatening food allergies. Given the scale and severity of the food allergy epidemic, urgent action is needed to change vaccine policy concerning vaccine specifications, manufacture, vaccine package insert documentation requirements."*

[17] "Predicting Post-Vaccination Autoimmunity: Who Might be at Risk?" Soriano A, et al. ***Journal of Pharmacological Research*** (2015) [Free complete text]

"The relationship between vaccines and autoimmunity is bi-directional [5] . On one hand, vaccines prevent infectious conditions, therefore preventing the development of overt autoimmune diseases which in some individuals are triggered by infections. On the other hand, many reports that describe post-vaccination autoimmunity strongly suggest that vaccines can indeed trigger autoimmunity.

Defined autoimmune disease that may occur following vaccinations include arthritis, lupus (systemic lupus erythematosus, SLE), diabetes mellitus, thrombocytopenia, vasculitis, dermatomyositis, Guillain-Barré syndrome and demyelinating disorders. Almost all types of vaccines have been reported to be associated with onset autoimmune inflammatory syndrome induced by adjuvants (ASIA).

"It has been postulated that autoimmunity could be triggered or enhanced by the vaccine immunogen contents, as well as by adjuvants, which are used to increase the immune reaction to the immunogen. Fortunately, vaccination-related ASIA is uncommon. Yet, by defining individuals at risk we may further limit the number of individuals developing post-vaccination ASIA. In this perspective we defined four groups of individuals who might be susceptible to develop vaccination-induced ASIA:

- patients with prior post-vaccination autoimmune phenomena,
- patients with a medical history of autoimmunity,
- patients with a history of allergic reactions,
- and individuals who are prone to develop autoimmunity (have a family history of autoimmune diseases; asymptomatic carriers of autoantibodies; carry certain genetic profiles

"Throughout our lifetime the normal immune system walks a fine line between preserving normal immune reactions and developing autoimmune diseases," says the paper. "The healthy immune system is tolerant to self-antigens. When self-tolerance is disturbed, dysregulation of the immune system follows, resulting in emergence of an autoimmune disease. Vaccination is one of the conditions that may disturb this homeostasis in susceptible individuals, resulting in autoimmune phenomena and ASIA

Fortunately, vaccination-related ASIA is uncommon. Yet, by defining individuals at risk we may further limit the number of individuals developing post-vaccination ASIA. It is assumed that four groups of individuals are at risk: patients with prior post-vaccination autoimmune phenomena, patients with a medical history of autoimmunity, patients with a history of allergic reactions, and individuals who are prone to develop autoimmunity.

Because of selection bias [in clinical trials] the occurrence of serious adverse reactions resulting from vaccinations in the real life where vaccines are mandated to all individuals regardless of their susceptibility factors may be considerable understated."

[18] ***Vaccines and Autoimmunity***, 2015 Edited by leaders in the field. This textbook includes 37 chapters by an international roster of scientists.

"The book is divided into three sections; the first contextualizes the role of adjuvants in the framework of autoimmunity, covering the mechanism of action of adjuvants, experimental models of adjuvant induced autoimmune diseases, infections as adjuvants, the Gulf War Syndrome, sick-building syndrome (SBS), safe vaccines, toll-like receptors, TLRS in vaccines, pesticides as adjuvants, oil as adjuvant, mercury, aluminum and autoimmunity. The following section reviews literature on vaccines that have induced autoimmune conditions such as MMR

and HBV, among others. The final section covers diseases in which vaccines were known to be the solicitor – for instance, systemic lupus erythematosus – and whether it can be induced by vaccines for MMR, HBV, HCV, and others."

[19] "Gastrointestinal Issues In Autism Spectrum Disorder," Elaine Y Hsiao, ***Harvard Review Of Psychiatry***, 2014

Abstract: "While autism spectrum disorder (ASD) is characterized by communication impairments, social abnormalities, and stereotypic behaviors, several medical comorbidities are observed in autistic individuals. Of these, gastrointestinal (GI) abnormalities are of particular interest given their reported prevalence and correlation with the severity of core autism-related behavioral abnormalities.

This review discusses the GI pathologies seen in ASD individuals and the association of particular GI conditions with known genetic and environmental risk factors for autism. It further addresses how GI abnormalities can affect the neuropathological and behavioral features of ASD, as well as the development of autism-related endophenotypes such as immune dysregulation, hyperserotonemia, and metabolic dysfunction. Finally, it presents emerging evidence for a gut-brain connection in autism, wherein GI dysfunction may contribute to the pathogenesis or severity of ASD symptoms."

Conclusions
"ASD is tremendously heterogeneous not only in the presence and severity of its diagnostic behavioral features, but also in the presence and severity of a wide range of medical comorbidities. The challenges faced in identifying the underlying causes, molecular biomarkers, and specific treatments for ASD warrant the need to study well-defined subclasses of autistic individuals. A preponderance of evidence suggests that a significant subset of autistic individuals exhibit GI abnormalities and that GI issues can contribute to the clinical manifestations of ASD-associated symptoms, including abnormal behavior, immune dysregulation, and metabolic dysfunction."
*Three of Dr. Wakefield's post-*Lancet* article are cited.

[20] "Methodological Issues And Evidence Of Malfeasance In Research Purporting To Show Thimerosal In Vaccines Is Safe," Brian Hooker et al. ***Biomed Research International, 2014*** [Open Access. Full Text]

Dr. Hooker and colleagues trace the route that led to the publication of the Madsen/Thorsen/Schendel, et al report in the journal *Pediatrics.* It was rejected for publication by *the Lancet* and by the *Journal of the American Medical Association (JAMA).* A written communication between Dr. Thorsen and CDC official, Coleen Boyle (2003) reveals that when the paper was first submitted to *Pediatrics* with the 2001 data included; it was criticized by one of the peer-reviewers:

"The drop of incidence shown for the most recent years is perhaps the most dramatic feature of the figure, and is seen in the oldest age group as well as the youngest." The reviewer questions the authors' failure to discuss *"the possibility that this decrease might have come about through elimination of [T]himerosal."*

That such a deliberately manipulated, fraudulent report was published in an "authoritative" "high impact" journal – whose editors knew that the 2001 data was omitted from the final version – reveals much about the corrupted vaccine literature. Hooker lists **165 published studies** that contradict the Danish CDC-Thorsen claimed findings. These studies reported Thimerosal to be harmful. They note that sixteen of these reports examined mercury's effect in infants and children; and these studies reported that the children suffered severe outcomes including, death, allergic reaction, malformation, auto-immune reaction, developmental delays, and autism.

[21] "Transcriptomic Analyses of Neurotoxic Effects in Mouse Brain After Intermittent Neonatal Administration of Thimerosal," Xialong Li, Fengqin Qu, Wenjuan Xe, Fengli Wang, Hongmei Lui, *Toxicological Sciences*, March 2014 [Chinese study]

Summary: "Although thimerosal has been removed from mandatory childhood vaccines in the United States, thimerosal-preserved vaccines are still widely used outside of the United States especially in developing countries. Notably, thimerosal-containing vaccines are being given to the newborns within the first 12-24 h after birth in some countries. Thimerosal-treated mice exhibited neural development delay, social interaction deficiency, and inclination of depression. Apparent neuropathological changes were also observed in adult mice neonatally treated with thimerosal. High-throughput RNA sequencing of autistic-behaved mice brains revealed the alternation of a number of canonical path- ways involving neuronal development, neuronal synaptic function, and the dysregulation of endocrine system. Intriguingly, the elevation of anterior pituitary secreting hormones occurred exclusively in male but not in female thimerosal-treated mice, demonstrating for the first time the gender bias of thimerosal-mercury toxicity with regard to endocrine system."

[22] "A Dose-Response Relationship between Organic Mercury Exposure from Thimerosal-Containing Vaccines and Neurodevelopmental Disorders," David A. Geier, Brian S. Hooker, Janet K. Kern, Paul G. King, Lisa K. Sykes and Mark R. Geier, *International Journal of Environmental Research Public Health*, 2014 [Open Access]

Summary: "A hypothesis testing case-control study evaluated concerns about the toxic effects of organic-mercury (Hg) exposure from thimerosal-containing vaccines on the risk of neurodevelopmental disorders (NDs) Automated medical records were examined to identify cases and controls enrolled from their date-of-birth (1991-2000) in the Vaccine Safety Datalink (VSD) project.

ND cases were diagnosed with pervasive developmental disorder (PDD), specific developmental delay, tic disorder or hyperkinetic syndrome of childhood. In addition, putative non-thimerosal-related outcomes of febrile seizure, failure to thrive and cerebral degenerations were examined. The cumulative total dose of Hg exposure from thimerosal-containing hepatitis B vaccine (T-HBV) administered within the first six months of life was calculated.

Routine childhood vaccination may be an important public health tool to reduce infectious disease-associated morbidity/mortality, but the present study significantly associates organic-Hg

exposure from T-HBV with an increased risk of an ND diagnosis. This study provides new epidemiological evidence supporting a significant relationship between increasing organic-Hg exposure from TCVs and the subsequent risk of an ND diagnosis.

[23] Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. Hsiao EY1, McBride SW2, Hsien S2, Sharon G2, Hyde ER3, McCue T3, Codelli JA4, Chow J2, Reisman SE4, Petrosino JF3, Patterson PH5, Mazmanian SK6 *Cell*, 2013 [California Institute of Technology]

Abstract: Neurodevelopmental disorders, including autism spectrum disorder (ASD), are defined by core behavioral impairments; however, subsets of individuals display a spectrum of gastrointestinal (GI) abnormalities. We demonstrate GI barrier defects and microbiota alterations in the maternal immune activation (MIA) mouse model that is known to display features of ASD. Oral treatment of MIA offspring with the human commensal Bacteroides fragilis corrects gut permeability, alters microbial composition, and ameliorates defects in communicative, stereotypic, anxiety-like and sensorimotor behaviors. MIA offspring display an altered serum metabolomic profile, and B. fragilis modulates levels of several metabolites. Treating naive mice with a metabolite that is increased by MIA and restored by B. fragilis causes certain behavioral abnormalities, suggesting that gut bacterial effects on the host metabolome impact behavior.

Taken together, these findings support a gut-microbiome-brain connection in a mouse model of ASD and identify a potential probiotic therapy for GI and particular behavioral symptoms in human neurodevelopmental disorders.

[24] "A Population-Based Cohort Study of Undervaccination in 8 Managed Care Organizations Across the United States," Jason M. Glanz, PhD; Sophia R. Newcomer, MPH; Komal J. Narwaney, MD, PhD; Simon J. Hambidge, MD, PhD; Matthew F. Daley, MD; Nicole M. Wagner, MPH, *JAMA Pediatrics*, January 2013

Summary: "The study examined trends of undervaccination in children aged 2 to 24 months (born between 2004 and 2008). Outcome Measures: Compared health care utilization rates between undervaccinated – 48.7% -- and age-appropriately vaccinated children.
In a matched cohort analysis, undervaccinated children had lower outpatient visit rates compared with children who were age-appropriately vaccinated. Children who were under-vaccinated because of parental choice had lower rates of outpatient visits, and lower rates of ED [emergency room] encounters compared with children who were age-appropriately vaccinated."

[25] Identification of unique gene expression profile in children with regressive autism spectrum disorder (ASD) and ileocolitis. Walker SJ1, Fortunato J, Gonzalez LG, Krigsman A. *PLoS One*, 2013

The finding of this Wake Forest study confirms both Dr. Wakefield's original case series study and the validity of the diagnostic methodology used by the team of medical experts who diagnosed the 12 children in the *Lancet* (1998) study. They correctly conducted the necessary

physiological examinations needed to obtain a valid, verifiable diagnosis which general practitioners had not.

Abstract: Gastrointestinal symptoms are common in children with autism spectrum disorder (ASD) and are often associated with mucosal inflammatory infiltrates of the small and large intestine. Although distinct histologic and immunohistochemical properties of this inflammatory infiltrate have been previously described in this ASD (GI) group, molecular characterization of these lesions has not been reported. In this study we utilize transcriptome profiling of gastrointestinal mucosal biopsy tissue from ASD(GI) children and three non-ASD control groups (Crohn's disease, ulcerative colitis, and histologically normal) in an effort to determine if there is a gene expression profile unique to the ASD(GI) group.

"Prospective controlled studies suggest that as many as 70% of autistic children exhibit chronic GI [gastrointestinal inflammation], diarrhea, constipation, abdominal distension, failure to thrive, weight loss, feeding problems, and abdominal pain related to extreme irritability, aggression, and self-injury."

"*retrospective chart review studies have shown no increase in GI symptoms in ASD children. [Yet] In ASD children who undergo endoscopic and histologic examinations, inflammatory pathology is reported with high frequency."*

Taken together, these results demonstrate that ASD(GI) children have a gastrointestinal mucosal molecular profile that overlaps significantly with known inflammatory bowel disease (IBD), yet has distinctive features that further supports the presence of an ASD-associated IBD variant, or, alternatively, a prodromal phase of typical inflammatory bowel disease.

[26] "Aluminum In The Central Nervous System (CNS): Toxicity In Humans And Animals, Vaccine Adjuvants, And Autoimmunity," Chris Shaw, L. Tomljenovic *Immunological Research*, 2013

Summary: "An overview of the neurotoxicity of aluminum and the various associated disease states. The literature demonstrates clearly negative impacts of aluminum on the nervous system across the age span. In young children, a highly significant correlation exists between the number of pediatric aluminum-adjuvanted vaccines administered and the rate of autism spectrum disorders.

Many of the features of aluminum- induced neurotoxicity may arise, in part, from autoimmune reactions, as part of the ASIA syndrome. Unlike dietary aluminum which will usually clear rapidly from the body, aluminum used in vaccines and injected is designed to provide a long-lasting cellular exposure. Thus, the problem with vaccine- derived aluminum is really twofold: It drives the immune response even in the absence of a viral or bacterial threat and it can make its way into the central nervous system. It is not really a matter of much debate that aluminum in various forms can be neurotoxic."

[27] "Aluminium Based Adjuvants And Their Effects On Mitochondria And Lysosomes Of Phagocytosing Cells,"Ohlsson L, Exley C, Darabi A, Sandén E, Siesjö P, Eriksson H, Journal of Inorganic Biochemistry, 2013 [Swedish study]

Abstract: Aluminium oxyhydroxide, Al (OH)3 is one of few compounds approved as an adjuvant in human vaccines. However, the mechanism behind its immune stimulating properties is still poorly understood. In vitro co-culture of an aluminium adjuvant and the human monocytic cell line THP-1 resulted in reduced cell proliferation. Inhibition occurred at concentrations of adjuvant several times lower than would be found at the injection site using a vaccine formulation containing an aluminium adjuvant.

Based on evaluation of the mitochondrial membrane potential, THP-1 cells showed no mitochondrial rupture after co-culture with the aluminium adjuvant, instead an increase in mitochondrial activity was seen… THP-1 cells are an appropriate in vitro model in order to investigate the mechanism behind the induction of a phagocytosing antigen presenting cell into an inflammatory cell by aluminium adjuvants."

"The immunopotency of aluminium has been known for at least 100 years and still today forms the basis for the use of aluminium salts as adjuvants in vaccinations and allergy therapies. What is then surprising is the uncertainty regarding their mechanism of action and burgeoning evidence of their toxicity in potentially susceptible individuals."

There is [sic] a perception that aluminium is a 'safe' metal with few if any signicant implications for human health. This is a view which though seemingly convenient for the aluminium industry is neither supported by observation; for example, aluminium is the cause of dialysis encephalopathy, nor by decades of animal experimentation demonstrating intoxication. It is truly an anomaly that the perceived innocuousness of aluminium in humans has persisted through to the present day and to the extent that there is no legislation whatsoever limiting human's exposure to aluminium. (Human Exposure to Aluminum, *Environmental Science Processes & Impacts*, 2013)

[28] "Autoimmune/Inflammatory Syndrome Induced By Adjuvants (ASIA) 2013: Unveiling The Pathogenic, Clinical And Diagnostic Aspects," Carlo Perricone, Serena Colafrancesco, Roei D. Mazor, Alessandra Soriano, Yehuda Shoenfeld, *Journal of Autoimmunity*, October 2013 [An Israeli / Italian study]

Summary: "This paper will focus on protean facets which are part of ASIA, focusing on the roles and mechanisms of action of different adjuvants which lead to the autoimmune/inflammatory response. The data herein illustrate the critical role of environmental factors in the induction of autoimmunity. Indeed, it is the interplay of genetic susceptibility and environment that is the major player for the initiation of breach of tolerance.

The data herein illustrate the critical role of environmental factors and the interplay of genetic susceptibility and environment in the induction of autoimmunity. Several neurologic demelinating diseases have been reported following vaccination, the main being Guillaine Barré syndrome (GBS). Another demyelinating disease associated with vaccines is the acute

disseminated encephalomyelitis (ADEM). This is an inflammatory disease of the central nervous system frequently occurring post-vaccination. Rabies, diphtheria tetanus polio, smallpox, measles, mumps, rubella, Japanese B encephalitis, pertussis, influenza, hepatitis B, and the Hog vaccines have been called to be involved."

[29] "Autoimmune/Inflammatory Syndrome Induced By Adjuvants (Shoenfeld's Syndrome): Clinical And Immunological Spectrum," Olga Vera-Lastra, Gabriela Medina, Maria Del-Pilar Cruz Dominguez, Luis J Jara, Expert Rev. *Clinical Immunology* 2013 [Mexican study]

Summary: "The activation of the immune system by adjuvants, a desirable effect, could trigger manifestations of autoimmunity or autoimmune disease. Recently, a new syndrome was introduced, autoimmune/inflammatory syndrome induced by adjuvants (ASIA), that includes post-vaccination phenomena, macrophagic myofasciitis, Gulf War syndrome and siliconosis. Various adjuvants used in vaccines enhance a specific immune response against antigens and may produce autoimmunity and AID both in experimental models and humans. The clinical and laboratory data support an association between adjuvants and autoimmune diseases."

[30] "The non-specific effects of vaccines and other childhood interventions: the contribution of INDEPTH Health and Demographic Surveillance Systems. Osman Sankoh, Paul Welaga, Cornelius Debpuur, Charles Zandoh, Stephney Gyaase, Mary Atta Poma, Martin Kavao Mutua, Manzoor Ahmed Hanifi, Cesario Martins, Eric Nebie, Moubassira Kagoné, Jacques BO Emina, and Peter Aaby, *International Journal of Epidemiology*, 2014 [Open Access Full Text] [Ghana Network study]

Summary:"Immunization has been advocated as the most successful public health intervention to improve child survival. Each year, immunization averts an estimated 2–3 million deaths from diphtheria, tetanus, pertussis (whooping cough) and measles. However, there is now strong evidence that vaccines have substantial non-specific (heterologous) effects in children in high-mortality regions, i.e. by changing mortality from infections unrelated to the vaccine-targeted infections.1–5

"Most childhood interventions (vaccines, micronutrients) in low-income countries are justified by their assumed effect on child survival. However, usually the interventions have only been studied with respect to their disease/deficiency-specific effects and not for their overall effects on morbidity and mortality. In many situations, the population-based effects have been very different from the anticipated effects; for example, the measles-preventive high-titre measles vaccine was associated with 2-fold increased female mortality; BCG [tuberculosis vaccine] reduces neonatal mortality although children do not die of tuberculosis in the neonatal period; vitamin A may be associated with increased or reduced child mortality in different situations; effects of interventions may differ for boys and girls.

The reasons for these and other contrasts between expectations and observations are likely to be that the immune system learns more than specific prevention from an intervention; such training may enhance or reduce susceptibility to unrelated infections…The perceived lack of biological plausibility has been a major obstacle in recognizing and further investigating non-specific

effects. Hence, it is important to consider immunological mechanisms that may mediate such effects…
Each individual has a unique lifelong history of infections and vaccinations, and each exposure leaves an imprint on the immune system that can affect future innate and adaptive immune responses to new pathogens…In some scenarios, beneficial heterologous immunity can provide partial protective immunity and be the difference between life and death. In other scenarios, detrimental heterologous immunity can lead to severe immunopathology. Hence, T-cell mediated heterologous immunity provides a plausible biological mechanism by which vaccines may affect the immune response to a subsequent unrelated infection and also explains how, in certain situations, a vaccine could have detrimental effects on the outcome of secondary infections.

[33] "Human Papilloma Virus Vaccine and Primary Ovarian Failure: Another Facet of the Autoimmune/Inflammatory Syndrome Induced by Adjuvants *American Journal of Reproductive Immunology*, 2013, Selena Colafrancesco, Carlo Perricone, Lucija Tomljenovic, Yehuda Shoenfeld [Israeli / Italian / Canadian study]

Summary: Post-vaccination autoimmune phenomena are a major facet of the autoimmune/inflammatory syndrome induced by adjuvants (ASIA) and different vaccines, including HPV, have been identified as possible causes.

"We documented here the evidence of the potential of the HPV vaccine to trigger a life-disabling autoimmune condition. The increasing number of similar reports of post HPV vaccine-linked autoimmunity and the uncertainty of long-term clinical benefits of HPV vaccination are a matter of public health that warrants further rigorous inquiry."

[34] "Application of Novel PCR-Based Methods for Detection, Quantitation, and Phylogenetic Characterization of Sutterella Species in Intestinal Biopsy Samples from Children with Autism and Gastrointestinal Disturbances," Brent L. Williams, Mady Hornig,Tanmay Parekh, and W. Ian Lipkin, *Journal of the American Society for Microbiology* (MBI), 2012)
[Columbia University study]

"*Gastrointestinal disturbances are commonly reported in children with autism and may be associated with compositional changes in intestinal bacteria. In a previous report, we surveyed intestinal microbiota in ileal and cecal biopsy samples from children with autism and gastrointestinal dysfunction (AUT-GI) and children with only gastrointestinal dysfunction (Control-GI).*

Many children with autism have gastrointestinal (GI) disturbances that can complicate clinical management and contribute to behavioral problems. Understanding the molecular and microbial underpinnings of these GI issues is of paramount importance for elucidating pathogenesis, rendering diagnosis, and administering informed treatment. Here we describe an association between high levels of intestinal, mucoepithelial-associated Sutterella species and GI disturbances in children with autism. These findings elevate this little-recognized bacterium to the forefront by demonstrating that Sutterella is a major component of the microbiota in over

half of children with autism and gastrointestinal dysfunction (AUT-GI) and is absent in children with only gastrointestinal dysfunction (Control-GI) evaluated in this study."

[35] "The spectrum of ASIA: 'Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants" N Agmon-Levin, GRV Hughes, Y Shoenfeld, *Lupus*, 2012

Summary: "Physicians are often puzzled by enigmatic medical conditions or the abrupt appearance of an immune-mediated disease. It seems that the role of adjuvants [aluminum in vaccines] in the pathogenesis of immune-mediated diseases can no longer be ignored, and the medical community must look towards producing safer adjuvants. Another cornerstone of ASIA is the complex interaction between autoimmunity and adjuvanted vaccines. On the one hand vaccines are beneficial for the vast majority of subjects including those who suffer from autoimmune-rheumatic diseases as delineated in this issue by van Assen and Bijl.16 On the other hand in a small minority of individuals vaccine can trigger the appearance of autoan- tibodies as documented by Vista et al.17 and Perdan-Pirkmajer et al.18 Moreover, a link between immunization and defined autoimmune diseases has been reported elsewhere and herein."

"A Saudi Sheikh, who suffered at the age of 27 from joints pains, rash and serological evidence of anti-Ro antibodies, was diagnosed with probable systemic lupus erythematosus (SLE) at that time. He was treated with Plaquenil for a year, but as no signs of SLE were apparent, treatment was stopped and he remained disease free for the next 12 years. At the age of 39 years, 2 weeks after immunization with the flu vaccine, his disease reemerged. This time he presented with severe arthritis and pericarditis, which required treatment with high doses of steroids.

This patient's story illustrates the acceleration of an autoimmune or immune-mediated condition following exposure to external stimuli. During the past year a new syndrome was introduced and termed ASIA, 'Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants'.[1] This syndrome assembles a spectrum of immune-mediated diseases triggered by an adjuvant stimulus."

[36] "Risk Of Febrile Seizures And Epilepsy After Vaccination With Diphtheria, Tetanus, Acellular Pertussis, Inactivated Poliovirus, And Haemophilus Influenzae Type B.," Sun Y, Christensen J, Hviid A, Li J, Vedsted P, Olsen J, Vestergaard M. *Jama*, 2012 [Danish study]

Summary: "Vaccination with whole-cell pertussis vaccine carries an increased risk of febrile seizures, but whether this risk applies to the acellular pertussis vaccine is not known. In Denmark, acellular pertussis vaccine has been included in the combined diphtheria-tetanus toxoids-acellular pertussis-inactivated poliovirus-Haemophilus influenzae type b (DTaP-IPV-Hib) vaccine since September 2002.

CONCLUSIONS: DTaP-IPV-Hib vaccination was associated with an increased risk of febrile seizures on the day of the first 2 vaccinations given at 3 and 5 months, although the absolute risk was small. Vaccination with DTaP-IPV-Hib was not associated with an increased risk of epilepsy."

[37] "Neurologic Adverse Events Following Vaccination," Sienkiewicz D., Kułak W., Okurowska-Zawada B., Paszko-Patej G., *Prog Health Sci*, 2012
[Polish scientists propose new vaccine schedule, express concern at high rate of vaccine adverse events.]

Summary: "The present review summarizes data on neurological adverse events following vaccination in the relation to intensity, time of onset, taking into account the immunological and non-immunological mechanisms. The authors described the physiological development of the immune system and the possible immune system responses following vaccination. Toxic property of thimerosal-a mercury-containing preservative used in some vaccines was presented. The neurological complications after vaccination were described. The role of vaccination in the natural course of infectious diseases and the current immunizations schedule in Poland was discussed.

According to researchers, a manifold incidence increase of psycho-neurological diseases such as autism, ADHD, mental retardation, epilepsy and others have been observed all over the world over the past twenty years. As stated, from the 1990s new vaccines for infants containing thimerosal began to be used in America. In the DTP, Hib and Hep B vaccines, children received a dose of 62.5 ug of mercury, which is 125-fold more than the dose considered safe (0.1ug/kg/day). These reports were the reason that Scandinavian countries already prohibited the use of mercury in 1990

Thus, it is not reasonable to assume that manipulation of the immune system through an increasing number of vaccinations during critical periods of brain development will not result in adverse neurodevelopmental outcomes. European countries have different models of vaccination that have been modified in recent decades. In Scandinavian countries, which have the lowest infant mortality, vaccinations are voluntary and infants receive their first vaccination at 3 months of age. In the first year of life, they receive 9 recommended vaccinations, and at 18 months—MMR. The acellular pertussis vaccine (DTaP) is used, as well as IPV. BCG and Hepatitis B vaccines are administered to children from high risk groups.

Reports in many Polish and foreign medical journals lead us to conclude that post-vaccinal complications among children can be observed in sporadic cases and that they are disproportionate to the benefits of vaccination in the elimination of dangerous diseases in childhood."

[38] Gastrointestinal Conditions in Children With Autism Spectrum Disorder: Developing a Research Agenda. Daniel L. Coury, Paul Ashwood, Alessio Fasano, George Fuchs, Maureen Geraghty, Ajay Kaul, Gary Mawe, Paul Patterson, Nancy E. Jones, *Pediatrics*, 2012

Autism spectrum disorders (ASDs) are a set of complex neurodevelopmental disorders defined behaviorally by impaired social interaction, delayed and disordered language, repetitive or stereotypic behavior, and a restricted range of interests. ASDs represent a significant public health issue with recent estimates indicating that as many as 1% of children in the United States are diagnosed with an ASD.[1,2]

Many individuals with ASDs have symptoms of associated medical conditions, including seizures, sleep problems, metabolic conditions, and gastrointestinal (GI) disorders, which have significant health, developmental, social, and educational impacts. Gastrointestinal complaints are a commonly reported concern for parents and may be related to problem behaviors and other medical issues such as dysregulated sleep (ATN Annual Registry Report, unpublished data, November 2009).[3] Despite the magnitude of these issues, potential GI problems are not routinely considered in ASD evaluations. This likely reflects several factors, including variability in reported rates of GI disorders, controversies regarding the relationship between GI symptoms and the putative causes of autism, the limited verbal capacity of many ASD patients, and the lack of recognition by clinicians that certain behavioral manifestations in children with ASDs are indicators of GI problems (eg, pain, discomfort, or nausea).

[39] *"Theoretical Aspects of Autism: Causes – A Review" and "Theoretical Aspects of Autism: Biomarkers—a Review*" Helen Ratajczak PhD, ***The Journal of Immunotoxicology*** (2011).

The author of these comprehensive reviews is a former senior scientist at a pharmaceutical company whose scientific career was focused on immunology and toxicology. Her multi-faceted reviews go way beyond Dr. Wakefield's findings; if brought to public attention, her findings would pose a far more critical threat to the vaccine industry and the CDC vaccination schedule.

"*In 1988, two doses of MMR II were recommended to immunize those individuals who did not respond to the first injection. A spike of incidence of autism accompanied the addition of the second dose of MMR II… the United Kingdom reported a dramatic increase in prevalence of autism to 1/64."Furthermore, an examination of the continuing increase in prevalence in autism in the context of the dates of spikes in increase in prevalence which point to the MMR II vaccine (which did not contain Thimerosal after 2000) suggests that something "new" caused the increase in incidence of autism."*

Dr. Ratajczak identifies that "new" component in the preparation of the MMR II vaccine and the chicken pox vaccine, as human DNA. She notes that at about the time that thimerosal was removed from childhood vaccines –with the exception of the flu vaccine – human DNA is currently included in the MMR II and chicken pox vaccines. She cites a Merck document, dated 2010.

"It is important to note that unlike the former MMR, the rubella component of MMR II was propagated in a human cell line derived from embryonic lung tissue. The MMR II vaccine is contaminated with human DNA from the cell line. This human DNA could be the cause of the spikes in incidence. An additional increased spike in incidence of autism occurred in 1995 when the chicken pox vaccine was grown in human fetal tissue.

The human DNA from the vaccine can be randomly inserted into the recipient's genes by homologous recombination, a process that occurs spontaneously only within a species. Hot spots for DNA insertion are found on the X chromosome in eight autism-associated genes involved in nerve cell synapse formation, central nervous system development, and mitochondrial function. This could provide some explanation of why autism is predominantly a disease of boys.

Taken together, these data support the hypothesis that residual human DNA in some vaccines might cause autism."

Ratajczak agrees that nobody has proven DNA causes autism; but argues nobody has shown the opposite, and scientifically, the case is still open.

[40] Alluminum Toxicity in Mitochondrial Dysfunction and ASD, Nancy Mullan MD, Amy Yasko PhD, AMD, FAAIM *Autism Science Digest*, 2013

"The cause of the high comorbidity between ASD and mitochondrialdysfunction remains obscure. Most ASD patients do not have a geneticabnormality that would explain the association. Aluminum offers another plausible explanation as to why the rate of autism didnot decline upon the removal of thimerosal from most vaccines. During the highly publicized phase-out period for mercury in 1999-2002, four doses of a new vaccine with high aluminum content were added to the CDC vaccination schedule. During 2005, another two doses of high-aluminum vaccine were added…

[41] "Mitochondrial Dysfunction Can Connect The Diverse Medical Symptoms Associated With Autism Spectrum Disorders," Richard E. Frye and Daniel A. Rossignol, ***Pediatric Research,*** 2012 [Free Full Text]

"Autism spectrum disorder (ASD) is a devastating neurodevelopmental disorder. Over the last decade, evidence has emerged that some children with ASD suffer from undiagnosed co-morbid medical conditions. One of the medical disorders that has been consistently associated with ASD is mitochondrial dysfunction. Individuals with mitochondrial disorders without concomitant ASD manifest dysfunction in multiple high energy organ systems, such as the central nervous, muscular and gastrointestinal systems. Interestingly, these are the identical organ systems affected in a significant number of children with ASD. This finding raises the possibility that mitochondrial dysfunction may be one of the keys that explains the many diverse symptoms observed in some children with ASD.

Mitochondrial dysfunction is the most common metabolic abnormality associated with ASD (Over the last decade, we have started to understand that some children with ASD suffer from undiagnosed co-morbid medical conditions such as abnormalities in the peripheral nervous, musculoskeletal, endocrine, gastrointestinal, immune, detoxification, redox regulation and energy generation systems (3). This has changed our view of ASD from a primary CNS disorder to a disorder that affects multiple physiological systems.

A large population-based study estimated the prevalence of mitochondrial disease in ASD to be approximately 7.2% while a more recent but small controlled study has suggested that the prevalence of mitochondrial dysfunction (at least as measured in lymphocytes) in ASD may be as high as 80% (12). Many clinical features as well as biochemical and physiological abnormalities associated with ASD could be related to mitochondrial disease and/or dysfunction."

[42] "Mitochondrial Dysfunction In Autism Spectrum Disorders: A Systematic Review And Meta-Analysis" Rossignol DA[1], Frye RE. *Molecular Psychiatry*, 2012
"[Our] findings suggest children with ASD have a spectrum of mitochondrial dysfunction of differing severity. Eighteen publications representing a total of 112 children with ASD and MD (ASD/MD) were identified. The prevalence of developmental regression (52%), seizures (41%), motor delay (51%), gastrointestinal abnormalities (74%), female gender (39%), and elevated lactate (78%) and pyruvate (45%) was significantly higher in ASD/MD compared with the general ASD population.

Most ASD/MD cases (79%) were not associated with genetic abnormalities, raising the possibility of secondary mitochondrial dysfunction. Treatment studies for ASD/MD were limited, although improvements were noted in some studies with carnitine, co-enzyme Q10 and B-vitamins*."*

By now it is also established the mitochondrial dysfunction is a common feature in autistic children and much higher than in the general population

The following peer-reviewed reports (dated from 2000 to 2011) confirm the validity of Wakefield's pioneering avenue of research, first reported as a small case series review in the controversial *Lancet* report. **The existence of these reports should have been known to editors at the *BMJ***. *But Godlee indicated in Nov. 2011: "We are unaware of any peer reviewed paper replicating Andrew Wakefield's research ."*

[43] Impaired Carbohydrate Digestion And Transport And Mucosal Dysbiosis In The Intestines Of Children With Autism And Gastrointestinal Disturbances. Williams BL1, Hornig M, Buie T, Bauman ML, Cho Paik M, Wick I, Bennett A, Jabado O, Hirschberg DL, Lipkin WI. *PLoS One*, 2011 [Columbia University]

Summary: Gastrointestinal disturbances are commonly reported in children with autism, complicate clinical management, and may contribute to behavioral impairment. Reports of deficiencies in disaccharidase enzymatic activity and of beneficial responses to probiotic and dietary therapies led us to survey gene expression and the mucoepithelial microbiota in intestinal biopsies from children with autism and gastrointestinal disease and children with gastrointestinal disease alone. Ileal transcripts encoding disaccharidases and hexose transporters were deficient in children with autism, indicating impairment of the primary pathway for carbohydrate digestion and transport in enterocytes.

Deficient expression of these enzymes and transporters was associated with expression of the intestinal transcription factor, CDX2. Metagenomic analysis of intestinal bacteria revealed compositional dysbiosis manifest as decreases in Bacteroidetes, increases in the ratio of Firmicutes to Bacteroidetes, and increases in Betaproteobacteria. Expression levels of disaccharidases and transporters were associated with the abundance of affected bacterial phylotypes.

"a relationship between human intestinal gene expression and bacterial community structure and may provide insights into the pathophysiology of gastrointestinal disturbances in children with autism.

Metabolic interactions between intestinal microflora and their hosts are only beginning to be understood. Nonetheless, there is already abundant evidence that microflora can have system-wide effects and influence immune responses, brain development and behavior.

"Taken as a whole, the picture that emerges is one in which GI symptomatic children with ASD in whom cellular infiltrate is present in the ileum and colon have a distinct molecular signature that is consistent with the larger disease categories of gastrointestinal disease, and more specifically, overlaps with Crohn's disease, ulcerative colitis, and autoimmunity. The shared uniquely expressed DETs seen in both the ileum and colon suggest that intestinal mucosal inflammatory infiltrates in the setting of GI symptomatic patients with ASD reflect a single unifying autoimmune process at play in both the small and large bowel."

These results indicate a relationship between human intestinal gene expression and bacterial community structure and may provide insights into the pathophysiology of gastrointestinal disturbances in children with autism. The authors cited three of Dr. Wakefield's publications

[44] 'ASIA' - Autoimmune/Inflammatory Syndrome Induced by Adjuvants,"by Yehuda Shoenfeld MD, ***Journal of Autoimmunity***, 2011

ASIA is a post-vaccine syndrome identified by Dr. Yehuda Shoenfeld, an internationally recognized authority of autoimmune diseases.

"The efficacy of most currently used vaccines depends on the presence of an adjuvant in conjunction with a foreign antigen corresponding to a component of an infectious agent… in the past, adjuvants were generally considered to be inert materials that posed little or no independent threat to the host. Alas, animal studies as well as reports of human diseases have clearly demonstrated the ability of adjuvants to inflict diseases by themselves.

A causal link between vaccines and autoimmunity was noted in 1976 during an outbreak of Guillain-Barré syndrome (GBS) that followed immunization with the "swine flu" vaccine. Causal relationships have also been accepted for transverse myelitis following an oral polio vaccine, autoimmune thrombocytopenia after measles-mumps-rubella, and arthritis following diphtheria-tetanus-pertussis. Unraveling the adjuvant diseases pathogenesis may facilitate the search for preventive and therapeutic interventions."

[45] "The Immunobiology Of Aluminium Adjuvants: How Do They Really Work?" Christopher Exley, Peter Siesjo, Hakan Eriksson, *Trends in Immunology* 2010,

Summary: "Aluminium adjuvants potentiate the immune response, thereby ensuring the potency and efficacy of typically sparingly available antigen. Their concomitant critical importance in mass vaccination programmes may have prompted recent intense interest in understanding how they work and their safety. Progress in these areas is stymied, however, by a lack of accessible knowledge pertaining to the bioinorganic chemistry of aluminium adjuvants, and, consequently, the inappropriate application and interpretation of experimental models of their mode of action.. In relation to this possible 'indirect adjuvanticity' there are burgeoning

examples in the scientific literature of aluminium salts inducing sen- sitization to substances that might not normally be considered as antigens. For example, such effects may contribute towards allergies to foods."

[46] "Sorting Out The Spinning Of Autism: Heavy Metals And The Question Of Incidence," Mary Catherine DeSoto and Robert T. Hitlan, *Acta Neurobiologica*, 2010

Summary: A review of the literature linking autism to environmental toxins.
"In this paper, we argue that increasingly over the past decade, positions that deny a link to environmental toxins and autism are based on relatively weak science and are disregarding the bulk of scientific literature. The question about toxic exposure and autism is open, with the weight of evidence favoring a connection that is not well understood. Although it is not possible to say with certainty, it seems likely that the connection would be mediated by genetic susceptibility and ability to detoxify. That is, some people have genotypes that confer higher susceptibility to toxic exposures. If so, then 50 years ago few people would have had enough toxic expo- sure to have the neurological changes that result in autism."

[47] "Influence Of Pediatric Vaccines On Amygdala Growth And Opioid Ligand Binding In Rhesus Macaque Infants: A Pilot Study," Laura Hewitson, Brian J. Lopresti, Carol Stott, *Acta Neurobiol Exp*, 2010

Summary: Infant monkeys administered vaccines according to CDC Vaccination Schedule had brain abnormalities in region responsible for social and emotional development.

"The data suggest that vaccine exposure may be asso- ciated with significant disturbances in central opioidergic pathways in this model… Volumetric analyses identified significantly greater total brain volume in exposed compared with unexposed animals at both measured time points. These results raise the possibility that multiple vaccine exposures during the previous 3–4 months may have had a significant impact on brain growth and development."

[48] "Hepatitis B Vaccination Of Male Neonates And Autism Diagnosis, NHIS 1997-2002. Gallagher CM, Goodman MS, ***Journal of Toxiclology & Environmental Health*** (2010) [New York State University, Stony Brook study]

"Universal hepatitis B vaccination was recommended for U.S. newborns in 1991; however, safety findings are mixed. The association between hepatitis B vaccination of male neonates and parental report of autism diagnosis was determined. This cross-sectional study used weighted probability samples obtained from National Health Interview Survey 1997-2002 data sets. Vaccination status was determined from the vaccination record.

Logistic regression was used to estimate the odds for autism diagnosis associated with neonatal hepatitis B vaccination among boys age 3-17 years, born before 1999, adjusted for race, maternal

education, and two-parent household. Boys vaccinated as neonates had threefold greater odds for autism diagnosis compared to boys never vaccinated or vaccinated after the first month of life. Non-Hispanic white boys were 64% less likely to have autism diagnosis relative to nonwhite boys. Findings suggest that U.S. male neonates vaccinated with the hepatitis B vaccine prior to 1999 (from vaccination record) had a threefold higher risk for parental report of autism diagnosis compared to boys not vaccinated as neonates during that same time period. Nonwhite boys bore a greater risk"

[49] "Interindividual Variations In The Efficacy And Toxicity Of Vaccines," Thomas C, Moridani M, *Toxicology* 2010,

Summary: "A number of currently available vaccines have shown significant differences in the magnitude of immune responses and toxicity in individuals undergoing vaccination. A number of factors may be involved in the variations in immune responses, which include age, gender, race, amount and quality of the antigen, the dose administered and to some extent the route of administration, and genetics of immune system. Hence, it becomes imperative that researchers have tools such as genomics and proteomics at their disposal to predict which set of population is more likely to be non-responsive or develop toxicity to vaccines.. With the increasing number of side effects associated with a number of vaccines reported over the years, it has become imperative to develop new technologies that can effectively assist in the development and evaluation of vaccines for efficacy and toxicity."

[50] "Timing of Increased Autism Disorder Cumulative Incidence," McDonald, ME, Pau, JF. *Environmental Science & Technology*, 2010
A report by scientists at the Environmental Protection Agency (EPA) who analyzed the cumulative incidence of autistic disorder during a10-year period (1987 – 1996) pinpointed a sharp "changepoint" year (1988) when the incidence of autism sharply increased. The "changepoint" year is concomitant with the year childhood vaccination schedules expanded. In the US, between 1988 and 1996, the following vaccines were added to the CDC vaccination schedule for children in the first 15 months of life.

- HiB - Improved Hib conjugate vaccine added in 1988.
- DTaP - Additional dose at younger age added around 1990.
- HiB - Three additional doses added to schedule in 1991.
- Hep B - Three doses - Added to childhood schedule in 1992.
- Chicken Pox - Approved in 1995, added to schedule in 1996

"*In the Danish, California, and worldwide data sets, we found that an increase in autism disorder cumulative incidence began about (the birth cohort years) 1988-1989.*"

[51] "Vaccines and Autoimmunity" by Professor Yehuda Shoenfeld, ***Nature Review Rheumatology***, 2009

"*In this article, on the basis of published evidence and our own experience, we discuss the various aspects of the causal and temporal interactions between vaccines and autoimmune phenomena, as well as the possible mechanisms by which different components of vaccines might induce autoimmunity.*"

[52] "A Role for the Body Burden Of Aluminium In Vaccine-Associated Macrophagic Myofasciitis And Chronic Fatigue Syndrome," Exley C, Swarbrick L, Gherardi RK, Authier FJ. *Medical Hypotheses*, 2009

Abstract: "Macrophagic myofasciitis and chronic fatigue syndrome are severely disabling conditions which may be caused by adverse reactions to aluminium-containing adjuvants in vaccines. While a little is known of disease aetiology both conditions are characterised by an aberrant immune response, have a number of prominent symptoms in common and are coincident in many individuals.

Herein, we have described a case of vaccine-associated chronic fatigue syndrome and macrophagic myofasciitis in an individual demonstrating aluminium overload. This is the first report linking the latter with either of these two conditions and the possibility is considered that the coincident aluminium overload contributed significantly to the severity of these conditions in this individual.

This case has highlighted potential dangers associated with aluminium-containing adjuvants and we have elucidated a possible mechanism whereby vaccination involving aluminium-containing adjuvants could trigger the cascade of immunological events which are associated with autoimmune conditions including chronic fatigue syndrome and macrophagic myofasciitis."

[53] "Delayed Acquisition Of Neonatal Reflexes In Newborn Primates Receiving A Thimerosal-Containing Hepatitis B Vaccine: Influence Of Gestational Age And Birth Weight" Hewitson L, Houser LA, Stott C, Sackett G, Tomko JL,Atwood D, Blue L, White ER, Wakefield AJ, *Neuro-Toxicology*, 2009 [Withdrawn by journal without explanation]

Abstract: This study examined whether acquisition of neonatal reflexes and sensorimotor skills in newborn rhesus macaques (Macaca mulatta) is influenced by receipt of the single neonatal dose of Hepatitis B (HB) vaccine containing the preservative thimerosal (Th). HB vaccine containing a standardized weight-adjusted Th dose was administered to male macaques within 24 hours of birth (n=13).

Unexposed animals received saline placebo (n=4) or no injection (n=3). Infants were raised identically and tested daily for acquisition of 9 survival, motor, and sensorimotor reflexes by a blinded observer. In exposed animals there was a significant delay in the acquisition of three survival reflexes: root, snout and suck, compared with unexposed animals. No neonatal responses were significantly delayed in unexposed animals compared with exposed. Gestational age (GA) and birth weight were not significantly correlated. Cox regression models were used to evaluate the main effects and interactions of exposure with birth weight and GA as independent predictors and time-invariant covariates.

Significant main effects remained for exposure on root and suck when controlling for GA and birth weight such that exposed animals were relatively delayed in time-to-criterion. There was a significant effect of GA on visual follow far when controlling for exposure such that increasing GA was associated with shorter time-to-criterion. Interaction models indicated that while there were no main effects of GA or birth weight on root, suck or snout reflexes there were various interactions between exposure, GA, and birth weight such that inclusion of the relevant interaction terms significantly improved model fit.

This, in turn, indicated important influences of birth weight and/or GA on the effect of exposure which, in general, operated in a way that lower birth weight and/or lower GA exacerbated the detrimental effect of vaccine exposure. This primate model provides a possible means of assessing adverse neurodevelopmental outcomes from neonatal Th-containing HB vaccine exposure, particularly in infants of lower GA or low birth weight.The mechanism of these effects and the requirements for Th is not known and requires further study.

[54] "Gastrointestinal Pathology in Autism: Description and Treatment," Arthur Krigsman, MD, *Medical Veritas,* 2007

Abstract: This paper, adapted from conference presentations, describes various lesions found in the gastrointestinal tracts of children with autism spectrum disorder (ASD) using endoscopy. Some of these lesions, which are illustrated in color, are common to children with ASD, while others are similar to those found in neurotypical children. While not curable, all of these lesions are treatable. What is exciting is that most of these children respond ex-tremely well to some combination of a restricted diet, anti-inflammatory medication, probiotics, antibiotics, antifungals, and digestive enzymes. [Includes a series of photographic illustrations]

[55] The Immune Response in Autism: a New Frontier For Autism Research, Paul Ashwood, Sharifia Wills, Judy Van de Water (MIND Institute UC Davis) ***Journal of Leukocyte Biology*** 2006

"Numerous studies report apparently conflicting results, and thus far, no consensus about the described immune findings has been reached. However, with increasing reports of immune dysfunction in autism, there is a growing awareness and concern that immune dysfunction may play a role in, if not all, at least a subgroup(s) of patients with autism. Moreover, various hypotheses have attempted to link dysfunctional immune activity and autism, such as maternal immune abnormalities during early pregnancy, increased incidence of familial autoimmunity, childhood vaccinations, and the generation of autism animal models based on immune parameters.*"*

[56] In 2006, Dr. Stephen Walker (Wake Forrest University) reported interim study findings at an International Meeting for Autism Research. He reported that a high percentage of autistic children had chronic intestinal bowel disease: of 82 children tested, 70 proved positive for the

measles virus in their intestine. What's more, the virus found: "***all are vaccine strain and none are wild measles.***" This is a replication of Dr. Wakefield's *Lancet* study. Indeed, Dr. Walker confirmed in the UK *Daily Mail* (May 28, 2006) that:

"Of [the] results we have in so far, all are vaccine strain and none are wild measles.
This research proves that in the gastrointestinal tract of a number of children who have been diagnosed with regressive autism, there is evidence of measles virus. What it means is that the study done earlier by Dr. Wakefield and published in 1998 is correct.
That study didn't draw any conclusions about specifically what it means to find measles virus in the gut, but the implication is it may be coming from the MMR vaccine. If that's the case, and this live virus is residing in the gastrointestinal tract of some children, and then they have GI inflammation and other problems, it may be related to the MMR."

Wake Forest issued a hasty [implausible] warning "against making connection between [the] presence of the measles virus and autism" – even though it is precisely the subject of the study. And the warning provides additional confirmation for making the connection:

"The vaccine is first given as part of a triple vaccine called MMR – for measles, mumps and rubella – at ages 12-18 months. That is shortly before a particular type of autism (regressive) begins to appear in children afflicted with the condition, which has fueled the speculation about a connection.(Wake Forest website)

[See the completed published Walker study (2013) above [4]

[57] "Suspected Side Effects To The Quadrivalent Human Papilloma Vaccine." Brinth L, Theibel AC, Pors K, Mehlsen J. *Danish Medical Journal*, 2005

Summary: "The quadrivalent vaccine that protects against human papilloma virus types 6, 11, 16 and 18 (Q-HPV vaccine, Gardasil) was included into the Danish childhood vaccination programme in 2009. During the past years, a collection of symptoms primarily consistent with sympathetic nervous system dysfunction have been described as suspected side effects to the Q-HPV vaccine. All 53 patients had symptoms consistent with pronounced autonomic dysfunction including different degrees of orthostatic intolerance, severe non-migraine-like headache, excessive fatigue, cognitive dysfunction, gastrointestinal discomfort and widespread pain of a neuropathic character."

[58] "Infection, Vaccines and Other Environmental Triggers of Autoimmunity" by Y. Molina and Y. Shoenfeld, ***Autoimmunity***, 2005
"Vaccines, in several reports were found to be temporally followed by a new onset of autoimmune diseases. The same mechanisms that act in infectious invasion of the host, apply equally to the host response to vaccination. It has been accepted for diphtheria and tetanus toxoid, polio and measles vaccines and GBS. Also this theory has been accepted for MMR vaccination and development of autoimmune thrombocytopenia, MS has been associated with HBV vaccination."

The vaccine most commonly associated with autism was the measles vaccine.
The same mechanisms that act in infectious invasion of the host apply equally to the host response to vaccination [1]. Based on these principles a killed vaccine would be less likely than a live attenuated vaccine to activate the innate immunity response [1]. Thus might be a risk that following a live attenuated vaccination an autoimmune disease or autoimmune symptoms may develop, using the same mechanism used by infections.

There have been over the last 15 years or so several reports of adverse autoimmune reactions to various vaccines. Mostly the connection between the vaccination and the autoimmune reaction was temporal and not causal. The vast majority of epidemiological studies could not find a causal link [54]. A causal relationship has been accepted by the institute of Medicine of the National Academy of Science in the USA for several different vaccines and three syndromes.

These include
(1) diphtheria and tetanus toxoid, polio and measles vaccines and GBS
(2) MMR vaccines and thrombocytopenia (ITP like) and
(3) rubella vaccine has been connected with acute and chronic arthritis in adult women The MMR vaccination has been associated also with IBD [55].

Many common infections can induce a transient rise in autoantibody production. A similar rise in autoantibody production has been observed after various vaccinations. Such autoantibodies usually resolve within a period of 2 months [55] but can persist in rare cases."

[59] "A Comparative Evaluation Of The Effects Of MMR Immunization And Mercury Doses From Thimerosal-Containing Childhood Vaccines On The Population Prevalence Of Autism," Geier DA, Geier MR. *Medical Science Monitor*, 2004

"There was a close correlation between mercury doses from thimerosal--containing childhood vaccines and the prevalence of autism from the late 1980s through the mid-1990s. In contrast, there was a potential correlation between the number of primary pediatric measles-containing vaccines administered and the prevalence of autism during the 1980s

There were statistically significant odds ratios for the development of autism following increasing doses of mercury from thimerosal-containing vaccines (birth cohorts: 1985 and 1990-1995) in comparison to a baseline measurement (birth cohort: 1984). The contribution of thimerosal from childhood vaccines (>50% effect) was greater than MMR vaccine on the prevalence of autism observed in this study.

The results of this study agree with a number of previously published studies. These studies have shown that there is biological plausibility and epidemiological evidence showing a direct relationship between increasing doses of mercury from thimerosal-containing vaccines and neurodevelopmental disorders, and measles-containing vaccines and serious neurological disorders. It is recommended that thimerosal be removed from all vaccines, and additional research be undertaken to produce a MMR vaccine with an improved safety profile."

They site Wakefield et al article, Enterocolitis in children with developmental disorders, in the American Journal of Gastroenterology (2000) which included 60 children. And they cite other investigators who suspected that the three-in-one MMR vaccine synergistically causes more severe adverse reactions. Therefore, they recommend separating the three components:
"We believe one might consider the option, in order to alleviate some of the adverse effects of MMR vaccine, of taking each component of this vaccine separately."

[60] "Immunological Findings in Autism," Cohly HH, Panja A. ***International Review of Neurobiology***, 2005
"Virus specific antibodies associated with measles virus have been demonstrated in autistic subjects. Environmental exposure to mercury is believed to harm human health possibly through modulation of immune homeostasis. A mercury link with the immune system has been postulated due to the involvement of postnatal exposure to thimerosal, a preservative added in the MMR vaccines… MMR vaccination may increase risk for autism via an autoimmune mechanism in autism. MMR antibodies are significantly higher in autistic children as compared to normal children, supporting a role of MMR in autism"

[61] "The Intestinal Lesion of Autistic Spectrum Disorder," Editorial. JR Jass (McGill University) ***European J Gastroenterology Hepatology,*** 2005

"This editorial briefly reviews the significance of lymphoid nodular hyperplasia in the intestinal tract of children with autistic spectrum disorder. The distinction between physiological and pathological lymphoid hyperplasia of the intestinal tract is of importance in the context of a possible causative link with autism. A primary intestinal lesion may occur as part of the broad spectrum of immunological disorders to which autistic children are prone. This could result in increased intestinal permeability to peptides of dietary origin which may then lead to disruption of neuroregulatory mechanisms required for normal brain development. Alternatively, there could be a primary defect in the translocation and processing of factors derived from the intestinal lumen.

These possibilities deserve further investigation and should not be lost in the fog of the controversy regarding the role of measles/mumps/rubella vaccination in the aetiology of autistic spectrum disorder."

[62] Immunological Findings In Autism. Cohly HH[1], Panja A. *International Review of Neurobiology, 2005* (University of Mississippi)

"The immunopathogenesis of autism is presented schematically in Fig. 1. Two main immune dysfunctions in autism are immune regulation involving pro-inflammatory cytokines and autoimmunity. Mercury and an infectious agent like the measles virus are currently two main candidate environmental triggers for immune dysfunction in autism. Genetically immune dysfunction in autism involves the MHC region, as this is an immunologic gene cluster whose gene products are Class I, II, and III molecules. Class I and II molecules are associated with antigen presentation. The antigen in virus infection initiated by the virus particle itself while the

cytokine production and inflammatory mediators are due to the response to the putative antigen in question.

Studies showing elevated brain specific antibodies in autism support an autoimmune mechanism. Viruses may initiate the process but the subsequent activation of cytokines is the damaging factor associated with autism. Virus specific antibodies associated with measles virus have been demonstrated in autistic subjects. Environmental exposure to mercury is believed to harm human health possibly through modulation of immune homeostasis. A mercury link with the immune system has been postulated due to the involvement of postnatal exposure to thimerosal, a preservative added in the MMR vaccines.

"Maternal antibodies may trigger autism as a mechanism of autoimmunity. MMR vaccination may increase risk for autism via an autoimmune mechanism in autism. MMR antibodies are significantly higher in autistic children as compared to normal children, supporting a role of MMR in autism."

[63] "Elevated Levels of Measles Antibodies In Children With Autism," VK Singh and RL Jensen ***Pediatric Neurology,*** 2003.

*"*Virus-induced autoimmunity may play a causal role in autism… The antibody to this antigen was found in 83% of autistic children but not in normal children or siblings of autistic children. Thus autistic children have a hyperimmune response to measles virus, which in the absence of a wild type of measles infection might be a sign of an abnormal immune reaction to the vaccine strain or virus reactivation*."*

[64] "Detection Of Measles Virus In Children With Ileo-Colonic Lymphoid Nodular Hyperplasia, Enterocolitis And Developmental Disorder" M Martin, V Uhlmann, A Killalea, O Sheils And JJ O'Leary, ***Nature: Molecular Psychiatry***, 2002

"A novel form of inflammatory bowel disease has been reported in a cohort of children with developmental disorder, manifesting predominantly as regressive autism (affected children). The intestinal pathology includes ileo-colonic lymphoid nodular hyperplasia (LNH) and a subtle enterocolitis. Clinical and pathological aspects of this disorder have previously been reported… The aim of this study was to examine for the presence of measles virus (MV) in ileal lymphoid tissues of affected children and controls… Overall, 73 of 77 (95%) affected children (median age 6 yrs; range 3–14; 65 male) contained MV genomes in ileal lymphoid tissue compared with five of 44 (11.4%) controls."

[65] "Abnormal measles-mumps-rubella antibodies and CNS autoimmunity in children with autism**"** Singh VK, Lin SX, Newell E, Nelson C (Utah State University), ***Journal of Biomedical Science***, 2002 [Free full text]

" many autistic children harbor elevated levels of measles antibodies, we conducted a serological study of measles-mumps-rubella (MMR) and MBP autoantibodies. Using serum samples of 125

autistic children and 92 control children, antibodies were assayed by ELISA or immunoblotting methods… Immunoblotting analysis revealed the presence of an unusual MMR antibody in 75 of 125 (60%) autistic sera but not in control sera. This antibody specifically detected a protein of 73-75 kD of MMR.

The MMR antibody in autistic sera detected measles HA protein, which is unique to the measles subunit of the vaccine. Furthermore, over 90% of MMR antibody-positive autistic sera were also positive for MBP autoantibodies, suggesting a strong association between MMR and CNS autoimmunity in autism.

Stemming from this evidence, we suggest that an inappropriate antibody response to MMR, specifically the measles component thereof, might be related to pathogenesis of autism."

[66] "New Evidence For A Viral Pathogenic Mechanism For New Variant Inflammatory Bowel Disease And Development Disorder?" by A Morris and D Aldulaimi, ***Molecular Pathology***, 2002

"We are all aware of the public unease about a potential link between vaccination with the triple vaccine MMR (mumps, measles, and rubella) and autism or bowel inflammatory conditions, with some hundreds of parents of afflicted children undertaking legal action against the manufacturers… epidemiologists are content that there is no significant association between MMR and either autism or bowel inflammatory conditions. However,
"Epidemiology is a pretty blunt tool and the studies done do not rule out the possibility that there may be at risk groups where a real link between MMR and autism/bowel inflammatory conditions exists…There is evidence that developmental disorders are associated with a functional disturbance of the brain–gut axis."

[67] "Pro-Inflammatory And Regulatory Cytokine Production Associated With Innate And Adaptive Immune Responses In Children With Autism Spectrum Disorders And Developmental Regression," Jyonouchi H, Sun S, Le H. *Journal of Neuro Immunology*, 2001;120:170-179.

Articles co-authored by Dr. Wakefield prior to the 1998 Lancet article and after:

[1] "Detection and Sequencing Of Measles Virus From Peripheral Mononuclear Cells From Patients With Inflammatory Bowel Disease And Autism." Kawashima H1, Mori T, Kashiwagi Y, Takekuma K, Hoshika A, Wakefield A. ***Digestive Disease & Sciences*** 2001.

> ***"****The sequences obtained from the patients with ulcerative colitis and children with autism were consistent with being vaccine strains.*"

[2] "Mumps, Measles, Rubella Vaccine: Through a Glass Darkly," Wakefield AJ, Montgomery SM. ***Adverse Drug Reaction & Toxicology Review***, 2000.

The authors reported that they had identified 170 cases of autism and bowel disease in children at the Royal Free Hospital who had the triple-dose MMR vaccine. Dr. Wakefield then publicly challenged the health department claim that the safety of the MMR "*has been proven.*"

"The argument is untenable. It cannot be substantiated by the science. That is not only my opinion but increasingly the view of healthcare professionals and the public…Tests have revealed time and time again that we are dealing with a new phenomenon. The Department of Health's contention that MMR has been proven to be safe by study after study after study just doesn't hold up. Frankly, it is not an honest appraisal of the science and it relegates the scientific issues to the bottom of the barrel in favour of winning a propaganda war.*"* (*The Telegraph*, 25, 2001)

[3] "Enterocolitis in children with developmental disorders," Wakefield AJ, Anthony A, Murch SH, Thomson M, Montgomery SM, Davies S, O'Leary JJ, Berelowitz M, Walker-Smith JA. ***American Journal of Gastroenterology***, 2000 [Retracted 2010]

Objective:
Intestinal pathology, i.e., ileocolonic lymphoid nodular hyperplasia (LNH) and mucosal inflammation, has been described in children with developmental disorders. This study describes some of the endoscopic and pathological characteristics in a group of children with developmental disorders (affected children) that are associated with behavioral regression and bowel symptoms, and compares them with pediatric controls.

Methods:
Ileocolonoscopy and biopsy were performed on 60 affected children (median age 6 yr, range 3-16; 53 male). Developmental diagnoses were autism (50 patients), Asperger's syndrome (five), disintegrative disorder (two), attention deficit hyperactivity disorder (ADHD) (one), schizophrenia (one), and dyslexia (one). Severity of ileal LNH was graded (0-3) in both affected children and 37 developmentally normal controls (median age 11 yr, range 2-13 yr) who were investigated for possible inflammatory bowel disease (IBD). Tissue sections were reviewed by three pathologists and scored on a standard proforma. Data were compared with ileocolonic biopsies from 22 histologically normal children (controls) and 20 children with ulcerative colitis (UC), scored in an identical manner. Gut pathogens were sought routinely.

Results:
Ileal LNH was present in 54 of 58 (93%) affected children and in five of 35 (14.3%) controls ($p < 0.001$). Colonic LNH was present in 18 of 60 (30%) affected children and in two of 37 (5.4%) controls ($p < 0.01$). Histologically, reactive follicular hyperplasia was present in 46 of 52 (88.5%) ileal biopsies from affected children and in four of 14 (29%) with UC, but not in non-IBD controls ($p < 0.01$). Active ileitis was present in four of 51 (8%) affected children but not in controls. Chronic colitis was identified in 53 of 60 (88%) affected children compared with one of 22 (4.5%) controls and in 20 of 20 (100%) with UC. Scores of frequency and severity of inflammation were significantly greater in both affected children and those with UC, compared with controls ($p < 0.001$).

CONCLUSIONS: A new variant of inflammatory bowel disease is present in this group of children with developmental disorders.

[4] "Detection of Measles Virus Genomic RNA in Cerebrospinal Fluid of Children with Regressive Autism: a Report of Three Cases," J.J. Bradstreet, M.D.; J. El Dahr, M.D.; A. Anthony, M.B., Ph.D.; J.J. Kartzinel, M.D.; A.J. Wakefield, M.B. *Journal of American Physicians and Surgeons, 2004*

[5] "Evidence for this link is controversial, reflecting the widely differing conclusions of basic and clinical science vs. epidemiology, although the association is supported by a recent report based upon the CDC ís Vaccine Adverse Events Reporting System (VAERS).

Autistic encephalopathy is a complex disorder in which there is clearly more than one potential mechanism for regression.Cofactors including genetic predisposition are likely to influence the presentation and timing of symptom development. The potential mechanisms of AE in these children include, but are not limited to, some or all of the following: a toxic gut-brain interaction such as occurs in hepatic encephalopathy; immunological disruption of central nervous system functions; and direct viral invasion of the brain."

Measles, mumps, and rubella viruses, in their natural form, have been linked to childhood developmental disorders including autistic spectrum disorder (ASD), disintegrative disorder, and developmental regression.

Deykin and MacMahon compared exposure patterns of 183 children with autism and 355 sibling controls to the encephalitogenic viruses, measles, mumps, rubella, and chickenpox. They found that autistic manifestations were associated with prenatal experience with measles and mumps. Ring et al. using statistical modelling of the number of autism births compared with epidemics of measles, rubella, poliomyelitis, viral meningitis, and viral encephalitis in Israel, found that children born during epidemics of measles were at greater risk of developing autism.13 ?33

[6] "Colonic CD8 and γδT-cell infiltration with epithelial damage in children with autism" RI Furlano, A Anthony, R Day, A Brown, L McGarvey, M Thomson, S E. Davies, M Berelowitz, A Forbes, AJ Wakefield, John A. Walker-Smith, and Simon H. Murch, ***Journal of Pediatrics***, 2001

[7] "The GutBrain Axis in Childhood Developmental Disorders" Wakefield, Andrew J. ***Journal Of Pediatric Gastroenterology And Nutrition***, 2002

"In addition to frequent gastrointestinal symptoms, children with autism often manifest complex biochemical, metabolic, and immunologic abnormalities that a primary genetic cause cannot readily account for. The gut–brain axis is central to certain encephalopathies of extracranial origin, hepatic encephalopathy being the best characterized. Certain commonalties between the clinical characteristics of hepatic encephalopathy and an increasingly common autistic phenotype (developmental regression in a previously normal child accompanied by immune-mediated gastrointestinal pathology) have led to the hypothesis that an analogous mechanism of toxic

encephalopathy may exist in patients with liver failure and some children with autism. Aberrations in opioid biochemistry are common to these two conditions, and evidence suggests that opioid peptides may be among the central mediators of the respective syndromes. Generating biologically plausible and testable hypotheses in this area may help to identify new treatment options in encephalopathies of extracranial origin."

[8] "Potential viral pathogenic mechanism for new variant inflammatory bowel disease," V Uhlmann, C M Martin, O Sheils, L Pilkington, I Silva, A Killalea, S B Murch, J Walker-Smith, M Thomson, A J Wakefield, and J J O'Leary ***Molecular Pathology,*** 2002 [Free full text]

The research team was headed by Professor John O'Leary, Chair of pathology at Coombe Women's Hospital, Dublin, The reported finding: Measles virus may act as an immunological trigger that links a new form of inflammatory bowel disease and developmental disorder. They found the measles virus in the guts of 75 children out of 91 with the variant form of bowel disease, but in only five out of 70 healthy children. More boys than girls were affected. The article was accompanied by a carefully worded editorial:

"This paper was submitted by a scientist of international reputation, and accepted for publication after peer review. It was recognised by the referees and the editors as a potentially important observation which raised many questions about the possible role of measles in the aetiology of a syndrome in children."

However, the article ruffled feathers puting Professor O'Leary on the defensive: "*I stand by the findings of our research, which raises many questions about whether measles virus has a role in bowel inflammation in developmental disorder.*"

The authors had their defenders: "New Evidence For A Viral Pathogenic Mechanism For New Variant Inflammatory Bowel Disease And Development Disorder?" by A Morris and D Aldulaimi, ***Molecular Pathology***, 2002

"We are all aware of the public unease about a potential link between vaccination with the triple vaccine MMR (mumps, measles, and rubella) and autism or bowel inflammatory conditions, with some hundreds of parents of afflicted children undertaking legal action against the manufacturers… epidemiologists are content that there is no significant association between MMR and either autism or bowel inflammatory conditions. However,

"Epidemiology is a pretty blunt tool and the studies done do not rule out the possibility that there may be at risk groups where a real link between MMR and autism/bowel inflammatory conditions exists…There is evidence that developmental disorders are associated with a functional disturbance of the brain–gut axis.""

Professor John Walker-Smith felt the need to write a letter in defense of the article in the Lancet, 2002 in which he states:

"I believe that the published data in peer reviewed journals show two things. First, a highly selected group of children with developmental disorder (many with regressive autism) exists,

who have an unusual gastrointestinal abnormality characterised by ileal-lymphoid-nodular hyperplasia and non-specific enterocolitis that is not classical inflammatory bowel disease. The immunopathology of this disorder has been studied by Furlano and colleagues, who have established clear differences from chronic inflammatory bowel disease.

Second, in such highly selected children, Uhlmann and colleagues have now provided new evidence that measles might be involved, by use of molecular techniques to show the presence of measles virus genomes in 75 of 91 children with ileal-lymphoid-nodular hyperplasia, enterocolitis, and developmental disorder, compared with five of 70 control children. Measles virus was mainly localised in dendritic cells in reactive follicular hyperplastic centres in the ileum. This localisation mirrors that of HIV-1.

There has been much criticism of Wakefield and colleagues' work. His results have been said to be refuted. Much of this criticism has been epidemiological. Yet, as Morris and Aldulaimi in their comment on the Dublin data state, "Epidemiology is a pretty blunt tool and the studies done do not rule out the possibility that there are at risk groups where a real link with [measles, mumps, rubella vaccine] MMR and autism/bowel inflammatory condition exists".

[9] "Spontaneous mucosal lymphocyte cytokine profiles in children with autism and gastrointestinal symptoms: mucosal immune activation and reduced counter regulatory interleukin-10," Ashwood P, Anthony A, Torrente F, Wakefield AJ. ***Journal of Clinical Immunology***, 2004

Abstract: A lymphocytic enterocolitis has been reported in a cohort of children with autistic spectrum disorder (ASD) and gastrointestinal (GI) symptoms. This study tested the hypothesis that dysregulated intestinal mucosal immunity with enhanced pro-inflammatory cytokine production is present in these ASD children.

Comparison was made with developmentally normal children with, and without, mucosal inflammation. Duodenal and colonic biopsies were obtained from 21 ASD children, and 65 developmentally normal paediatric controls, of which 38 had signs of histological inflammation. Detection of CD3+ lymphocyte staining for spontaneous intracellular TNFα, IL-2, IL-4, IFNγ, and IL-10, was performed by multicolor flow cytometry. The data provide further evidence of a diffuse mucosal immunopathology in some ASD children and the potential for benefit of dietary and immunomodulatory therapies.

[10] "The Significance Of Ileo-Colonic Lymphoid Nodular Hyperplasia In Children With Autistic Spectrum Disorder," Wakefield AJ, Ashwood P, Limb K, Anthony A. ***European Journal of Gastroenterology Hepatology***, 2005.

*"*The prevalence of LNH was significantly greater in ASD children compared with controls in the ileum (129/144 (90%) vs. 8/27 (30%), $P < 0.0001$) and colon (88/148 (59%) vs. 7/30 (23%), $P = 0.0003$), whether or not controls had co-existent colonic inflammation*."*

[11] "Immune Activation Of Peripheral Blood And Mucosal CD3+ Lymphocyte Cytokine Profiles In Children With Autism And Gastrointestinal Symptoms," Ashwood P, Wakefield AJ. ***Journal of Neuroimmunology***, 2006.

[12] "Intestinal Lymphocyte Populations In Children With Regressive Autism: Evidence For Extensive Mucosal Immunopathology," Ashwood P, Murch SH, Anthony A, et al. Journal of Clinical Immunology, 2003; 23:504-517.

[13] "Mucosal and Peripheral Blood Lymphocyte Cytokine Profiles In Children With Regressive Autism And Gastrointestinal Symptoms: Mucosal Immune Activation And Reduced Counter Regulatory Interleukin-10." Ashwood P, Murch SH, Anthony A, et al. *Gastroenterology*, 2002

[14] "Detection and Sequencing Of Measles Virus From Peripheral Mononuclear Cells From Patients With Inflammatory Bowel Disease And Autism." Kawashima H1, Mori T, Kashiwagi Y, Takekuma K, Hoshika A, Wakefield A. ***Digestive Disease & Sciences*** 2001.
"*The sequences obtained from the patients with ulcerative colitis and children with autism were consistent with being vaccine strains.*"

[15] Ileal-Lymphoid-Nodular Hyperplasia, Non-Specific Colitis, And Pervasive Developmental Disorder In Children.Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Harvey P, Valentine A, Davies SE, Walker-Smith JA. *TheLancet*. 1998 Feb. Erratum in: Lancet. 2004 Mar 6;363(9411):750.
Retraction in: Lancet. 2010 Feb.

[16] "Acute Encephalopathy Followed By Permanent Brain Injury Or Death Associated With Further Attenuated Measles Vaccines: A Review Of Claims Submitted To The National Vaccine Injury Compensation Program," Weibel RE, Caserta V, Benor DE. 1998;101:383-387.

Ekbom A, Daszak P, Kraaz W, Wakefield AJ. Crohn's Disease After In Utero Measles Virus Exposure. *Lancet* 1996;348: 515–17.
Abstract
An epidemiological association between Crohn's disease and measles virus exposure in early life has been suggested in case-control studies.

METHODS:
To determine absolute risk estimates for in-utero measles virus exposure and Crohn's disease, maternity charts for all 25000 deliveries at University Hospital, Uppsala, between 1940-49 were reviewed: four cases of measles infection in the mother during pregnancy were identified. The children and two of their mothers were interviewed and case records reviewed. Three offspring had undergone multiple intestinal resections; tissue from these cases were examined by routine histology, and for measles-virus nucleoprotein antigen by immunohistochemistry and immunogold electronmicroscopy.
FINDINGS:

Three of the four children had Crohn's disease. In each the disease was preceded by recurrent, antibiotic-resistant pneumonia. They had extensive ileal and colonic disease; two patients required intravenous feeding. The only offspring to have had measles as a child did not develop Crohn's disease. Measles virus antigen was detected in foci of granulomatous and lymphocytic inflammation in all children with Crohn's disease.

INTERPRETATION:

The data indicate that exposure of mothers to measles virus in utero is a risk factor for Crohn's disease in their children. Exposure at this time may lead to persistent infection, or modify the response to infection in later life, leading to persistence of measles virus.

[17] Is Measles Vaccination A Risk Factor For Inflammatory Bowel Disease? N.P Thompson, Prof RE Pounder, AJ Wakefield, SM Montgomery, *The Lancet*, 1995.

Measles virus may persist in intestinal tissue, particularly that affected by Crohn's disease, and early exposure to measles may be a risk factor for the development of Crohn's disease. Crohn's disease and ulcerative colitis occur in the same families and may share a common aetiology. In view of the rising incidence of inflammatory bowel disease (Crohn's disease and ulcerative colitis), we examined the impact of measles vaccination upon these conditions.

Prevalences of Crohn's disease, ulcerative colitis, coeliac disease, and peptic ulceration were determined in 3545 people who had received live measles vaccine in 1964 as part of a measles vaccine trial. A longitudinal birth cohort of 11,407 subjects was one unvaccinated comparison cohort, and 2541 partners of those vaccinated was another. Compared with the birth cohort, the relative risk of developing Crohn's disease in the vaccinated group was 3.01 (95% CI 1.45-6.23) and of developing ulcerative colitis was 2.53 (1.15-5.58). There was no significant difference between these two groups in coeliac disease prevalence. Increased prevalence of inflammatory bowel disease, but not coeliac disease or peptic ulceration, was found in the vaccinated cohort compared with their partners. These findings suggest that measles virus may play a part in the development not only of Crohn's disease but also of ulcerative colitis.

[18] Lewin J, Dhillon AP, Sim R, Pounder RE, Wakefield AJ. Confirmation of Persistent Measles Virus Infection Of Intestinal Tissue By Immunogold Electron Microscopy. *Gut*, 1995; 36: 564–69.

This study sought to investigate persistent measles virus infection of the intestine: a novel protocol for immunogold electron microscopy was developed using a polyclonal anti-measles nucleoprotein antibody on reprocessed, formalin fixed paraffin wax embedded tissue sections. Antibody binding was detected using both immunoperoxidase and light microscopy on tissue sections, and 10 nm gold conjugated secondary antibody and electron microscopy on ultrathin sections. The techniques were validated using both measles infected vero cells and human tissues with established measles infection: these included brain affected by subacute sclerosing panencephalitis and acute measles appendicitis. The technique was applied subsequently to six untreated cases of granulomatous Crohn's disease, and two cases of ileocaecal tuberculosis, a granulomatous control.

Mumps primary antibody--applied to both mumps infected vero cells, and measles infected vero cells and tissues studied by immunoperoxidase, and measles antibody on mumps infected cells studied by immunoperoxidase and immunogold--were used as specificity controls: the primary antibodies identified their respective target antigen and there was no antibody cross reactivity. Measles virus nucleocapsids labelled with gold conjugated antibody in both infected cells and tissues, including foci of granulomatous inflammation in five of six cases of Crohn's disease: in the fifth case, the granuloma could not be identified in ultrathin section. In one of the tuberculosis cases, a low level of signal was noted while the second case was negative. Labelling adopted a characteristic pattern in all infected tissues, strengthening the specificity of these findings. This study provides the first direct confirmation of persistent measles virus infection of the intestine.

[20] Ekbom A, Wakefield AJ, Zack M, Adami HO. Perinatal Measles Infection And Subsequent Crohn's Disease. *Lancet* 1994;344: 508–10.

Abstract

Although the aetiology of Crohn's disease is unknown, morphological and epidemiological studies have implicated measles virus as a potential component cause, particularly when exposure occurs in utero or early in life. An increased incidence of Crohn's disease among people born during measles epidemics would support this hypothesis. We identified all individuals born in four counties in central Sweden in 1945-54 who had had Crohn's disease diagnosed before the age of 30 years. Yearly reports compiled in these counties revealed that five measles epidemics had affected all four counties during the trial period. After adjusting for monthly differences in the number of livebirths in the four counties, we calculated the expected number of patients with Crohn's disease and ulcerative colitis born during the 3-month period after the peaks of the epidemics.

The number of people with Crohn's disease significantly exceeded that expected: 57 versus 39.0 (standardised incidence ratio 1.46, 95% CI 1.11-1.89). For patients with ulcerative colitis, the observed number (42) was close to that expected (46.8). Our results strengthen the hypothesis that measles is related to Crohn's disease and that the perinatal period is a time of vulnerability.

As Dr. Wakefield's research findings linking gastrointestinal disease with ASD have been validated and amplified in numerous studies, the attacks on his professional reputation, and the effort to invalidate the science, have intensified rather than abated? Why?

This (partial) Bibliography drew on compilations of others, notably by J.B. Hadley, Jr., http://www.morehealthlesshealthcare.com/vaccines/the-study-behind-the-vaccine-austim-link/

*****