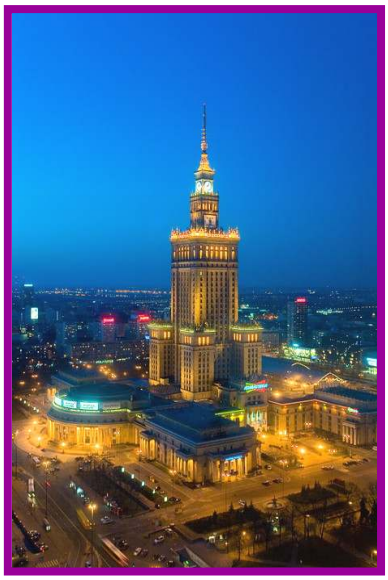
AUTISM AND VACCINATIONS: IS THERE A LINK?

International Conference

October 25-26, 2008,
Warsaw University, Miecznikowa 1
Warsaw, Poland



Sobieskiego 9, Warsaw

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AGENDA

October 25

8:00 - 9:00 **Registration**

9:00 – 9:30 **Prof. Maria Dorota Majewska** (Poland) Vaccines and Neurodevelopmental Disorders: Why we Must Continue to Study this Problem?

9:30- 10:30 **Dr Stefanie Cave** (USA) Vaccines: Have we Gone Too Far?

10:30-10:45 coffee break

10:45-11:45 **Dr Mark Geier & David Geier** (USA) Understanding the Biochemical Basis of Mercury-Induced Autism Spectrum Disorders

11:45-12:45 **Dr M. Catherine De Soto** (USA) Blood Levels of Mercury are Related to Diagnosis of Autism: Reanalysis of an Important Data Set

12:45-13:45 **Dr Joahim Mutter** (Germany) Mercury and Autism, Toxicology of Mercury

13:45-14:45 Lunch

14:45- 15:45 **Dr Boyd Haley** (USA) The Effects of Synergistic Toxicities and Genetic Susceptibilities on the Induction of Oxidative stress and its Relationship to Autism and other Neurological Disorders: New Treatment Possibilities

15:45-16:45 **Dr Mark Geier & David Geier** (USA) Understanding the Biochemical Basis of the Treatment of Autistic Disorders: An Overview of the Importance of Hormones (Testosterone & Estrogen)

16:45-17:45 **General Discussion**

Adjourn

October 26

9:00- 9:30 **Dr Mark Geier & David Geier** **(US)** Understanding the Role of Childhood Vaccinations as a Cause of Sudden Infant Death Syndrome (SIDS)

9:30-10:30 **Prof. Jozef Prandota** (Poland) Vaccines and SIDS, a Potential Pathomechanism

10:30-10:45 Coffee break

10:45- 11:45 **Dr Magdalena Cubala** (Poland/GB) Most Frequent Metabolic Abnormalities Observed in Autism and Current Methods of Autism Treatment

11:45 – 12:15 **Dr Lorene Amet** (GB) Prevalence and Functional Analysis of Self Injurious Behaviours in Autism: Underlying Clinical and Pain Issues - Implications for Behaviour Management Strategies

12:15-12:45 **Dr Beata Kazek** (Poland) Serotonergic Disturbance in Autism

12:45 - 13:15 **Dr Ewa Urbanowicz** (Poland) Childhood Vaccinations and Autism: Medical Establishment Conspiracy or Mass Hysteria?

13:15-14:15 Lunch

14:15-14:45 **Dr Mieszko Olczak & Msc Michalina Duszczyk** (Poland). "Postnatally administered Thimerosal in rats: a model of autism?"

14:45-15:15 **Dr Elzbieta Zieminska** (Poland). Role of glutamate receptors and calcium imbalance in thimerosal neurotoxicity: in vitro study

15:15-16:15 **General Discussion and conclusions (M.D. Majewska)**

ABSTRACTS

Vaccines and Neurodevelopmental Disorders: Why We Must be Concerned and Continue to Study this Problem

Maria Dorota Majewska, Ph.D., Professor, Marie Curie Chair, EC, Institute of Psychiatry and Neurology, Warsaw, Poland

Abstract:

The common belief, strengthened by the medical establishment, holds that vaccinations were responsible for the dramatic decrease in developed countries of deaths due to infectious diseases such as pertussis, diphtheria, measles, scarlet fever, polio, tuberculosis and other. As a result of this conviction, a majority of infants are being vaccinated with ever increasing number of vaccines, some of which are delivered in combinations of 3 to 8 antigen types in a single shot. In several countries, including Poland, the newborns in the first hours of life receive two vaccinations – BCG (against tuberculosis) and Hep B (against hepatitis B). During the first 18 months of life Polish children receive 16 obligatory (enforced by law) vaccinations against 10 diseases (tuberculosis, hepatitis B, diphtheria, pertussis, tetanus, poliomyelitis, measles, mumps, rubella and infections caused by Haemophilus influenzae). Many children receive additional recommended immunizations against: Streptococcus pneumoniae, Nisseria meningitidis, rotavirus, influenza virus, herpes virus varicellae and hepatitis A virus, totaling in a frightening number of 26 vaccine injections in the first 2 years of life.

However the national statistics of developed countries contradict the prevailing vaccination myths. The "Vital Statistics of the United States" show that death numbers due to major infectious diseases markedly declined before the introduction of vaccines against these diseases, due to improved hygiene, nutrition and living standards of the population. Also several epidemiological studies documented that many vaccines have questionable efficacy in preventing diseases. For example, for BCG vaccine the efficacy in preventing TB has been reported by different studies to be between 0% and 80%. In several epidemiological studies this vaccine failed or was shown to lead to a greater incidence of TB in the vaccinated populations, than in nonvaccinated. In Poland mass BCG vaccinations have been compulsory since 1955 and more than 95% of the population has been vaccinated. In spite of this, Poland has a 3-4 times greater incidence of TB (about 22 per 100 000) than most Western European countries or the US, where compulsory BCG vaccination have been abandoned. Similar situations appear to exist in other Central and Eastern European countries. Many outbreaks of pertussis, measles or polio in highly vaccinated populations have been reported in different countries and studies revealed that certain vaccines, particularly DPT and polio vaccine increase infants' mortality and can produce life-threatening adverse events in children and adults. Moreover, the "Vital Statistics of the United States" show that influenza and pneumonia mortality rates in the US markedly increased after the introduction of flu vaccines, proportionally to the percent vaccination coverage of the population.

Simultaneously with the growing number of vaccinations, a dramatic increase of neurodevelopmental disorders (such as autism, ADHD, learning disabilities, mental retardation, epilepsy) and other chronic debilitating diseases (diabetes type I, asthma, allergies) has been observed in children around the world. Mounting epidemiological and clinical data, as well as experimental findings have documented, that increase of incidence of

these diseases might be iatrogenic, due to excessive vaccination of children. According to the EUVAC database, Poland and some other Eastern European countries have outdated infant immunization programs, as they require obligatory immunization of all newborns in the first hours of life with BCG and Hep B vaccines. In Western European countries only infants from high-risk groups receive these vaccines and most vaccines are delayed until the 2^{nd} - 3^{rd} month of life or later age. Overall, comparing to western European countries, Polish children receive obligatory vaccines at earlier age and some with questionable quality, which may be harmful.

Vaccines challenge the immune system to produce antibodies, but may also cause its dysregulation and autoimmune diseases. They often contain toxic additives, such as thimerosal (mercury compound), aluminum salts, formaldehyde, foreign proteins and genetic materials, among others, which might poison vulnerable children and cause irreversible developmental injuries or severe life-long diseases. In developed countries, the personal and societal costs due to iatrogenic, likely vaccine-induced, diseases appear now to exceed the costs and dangers of treatable infectious diseases. The epidemiological numbers speak for themselves. The incidence of TB in Poland was 1 in 4500 (2004) and hepatitis B - 1 in 16 000 (2001), whereas the current prevalence of diseases, which might be caused by excessive vaccinations such as autism is approximately: 1 in 150 (Europe, US), ADHD – 1 in 10-20 (Europe, US), type 1 diabetes among children - 1 in 220-580 (US) and 1 in 48 (Finland), asthma 1 in 15 (US) and 1 in 6 (UK). The incidence of these diseases has been dramatically increasing over the past 2 decades, suggesting that we have new epidemics. Moreover, the psychological studies conducted in the UK by prof. Michael Shayer revealed a marked decline of intellectual capacities of school children, comparing to those from earlier generation. Similar are the observations of teachers in other countries. It is very likely, that this is a population effect of excessive vaccinations. The societal costs of such generational decrease of intelligence are not measurable, but could be staggering.

The alarming increase of neurodevelopmental disorders and chronic diseases, which appear to be directly related to iatrogenic effects of vaccinations, demand urgent attention of the governments as well as national and international health organizations, and reevaluation of true benefits and costs of current vaccination programs. It became evident, that in developed countries the risks now far outweigh the benefits. It is unacceptable, that any healthy child should die or become permanently debilitated due to vaccinations against treatable infectious diseases. Many developed countries reduced the number of infant vaccinations and moved them to later stages of development, i.e. after 2-3 months of age for the majority of children, except for those from high-risk groups. Also, the role of the pharmaceutical industry, which is pushing for more and more vaccination, should be critically examined. It is perhaps not accidental, that the same companies, which produce and aggressively promote new vaccines, also produce medications to treat debilitating life-long diseases caused by their vaccines.

At the Institute of Psychiatry and Neurology we are conducting a series of clinical and preclinical studies to examine a potential link between vaccinations and autism in children and to evaluate the neurotoxic effects of vaccine preservative, thimerosal, in developing rodents. Preliminary data from both lines of studies will be discussed in the presentations given by Dr. Ewa Urbanowicz and Dr. Mieszko Olczak.

Study sponsors: European Commission and Ministry of Science and Higher Education, Poland.

Vaccines: Have we Gone too Far?

Stephanie F. Cave, M.D., M.S., FAAFP
Clinical Faculty, Louisiana State University Medical School, Louisiana, USA

Abstract:

Medicine has defined autism as a psychiatric problem since it was first described by Leo Kannerin 1943. The number of autistic children remained steady at approximately 1/10000 for years until the 1990's. From 1991 to the present time the incidence of autism has increased rapidly. In 2008 medicine is faced with the reality that 1/150 children have been diagnosed autistic. Many have questioned the possibility of an epidemic, but studies by The Mind Institute, U.C. Davis showed very clearly that we are dealing with an epidemic that cannot be explained by changes in diagnosis or migratory patterns.

The cause of this epidemic has not been explained, but there have been several hypotheses that could explain the phenomenon. One of these implicates vaccines because they contain many environmental toxins like ethyl mercury and aluminum and live viruses like measles, mumps, rubella, and varicella. Jill James et al. have published studies suggesting a genetic predisposition in families of these children leaving them with a methylation problem and a deficiency in glutathione. The result of this is that the children cannot detoxify heavy metals. Vargas has shown ongoing inflammation in the brain and other studies are now showing that many of these children have mitochondrial dysfunction. The Hannah Poling case in the United States Vaccine Court was a landmark case in this epidemic. Hannah was found to have mitochondrial dysfunction. The impact of having nine vaccines on one day resulted in the child having autistic behavior. Hannah was awarded funding for future medical care. There are many other families who hope through this case to gain access to funds to help them to properly care for their children.

Understanding the Biochemical Basis of Mercury-Induced Autism Spectrum Disorders

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Abstract:

This presentation will provide an overview of the biochemical basis of mercury-induced autism spectrum disorders. Mercury has become a ubiquitous cause of potential harm from environmental sources (methylmercury in fish or mercury vapor power from coal-burning power plants) and medicinal sources (Thimerosal-containing vaccines/biologics or dental amalgams). Specific emphasis will paid to Thimerosal which has been marketed as an antimicrobial agent in a range of products, including topical antiseptic solutions and antiseptic ointments for treating cuts, nasal sprays, eye solutions, vaginal spermicides, diaper rash treatments, and perhaps most importantly as a preservative in vaccines and other injectable biological products, including Rho(D)-immune globulin preparations, despite evidence, dating to the early 1930s, indicating Thimerosal to be potentially hazardous to humans and ineffective as an antimicrobial agent.

Evidence will be presented showing that exposure to mercury can cause immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with autism, and the similarities extend to neuroanatomy, neurotransmitters, and biochemistry. Further, evidence will be presented showing an increased body burden of mercury in autism spectrum disorder patients with: (1) increased pre- and postnatal mercury exposure, (2) significant increases in the mean mercury level in the baby teeth, (3) significant elevations in urinary and fecal mercury concentrations following chelation therapy, (4) significant elevations in urinary porphyrins associated with mercury toxicity, and (5) a significant decrease in the rate of mercury excretion documented in first baby haircuts.

This presentation will clearly establish, given the known developmental neurotoxicity attributed to mercury and the known biochemical and genomic susceptibility factors to mercury toxicity present in many patients diagnosed with an autism spectrum disorder, that mercury exposure plays a causal role in a significant number of autism cases.

Blood Levels of Mercury are Related to Diagnosis of Autism: Reanalysis of an Important Data Set.

Dr. M.Catherine De Soto and Dr. Robert T. Hitlan
University of Northern Iowa, Cedar Falls, Iowa, United States

Abstract:

The question of what is leading to the apparent increase in autism is of great importance. Like the link between aspirin and heart attack, even a small effect can have major health implications. If there is any link between autism and mercury, it is absolutely crucial that the first reports of the question are not falsely stating that no link exists. We found a mistake in the only published article (Ip et al, J Child Neurol, 2004) that directly compared blood levels of mercury in autistic children to levels in normally developing children. The authors of the widely cited 2004 publication concluded that "there is no causal relationship between mercury as an environmental neurotoxin and autism." We obtained and reanalyzed their data set and documented that the original statistics were in error and that a significant relation does exist between the blood levels of mercury and diagnosis of an autism spectrum disorder, resulting in a formal erratum being published. Moreover, the hair sample analysis results offer some support for the idea that persons with autism may be less efficient and more variable at eliminating mercury from the blood (J. Child Neurol., 2007). The content of the talk will include the speaker's views on key aspects of the body of research on mercury and autism. That exposure to mercury causes negative changes in developing brains is a known fact that scientists do not dispute, while the extent of these changes that are due to environmental exposure is an open question within some broad bounds. That genetic differences among individuals account for the lion's share of who does and who does not get autism today is beyond dispute. But the heritability statistic is often misunderstood. High heritability poses no problem for macro-level environmental changes to cause a several fold increase in a trait's prevalence.

The story behind how the mistake was found will be shared and an interesting analysis of public and professional reaction will be provided. Finally, the authors' recent research on evidence for prenatal mercury effects will be considered. Specifically, in the United States, state autism rates vary by a factor of five-fold across states. Analysis of indicators of mercury pollution within a state shows this to be a surprisingly strong predictor of the state's autism prevalence.

The Toxicology of Mercury and the Relation to Autism

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Abstract

Mercury in all forms is known to be very toxic, even at very low doses. It is more toxic for neurons or protein folding than lead or cadmium and other metals because it has an extremely high affinity due to "covalent bond" formation with thiol groups, causing irreversible inhibition (binding-constant $10^{30\text{-}40}$). This might explain the exceptionally long half-life of mercury in not renewing tissue (e.g. brain) from several years to decades and the fact that mercury accumulates in such tissues over time of exposure. Both in vitro- and animal model studies have shown that only mercury in very low concentrations was able to damage brain neurons in multiple ways.

Over the last decades, mercury levels in the environment, and hence in animal- and human tissues, have been rising. In developed countries, main human sources of mercury are iatrogenic (dental amalgam, thimerosal) and fish consumption. According to the WHO (2005), there exist no safety levels, below which the adverse biological effects are excluded.

Mercury vapour or ethylmercury from thiomerosal may be more neurotoxic than methyl mercury found in fish. Recent publications have shown that pre- and postnatal exposure to mercury may increase the risk for neurodevelopmental disorders and autism. It was also shown in several studies, including autopsy studies, that it is not possible to estimate human mercury burden in living subjects through biomonitoring of mercury levels in blood, urine or hair. Furthermore, genetic polymorphism and exposure to other xenobiotics may lead to increased mercury toxicity and accumulation in tissues in some individuals, but decreased mercury excretion and thus, to low mercury levels in biomarkers.

These mechanisms were proposed in persons with autism. The reason, why these data are not officially acknowledged is based on the toxicological dogma, that mercury levels in body fluids have to correlate with mercury levels in tissues (or with the severity of clinical symptoms) as well as the dogma, that there exist safe levels of mercury. Based on the new scientific data, these views have to be revised.

Keywords**:** amalgam, mercury, toxicity, thimerosal, autism, ethylmercury

The Effects of Synergistic Toxicities and Genetic Susceptibilities on the Induction of Oxidative stress and its Relationship to Autism and other Neurological Disorders: New Treatment Possibilities

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Abstract:

Data now exists that strongly supports the concept that there is a genetic subset of the human population that is unable to effectively excrete mercury from low level exposures. This leads to retention toxicity in this subset at levels of exposure that is easily excreted by the bulk of the healthy population. Autistic children seem to fit into this subset as well as aged Alzheimer's disease subjects. The observed low levels of mercury in the blood, urine and hair of autistics, when compared to the higher levels retained in their other body tissues, indicates that retention toxicity occurs. This susceptible subset of the population, due to the low frequency, is very likely to be overlooked or not be apparent in most epidemiological studies that consider general populations. However, individuals with the inability to excrete mercury would be expected to develop neurological problems such as autism, AD, etc. Sorting out these individuals and comparing their toxicity status to the general, healthy population produces results strongly indicating that mercury exposures may be the cause of their neurological problems. It is consistent that many with neurological illnesses, especially autistic children, display low glutathione levels indicating that they are suffering from oxidative stress. Other factors, such as lipid peroxidation indicate that oxidative stress, or low glutathione, is prevalent in autistic children. Oxidative stress can be caused by many toxicants and removal of many toxicants from the body requires adequate glutathione. Therefore, low glutathione levels caused by a toxic exposure can put the human body on a track where other toxins (if exposed) are retained. This can keep the body in a constant abnormal redox state where maximum health is not obtained. But this represents a treatable situation with proper antioxidant therapies. This talk will address the logic of the initiation of oxidative stress in infants by early stage vaccinations and how the oxidative stress induced remains in even the older autistic children. The treatment of oxidative stress and reversal of this will be discussed.

The retention and toxicity of mercury and mercury compounds is known to be enhanced by the presence of other synergistic factors that may or may not have toxicity by themselves. Such non-toxic compounds include antibiotics, a milk diet and male hormone. Toxic compounds such as other heavy metals (lead, aluminum) are well known to dramatically increase the toxicity of low levels of mercury exposures. Therefore, unless a total knowledge of the exposure to synergistic toxins is known it is impossible to define a safe level of mercury exposure for humans in the environment.

Data will be presented showing the actual mercury vapor release from five amalgam sources. The International Academy of Oral and Medical Toxicology aided in the dental production of 90 single spill amalgam fillings made in plexiglass molds so that all are about the same size and weight. Nine different dentists made these fillings in their offices using amalgam materials from different manufacturers. The emission of mercury from each of these fillings has been determined based on micrograms/mg material and micrograms/cm^2 surface area. The results of this study show that 4 to 20 micrograms are released per cm^2 per day by.

This is hundreds of times higher than that estimated by spokespersons for the American Dental Association.

Recent research was published in JAMA from the latest NIH study called the "children's amalgam trials", or CAT studies, which concluded that amalgams are safe for use in children. However, this research showed that boys who received amalgams excreted no more mercury into their urine by the end of the 7 year study than did the amalgam free boys. Girls, in contrast, excreted mercury in the urine at levels much greater than boys from the very start and did not lose this ability after 7 years when compared to the amalgam free girls. This means the boys are retaining much more mercury than the girls and it is well recognized that autism and other child neurological illnesses are vastly higher in boys than girls. Further, the loss of excretion through the urine may indicate kidney damage in the boys, or it may reflect the fact that testosterone, which enhances mercury retention and toxicity, is increasing as these boys from 7-8 to 14-15 years of age. Several studies documented higher exposure to androgens of autistic children during fetal life, as increased levels of testosterone were measured in the amniotic fluid of women who give birth to autistic children. Synergistic toxic effects of mercury and testosterone may also explain why boys or young men more often die of 'sudden cardiac death' or 'idiopathic dilated cardiomyopathy, IDCM' during high school or college athletic events, as these subjects - according to a publication in the J. American Cardiology in 1999 - have 178,400ng/gram of mercury in heart tissue compared to 8ng/gram for comparative controls, a 22,000 fold increase. This indicates that the populations most at risk for mercury toxicity from amalgams are those with increased testosterone levels.

Recent research shows that 85% of dentists/hygienist have urinary porphyrin profiles that indicate that mercury exposure is affecting their ability to make heme. About 15% of this 85% appear to be more dramatically affected due to a polymorphism in the CPOX-4 gene. Research from France has shown that autistic children have urinary porphyrin profiles consistent with them being mercury toxic. Porphyrin profiles are the most sensitive and definitive measure of heavy metal toxicity, especially for mercury. Porphyrin synthesis is the major pathway for heme synthesis and heme carries oxygen and is also necessary for other biochemical functions, including detoxification. The prevailing paleness of autistic children implies that they do have a heme production problem.

Further, an evaluation of the relative toxic effects of mercury and thimerosal shows that the younger the infant the more toxic and lethal the effects can be. An evaluation of synergistic toxicities, genetic susceptibility and infant age will be presented along with the basic biochemical and cellular level research that strongly supports the thimerosal causation of autism hypothesis. It is now well known that mercury in the fetal cord blood is much higher than in the mother's blood indicating that the fetus is being exposed to larger amounts of mercury per unit body weight than is the mother.

Finally, current compounds being used to treat toxic or oxidative stress afflicted individuals are not very effective and may cause renal problems. We will describe a new type of antioxidant that increases body glutathione levels which likely provides for a safer treatment for toxic/oxidative stress in individuals. These compounds have been proven not to be toxic at levels over 1,000 times the levels that would be used in oxidative stress therapy to enhance the bodies' glutathione levels.

Understanding the Biochemical Basis of the Treatment of Autistic Disorders: An Overview of the Importance of Hormones (Testosterone & Estrogen)

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Abstract:

The American College of Medical Genetics, a recognized board of the American Medical Association, has recently issued guidelines recommending the routine evaluation and management of all patients diagnosed with an autism spectrum disorder by clinical geneticists. According to the newly published practice guidelines from the American College of Medical Genetics, "The primary role of the geneticist in this process is to define etiology, if possible, and to provide counseling and contribute to case management based on the results of such investigations." In response, the Genetic Centers of America has launched a landmark, national outreach program to provide clinical genetic services to the underserved population of persons diagnosed with an autism spectrum disorder. The Genetic Centers of America, involved in the management of clinical medical genetic evaluations for more than 28 years, presently has one of the United States' largest private clinical genetics practices involved in the management and treatment of patients diagnosed with as ASD. Further, the Genetic Centers of America, working in collaboration with the not-for-profit 501(C)3 Institute of Chronic Illnesses, Inc. and the not-for-profit 501(C)3 CoMeD, Inc., has been involved in more than 20 recent peer-reviewed studies helping to define the etiology and management of patients diagnosed with an autism spectrum disorder.

This presentation will examine the issue, how hormones such as testosterone and estrogen play an important role in the clinical presentation of patients diagnosed with an autism spectrum disorder, and how treatment of hormonal abnormalities oftentimes results in significant clinical improvements in patients diagnosed with an autism spectrum disorder. The sex difference in the occurrence of autism spectrum disorder cases may reflect a male vulnerability (male/female ratio = 3:1), a contention supported by multiple lines of evidence.

Evidence will presented showing that individuals with an autism spectrum disorder tend to display a hypermasculine profile on many cognitive tasks. Others have observed that individuals with an autism spectrum disorder also have lower-than-expected 2nd to 4th digit (2D:4D) ratios, which is correlated with higher ratios of fetal testosterone to fetal estrogen, as well as lower verbal and higher numerical intelligence. Some neuroanatomical studies comparing the brains of individuals with and without an autism spectrum disorder reveal structural differences associated with high levels of fetal testosterone. Clinical examination of patients with an autism spectrum disorder has revealed that on average, girls with an autism spectrum disorder show a significant delay in the onset of menarche are more likely to display elevated rates of testosterone-related disorders than neurotypical controls. Other studies have

shown elevated blood levels of testosterone in patients diagnosed with an autism spectrum disorder in comparison with controls.

Evidence will be presented showing that therapies designed to help treat elevated testosterone levels in patients diagnosed with an autism spectrum disorder have helped to improve clinical outcomes. Clinical data will presented from hormone therapy conducted on 200 patients diagnosed with an autism spectrum disorder that significantly lowered testosterone and significantly improved socialization, sensory/cognitive awareness, and health/physical/behavior skills, with few non-responders and minimal adverse clinical effects to the therapy. Further, will presented on how such therapy significantly helped to ameliorate hyperactivity/impulsivity, stereotypy, aggression, self injury, abnormal sexual behaviors, and/or irritability behaviors that frequently occur in those with an autism spectrum disorder diagnosis.

Understanding the Role of Childhood Vaccinations a Cause of Sudden Infant Death Syndrome (SIDS)

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Abstract:

This presentation will provide an overview of historical and recent studies that have examined the relationship between childhood vaccines as a significant cause of sudden infant death syndrome (SIDS). Specific evidence will presented concerning epidemiological studies examining the relationship between the administration of whole-cell pertussis-containing vaccines (DTP) and SIDS episodes. Evidence presented will include analyses of the rate of reported SIDS episodes reported to the Vaccine Adverse Event Reporting System (VAERS) database, a US national registry of vaccine-associated adverse events, following DTP vaccines in comparison to acellular pertussis-containing vaccines (DTaP), as well as observational epidemiological studies examining the death rate observed among children receiving DTP vaccines in comparison to unvaccinated populations from several different countries.

The presentation will also examine biologic mechanisms for the increased reactogenicity of whole-cell pertussis vaccines, which may stem from the fact that whole-cell pertussis vaccines contain 3,000 different proteins, whereas DTaP contains two to five proteins. Whole-cell pertussis vaccine contains known neurotoxins including: endotoxin, pertussis toxin and adenylate cyclase. Finally, the presentation will provide an overview of compensation provided by the US government to children that as a result of childhood vaccines as part of the National Vaccine Injury Compensation Program (NVICP) and a global view regarding the continued use of whole-cell pertussis vaccines.

Pathophysiology of Vaccination-Associated Adverse Events

Professor Józef Prandota, M.D.
Department of Social Pediatrics, University Medical School Wroclaw, Poland

Abstract:

DTP vaccination. A report in 1987 documented death of twins 2-3 hrs after DTP immunization, which may suggest genetic predisposition to SIDS. In mice, administration of the whole-cell diphtheria and tetanus toxoids and pertussis vaccine adsorbed caused an increase of liver and spleen weights lasting 7 to 14 days following DTP vaccination. Histopathologic tissue examination showed random, multifocal inflammation with hepatocyte necrosis. DTP vaccination caused also marked dose- and time-dependent depression in the expression of mRNA for isoenzymes of CYP450 in the livers of mice, and these effects were preceded by marked increases in mRNA expression for proinflammatory cytokines IL-1, IL-6, TNF, INF-γ, and inducible NO synthase. The wild-type diphtheria and tetanus toxoids and whole-cell pertussis vaccines decreased microsomal CYP450 levels by 50%, paralleling the results in prolongation of the hexobarbital-induced sleeping time in mice.

Clinical studies showed that DTP vaccination revealed latent urinary tract diseases, such as steroid-sensitive nephrotic syndrome, acute renal failure, pyelonephritis, and urinary infection/inflammation in infants and young children. Genetic polymorphisms of various interleukins (e.g. IL-10-592*A gene, the constellation of TNF-α and IL-6 genetic variants) may also predispose some infants to a more than usually intense inflammatory response after various vaccinations. It must be emphasized that IL-1β, TNF-α and IL-6 induce considerable increases in glucocorticosteroids (GS) binding and GS receptor levels thus markedly decreasing total body pool of these hormones. Since GS promote a Th2 type cytokine response by CD4+ T cells, their lack or significant deficiency may cause that some genetically predisposed infants become more vulnerable to various harmful factors.

Autoimmune hemolytic anemia (AIHA) is developing sometimes in infants and young children after DTP vaccination. In one case, RBCs from an Mk homozygote were found compatible with the patient's autoantibody. The DAT was positive (3+) with only anti-C3 on presentation. An IgM cold reactive autoantibody with probable anti-Pr specificity and high thermal amplitude (370C) was identified in the serum. In another case, the DATs performed with anti-C3d were positive, and the DAT using anti-IgG was strongly positive. It was suggested that AIHA could be secondary to the imbalance between IL-10 and IL-12 because decreased production of Th1 type cytokines and prevalent Th2 ones leading to autoantibodies production.

Thiomerosal (ethylmercury, EtHg). Hg(2+) accumulates in all organs, including the brain, and in genetically susceptible rodents produced mercury-induced autoimmunity (HgIA). Inorganic Hg (HgCl2) created HgIA with T cell-dependent polyclonal B cell activation and hypergammaglobulinemia, dose- and H-2 dependent production of anti-fibrillarin autoantibodies (AFA), and systemic vessel wall immune-complex (IC) deposits. EtHg administered to H-2s mice also caused development of AFA and IC deposits. IFN-γ and IL-6, but not IL-4, were important for induction of AFA. EtHg induced a persistent Th1-skewed response irrespectively of the dose and time used. The autoimmunogenic effect of EtHg might be entirely due to Hg(2+) formed from EtHg in the body.

Most Frequently Occurring Biological Disorders Related to Etiology of Autism and the Methods of Treatment

Magdalena Cubala-Kucharska, M.D., specialist in autism, Breakspear Medical Hospital Hertfordshire House Wood Lane Hemel Hempstead Hertfordshire HP2 4FD, UK

Abstract:

Autism is an developmental disorder. The initial symptoms can often be observed in early stages of childhood. The most common symptoms of autism are disruptions of social interactions, lack of communication skills, repetitive and ritualistic behaviours, self-stimulation, tantrums and sometimes aggression.

The medical understanding of autism has changed since it was first defined by Kanner. Nowadays science already identifies many biological disorders associated with this disease, which might play a role as etiological factors.

The picture of structural and biochemical changes in autistic spectrum disorders remains still unclear and requires further investigations, nevertheless, current scientific findings tend to define autism as a disease affecting the brain rather than a "disease of the brain".

Methods:

A review of current medical papers related to Autism Spectrum Disorders and a review of author's cases.

Aims:

The aim of this presentation is to show the most frequently occurring disorders related to autism and an evaluation of most commonly used methods of treatment.

Disorders frequently occurring in autism:

1) gastrointestinal tract disorders, including dysbiosis, inflammation, pancreatic exocrine insufficiency, coeliac disease, maldigestion, malabsorption, food intolerance, food allergies.
2) vitamin deficiencies, malnutrition
3) immune system disorders, disproportionate subpopulations of lymphocytes, chronic inflammation
4) disorders of main biochemical pathways of the organism, including methylation, transsulphation, oxidative stress, lactic acidosis, disorders of metabolism of neurotransmitters, including serotonin, dopamine, catecholamines, disorders of metal ion transportation and electrolytes
5) detoxification problems resulting from toxic exposure to most common environmental toxins such as pesticides, heavy metals, xenotoxins and difficulties in detoxifying of endotoxins like ammonia, arabinitol, propionic acid etc.
6) chronic infection of bacterial and viral origin, streptococcal, retroviral and others
7) genetic and epigenetic abnormalities

All the disorders mentioned above affect children with autism spectrum disorders to a different extent. Proper diagnosis followed by targeted treatment and supplementation in conjunction with diet and rehabilitation may lead to improvement in functioning.

Methods most commonly proposed in an ASD treatment are as follows:

1) gluten and casein free diet
2) treatment of inflammation of gastrointestinal tract
3) antioxidants
4) supplementation to remedy food deficiencies
5) treatment of disordered metabolic pathways
6) immunomodulatory treatment
7) detoxification/removal of toxic exposure
8) treatment of chronic infections and inflammation

Conclusions

Autism as a disease affects profoundly the functioning of patients and their families, resulting in irreversible social impairment and dramatic dysfunction. Each case of autism requires profound medical insight in order to diagnose possible metabolic, infectious or immune disease or toxic exposure, in order to better identify the underlying cause and implement early medical intervention. This should lead to an improvement in functioning of affected children and help them to obtain the highest possible grade of independence.

Prevalence and Functional Analysis of Self Injurious Behaviours in Autism: Underlying Clinical and Pain Issues - Implications for Behaviour Management Strategies

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Abstract:

Background: Challenging behaviour (CB) constitutes the prime reason for temporary and permanent exclusion of individuals with an Autism Spectrum Disorder (ASD). It causes major barriers to effective education and social development. Importantly, CB constitutes one of the most obvious hallmarks of a developmental difficulty, often a first sign of concern raised by parents and a red flag for autism. Currently there are very few reports that address the issues of prevalence of CB in autism.
Aims: To investigate the prevalence and nature of challenging and self injurious behaviours (SIB) in ASD. Sample: Sixty families of ASD children, age ranging from 2-17 with an average age of 8 years old, took part in a semi-quantitative parental survey. Forty six children had a diagnosis of Autism (77%), 4 had a diagnosis of PDD-NOS (Pervasive Development Disorder Not Otherwise Specified, 7%), 7 had a diagnosis of Asperger's Syndrome (12%), one had a diagnosis of Tourette Disorder (1.5%), one had Cerebral Palsy (1.5%), two had a diagnosis of ADHD (3%). There were 45 boys and 15 girls making a sex ratio of 3:1. The children's developmental histories indicated that on average 60% of the children developed regressive autism after a period of normal development.
Methods: A parental questionnaire was designed to cover areas of development, clinical and behavioural presentation. Three case studies were conducted on some of these children presenting with the most severe chronic SIB. A behavioural functional analysis and assessment of pain based on the Non-Communicative Children's Pain Checklist-Postoperative Version (NCCPC-PV) were carried out. Medical investigation by enteroscopy and biopsy were conducted in hospital environment for 2 of these children. Laboratory testing was conducted in NHS and private laboratories to survey possible immune and inflammatory abnormalities and base line metabolic and neurotransmitter levels.
Results: It was found that 60% of the group of children sampled displayed CB (aggression to others and property, sudden outbursts of behaviour) and 51% displayed SIB. The SIBs that were reported included hand biting, hitting arms, hitting face, head banging, scratching, poking and stabbing, banging chest, throwing self on floor/ walls and pulling hair. The case studies revealed that the occurrence of SIB correlated with expression of pain. Clinical investigations of these three children combined with a functional behavioural analysis indicated that inflammatory gastro-intestinal deregulations were the most likely cause of their pain and self injurious behaviour.
Discussion: These findings bear important implications for the management of SIB in autism. It is paramount to recognize that some of the most challenging behaviours seen in autism can be caused by undiagnosed and untreated underlying medical and physiological deregulations.

Serotonergic Disturbance in Autism

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Abstract

Objective: The etiology and pathogenesis of autistic spectrum disorders (ASD) are still unknown. In ASDs patients abnormal levels of neurotransmitters have been observed, including gamma-aminobutyric acid, opiates, glutamine acid and catecholamines. One of the theory indicate dysregulation of serotonergic system. Platelet hyperserotonemia has been detected in 25-60% of autistic children. Although serotonin is a neurotransmitter of the nervous system it can also be found extraneuronally in blood platelets and the intestinal mucous membrane cells. 5-HT is synthesized in neurons and enterochromaffin cells of the intestinal mucosa (1-2% of the whole body 5-HT is present in the CNS whereas 95% in the gastrointestinal tract). Over the last years, attention has been paid to higher incidence of gastrointestinal (GI) problems in people with impaired development, mainly ASD, compared to the population of healthy children

Aims was to asses frequency of GI problems and compare the expression of serotonin receptor 5-HT_{2A} in autistic and non autistic group - platelet mRNA receptor 5- HT_{2A} were analyzed. In a subgroup of patients with gastrointestinal problems the upper gastrointestinal tract endoscopy was performed and additionally the expression of 5-HT_{2A} serotonin receptor in duodenum were assessed. The results were statistically processed.

Results: Statistically significant differences between examined and control group has been proven in gastrointestinal problems. Greater concentration of platelet mRNA 5-HT_{2A} receptor in examined group was assessed. Intrinsic autistic group analysis did not show any difference in serotonin profile.

Conclusions: Gastrointestinal disorders occur more frequently in autistic patients at the developmental age than in their non-autistic peers. Significantly increased platelet level of 5-HT_{2A} mRNA in examined group suggest serotonin system dysregulation at the molecular level. The question about any coincidence between serotonin disturbance and GI problems is still open.

Vaccination-Conspiracy of Silence or Collective Hysteria?

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Abstract:

The parents of the children diagnosed with autism expect the doctors to answer the question: why at certain point in their healthy growing children there was a sudden appearance of this disorder? For many years, the hypothesis that vaccinations may be triggering the symptoms of autism has been a reoccurring subject, provoking serious controversies and continuous discussions. Parents facing various contradictory information about vaccination may ask themselves a question, whether their child should be vaccinated. The growing number of parents fears that the vaccination may cause such disorders as autism, hyperactivity, developmental delay, attention deficit disorder, diabetes or SIDS.

It is no longer questioned, that since making vaccinations generally available, the incidence of the potentially fatal illnesses, such as measles or diphtheria, or illnesses causing serious complications resulting in permanent damages, has significantly decreased. Therefore the opinion is often expressed, that the vaccinations have changed medicine and the world.
Before vaccines, the US parents could expect that every year:
- Polio would paralyze 10.000 children
- Rubella could cause birth defects and mental retardation In as many as 20.000 newborns,
- Measles would infect about 4 million children, killing 3.000,
-A bacterium called *Haemophilus influenzae* type b (Hib) could cause meningitis in 15.000 children, leaving many with permanent brain damage.
(The information given above were taken from the article published by Vaccine Education Center- Children's Hospital of Philadelphia).

It has been estimated, that currently the vaccinations in the period of the first two years protect children from 16 illnesses preventing 14 million illnesses and 33 thousand deaths per year. (The information given by Anne Schuchat- the director at CDC′s National Center for Immunization and Respiratory Diseases). Therefore, the rationale for further protection of the children and other people from the risk of falling ill seems obvious

Yet again, if in our work we continue to meet parents, who inform us that after immunization their children changed their behaviour in the way, which suggests the development of autism symptoms, our belief in lack of connection between the vaccination and autism might be temporarily questioned. This is my personal experience. In our practice, while meeting the autistic children we want to know how to help, how to protect and how not to harm. This is our dilemma and an obligation of every conscientious physician.

In my presentation, I would like to introduce the subjective opinions of the group of 40 parents of autistic children, who participate in our clinical study, on the subject of correlation between the vaccinations and the appearance of autism symptoms in their children. We can be yet again divided by their opinions. The first group would say that it is the collective hysteria, caused by the suggestions made in media. The second group would claim that the vaccination is the cause of autism in their children. Such antagonistic attitudes are not new for medical sciences and prove, that the scientific investigations of this problem must continue to be carried out to gain further knowledge. The example of actions and scientific research of John Poling, a neurologist and father of an autistic girl, shows, that it is necessary

to search for further solutions without rising prejudiced and antagonistic attitudes, bearing in mind that every treatment brings both risk and benefits.

Role of Glutamate Receptors and Calcium Imbalance in Thimerosal Neurotoxicity: in vitro study

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Abstract:

Neurotoxic effects of thimerosal have been usually ascribed to its ability to oxidize –SH groups, leading to glutathione depletion and oxidative stress, to interference with NGF signal transduction, or to activation of mitochondrial and JNK signaling pathways of apoptosis. However apart from these putative mechanisms, one should also consider a known calcium releasing potential of thimerosal, that may significantly alter the activity and signal transduction in glutamate receptors and influence mitochondrial potential. Due to affinity of thimerosal to sulfhydryl groups, it may potentiate activity of IP3 and/or ryanodine receptors, and inhibit Ca^{2+} entry through NMDA receptors and VOCCs. However the exact role of NMDA receptors (NMDA-Rs) and group I metabotropic glutamate receptors (mGluRs GI) in thimerosal neurotoxicity remains obscure.

The aim of present study was to evaluate the role of calcium imbalance and excitotoxicity mediated by glutamate receptors, as well as mitochondrial pathology in the neurotoxic effects of thimerosal, considering also the effect of proteins and sulfur containing amino acids present in the incubation medium. In all these experiments primary cultures of rat cerebellar granule cells were used. Neurotoxicity was induced in acute approach by 10 min incubation with 5 and 15 μM thimerosal, or subchronically, by 48 h exposure to this compound at submicromolar concentrations. Neuronal survival was evaluated with propidium iodide staining. Changes in the intracellular concentrations were assessed using fluo-3 fluorescent calcium probe and confocal microscope, moreover ^{45}Ca uptake was measured. Changes in the mitochondrial potential were detected using rhodamine 123 fluorescent probe.

Our results demonstrated acute and chronic neurotoxicity of thimerosal. Acute exposition of the cells to thimerosal did not induce ^{45}Ca uptake, and thimerosal inhibited glutamate-evoked radioactive calcium influx, indicating that this compound may inhibit activation of NMDA receptor channels. Nevertheless, NMDA channel blockers, as well as mGluRs GI antagonists and heparine induced partial neuroprotection. Thimerosal induced significant increases in the intracellular calcium concentrations, comparable to effects of established calcium releaser thapsigargin. Effects of both these compounds were inhibited by bastadin in the presence of ryanodine, whereas ryanodine alone given at high micromolar concentration and FK-506 were inactive. Partial inhibition of calcium release by heparine and mGluRs GI receptor antagonists point to enhanced signaling via IP3 receptor pathway. Our results did not demonstrate any significant effect of 25 μM thimerosal alone on swelling and membrane potential in isolated brain mitochondria, or on their calcium-evoked changes, whereas in cultured neurons thimerosal induced a rapid drop in mitochondrial membrane potential sensitive to heparine and antagonists of mGluRs GI, probably reflecting redistribution to mitochondria of Ca^{2+} released from the intracellular stores.

To sum up, our results suggest that thimerosal-induced calcium imbalance and dysfunction of glutamate receptor signaling may play a significant role in its neurotoxicity.

The exact mechanisms of responses to thimerasol, involving interplay between intracellular calcium channels and mGluRs GI as well as NMDA-Rs, possibly via PSD proteins, require further investigations.

Vaccine Preservative, Thimerosal, Causes Wide-Spread Neurodevelopmental Disturbances in Young Rats

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Abstract

Autism Spectrum Disorders is a group of neurodevelopmental disorders/diseases, which affect ever increasing number of children and adults world-wide. Currently 1 child in 150 (in some estimates 1 in 60) is affected with autism, while in 1970 it was 1 child in 2000. Thimerosal (ethyl(2-mercaptobenzoato-(2-)-O,S), an organomercury compound containing approximately 49% of mercury by weight, which was (and still is) commonly used as vaccine preservative, is one of the main agents suspected to be responsible for current autism epidemics. Thimerosal, like other mercury compounds, is neurotoxic. It is metabolized in the body to other organic (ethyl-mercury) and inorganic mercury compounds, which accumulate in the brain and in other organs, and impair their function.

In this study, we examined the potential neurotoxic effects of thimerosal, which was administered to rat pups i.m. on postnatal days 7, 9, 11, 14 in four equal doses, mimicking infants' immunization scheme. We monitored mercury distribution to different organs, general animal development, conducted several behavioral tests and examined the brains for neuropathological changes. The following behavioral tests were chosen to monitor alterations of rats' behaviour in the context of behaviors observed in Autism Spectrum Disorders: motor activity in the open filed, pain reaction and pain sensitivity (hot plate), social interactions, learning and memory (water maze). Brain histopathological observations (H&E and immunohistochemistry – GFAP, neurofilaments, synaptophysins) were carried out as well.

Mercury from postnatally administered thimerosal accumulated in several organs and remained there in large amounts for at least 30 days. Kidneys accumulated the largest amounts of mercury; 1 to 14 days after thimerosal injections they contained 3,5 to 4 times more mercury/kg, than the originally injected amount (calculated per body/tissue weight). The liver also contained large amounts of mercury at least for 14 days after thimerosal injection. The brain contained 13-18 % of the amount of mercury originally injected i.m., calculated per tissue/body weight. Mercury remained in the brain in significant amounts at least for 30 days after thimerosal injection.

The animals exposed postnatally to thimerosal had noticeably impaired locomotor activity. They were significantly slower in the open field and in water maze, and exhibited more anxiety than control rats. They had markedly impaired pain reactions, measured in hot plate test and their social interactions were disturbed.

The brain weights of thimerosal injected rats were significantly reduced and there were wide spread morphological and pathological changes in several brain regions, particularly in the cerebral cortex, striatum, amygdale, hippocampus and the cerebellum.

The multiple behavioral and neuropathological changes observed in young rats exposed postnatally to thimerosal confirm that this vaccine preservative is neurotoxic to the developing mammalian organisms. As such it could be responsible, in part, for the brain and other organs damage in children, exposed to it in many vaccines.

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