Vaccines and Autism: Is there a link?

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Abstract
There has been a worldwide increase in autism cases in the past few decades, but the cause of it is unclear. It has been suggested that vaccines may be contributing to the rise in autism rates. One claim is that the MMR vaccine can cause intestinal inflammation that may lead non-permeable peptides to be transferred to the brain where it will affect neurodevelopment. This may lead to autism with symptoms of developmental regression and gastrointestinal problems. Another major hypothesis that has received much attention is that a mercury-containing compound, thimerosal, found in many vaccines, can have toxic effects on the central nervous system. By retrieving studies from databases such as Ebsco, Proquest, and Pubmed found in the Touro College Library, this review investigates if there is any truth to these claims. No evidence of a direct link between vaccines and an increase in autism cases have been found.

Introduction
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Introduction
Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that impairs a child's ability to interact and communicate with others. It is commonly associated with certain behaviors such as difficulty making conversation, delayed language acquisition, and poor motor skills. Autism seems to originate from very early brain development. The most obvious symptoms of the disorder, however, usually begin to show between the ages of 2 and 3. (Autism Speaks, 2016) Autism diagnoses have greatly increased in the past few decades. According to statistics from the U.S. Centers for Disease Control and Prevention, the prevalence of autism in 1000 children was approximately 6.7 in the year 2000 and 14.7 in 2010, a significant increase. (Data & Statistics, 2015).The cause for this dramatic increase is unknown and has been the subject of much investigation. It is believed that genes play a role in an increasing risk for autism (Mascarelli, 2010). However, environmental factors play a part in most cases of autism too. There has been a growing concern of a possible link between vaccines and autism. Two separate theories have been proposed over the years. One is that the Measles-Mumps-Rubella (MMR) vaccine causes autism. The other is that thimerosal, a mercury containing preservative found in many vaccines can lead to damage in the brain. Researchers have sought to discover if there is any truth to these claims.

Methods
Information and research was obtained through databases such as Ebsco, Proquest, and Pubmed. Access was provided by the Touro College Library. Google Scholar was also used to find research articles. Keywords like vaccines, autism, and thimerosal were used to search for relevant material. In addition, references in these articles were retrieved and used as additional sources for further research.

Discussion
MMR Vaccine
In 1968 a link was suggested between the Mumps, Measles, and Rubella (MMR) vaccine and the onset of ASD. Unusual bowel symptoms were described among 12 children who showed developmental regression like losing acquired skills despite previous normal progress. Eight out of the twelve children who had gastrointestinal signs had reported their first symptoms of autism within a month of receiving the MMR immunization. It was concluded that the MMR vaccine caused intestinal inflammation allowing usually non-permeable peptides to be translocated to the bloodstream and ultimately to the brain, where they affected development. (Wakefield, et al. 1998) Although the sample was small with only a dozen children and the results were never replicated, the study received lots of attention from the public, and served as the foundation for much controversy in the years to come. Parent's anecdotes of their own personal experiences were enough for many to keep this alive. As a result, many refused to vaccinate their children worrying about their safety, and outbreaks of vaccine preventable diseases began reappearing in certain areas. The MMR-autism controversy was responsible for a significant decrease in immunizations following that year. The MMR immunization rates in the United Kingdom dropped from 90% in 1988, when they were first introduced, to 80% in 2004, after the article had been read by the public. (Kolodziejski, 2014)

Possible Developmental Regression and Gastrointestinal Symptoms Associated with MMR
Whether MMR is really associated with autism has been under constant debate. There have been many studies done to see if the link exists. Fombonne and Chakrabarti (2001) tested out

the hypothesis that a form of autism existed involving developmental regression and gastrointestinal symptoms caused by the MMR vaccine. It was proposed that if one or more of the following predictions were proved by the data collected, the hypothesis could be validated. The first prediction was that childhood disintegrative disorder (CDD) had become more common. Another is that the average age of first parental concern in autistic children in those who received the MMR vaccine is closer to the mean age of immunization than in those who were not vaccinated with MMR. The third prediction was that developmental regression in those who are vaccinated with MMR had become more frequent. If the age of onset of autism with regression is closer to MMR-vaccination as opposed to those who did have autism without regression, it could also prove that MMR could have caused autism. Another prediction is that those with regressive autism have different symptoms. Finally, those with regressive autism would have gastrointestinal signs and/or inflammatory bowel disorder.

Three samples, 1 epidemiological (n=96) and 2 clinical samples, a pre-MMR (n=68) and a post-MMR (n=98) were used to gather information. In order to assess age of first onset of autistic signs, the parents were asked how old their child was when they first became concerned with his/her development. Regression was noted when a loss of skill, such as language was confirmed based on certain criteria. Assessment of bowel symptoms was done by retrieving data from both the parents and pediatrician.

The first prediction of childhood disintegrative disorder (CDD) increasing was not supported by the data as only one boy met the criterion for CDD, which seems likely to have originated from brain pathology before the MMR immunization was even given. In this epidemiological sample where nearly all the children were vaccinated, it can be assumed that CDD is not increased with vaccine exposure. Second, there was no difference in age of first parental concern in two of the samples exposed to MMR (19.3 and 19.2) compared to the pre-MMR clinical sample (19.5). Third, the rate of regression for the post-MMR sample (15.6%) was lower than the rate in the pre-MMR sample (18.4%). This rules out MMR-induced regressive autism as a cause for the dramatic increase in autism cases. In the epidemiologic sample, 18.8% had gastrointestinal symptoms. Constipation was the most common symptom (9.4%), and no inflammatory bowel disorder was reported. Only 2.1% of the sample experienced both developmental regression and gastrointestinal symptoms, a rate which shows no association between the two. None of the 6 predictions were supported in this study, and no evidence was found to show a distinct syndrome of MMR-induced autism. (Fombonne E, Chakrabarti S, 2001).

Measles Virus RNA in Patients with Autism

There are studies that have reported Measles Virus (MV) RNA in bowel biopsies in autistic children, showing a possible link between intestinal inflammation and the measles virus. A study done by Kawashima et al (2000), examined children with gastrointestinal problems to see if they have the measles virus and if they did, if it derived from wild strains or vaccine strains. Eight of the patients had Crohn's disease, 3 had ulcerative colitis, and 9 had autistic enterocolitis. One of the patients with Crohn's disease, 1 with ulcerative colitis, and 3 of 9 with autism were positive for the virus, while the controls were all negative. The measles virus found in the patient with Crohn's disease proved to have characteristics of wild-strain virus, while the one with ulcerative colitis and in the autistic patients had vaccine strains.

A study including 125 autistic children and 92 control children. MMR antibodies were first measured by ELISA in sera of 24 randomly selected autistic children, 16 normal children, and 14 children with other developmental problems. Autistic children had a higher number of MMR antibodies compared to the other children. Soon after all of the 217 children were checked for MMR antibodies by immunoblotting assay for serum screening. They found that 75 (n=125) autistic children's sera were positive for an unusual MMR antibody, whereas none of the control sera had the antibody. A protein band was detected in the antibody which was immunopositive for measles HA protein but not for measles nucleoprotein and rubella or mumps viral proteins. The results showed that autistic sera detected measles HA protein in the MMR antibody. It is suggested that an inappropriate antibody response to MMR might be related to the development of autism. (Singh, et al, 2002)

However, despite those few studies, many studies have been done that disprove the link between autism and MMR including a few that failed to detect MV-RNA in cases of autism. A case control study tested for the presence of measles virus (MV) RNA in bowel tissue in children with ASD. The purpose was to see if those with GI disturbances and autism are more likely to have MV RNA in their bowel tissue than those with GI symptoms but no autism. This can determine if MMR is linked to this type of autism. The ileal and cecal tissues of 25 children with GI disturbances and autism and 13 children with GI disturbances but no autism were analyzed for MV RNA in 3 different laboratories. The timing of the autistic and gastrointestinal symptoms in respect to MMR immunization was also documented. The results showed no difference in MV RNA findings in the case group and the control group. The timing of the vaccine in regards to the GI symptoms and autism onset were inconsistent with the theory that MMR triggers either the GI symptoms or autism. (Hornig, et al, 2008)

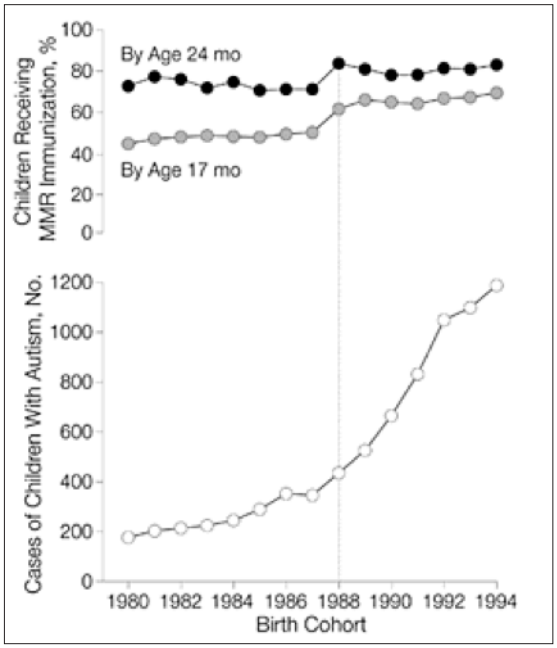
A 14 year prospective study reviewed the number of vaccines that were given from the time The National Board of Health and National Public Health Institute launched their MMR vaccination program in 1982 till the year 1996. 3 million vaccines were given during that period of time and 31 cases of gastrointestinal symptoms were reported after vaccination, ranging from 20 hours to 15 days. Fifty five percent (n=17) had symptoms of diarrhea and vomiting, 23% (n=7) had gingivostomatitis, 16% (n=5) had vomiting only, and (n=2) had abdominal pains. The symptoms usually lasted about a week. None of the children developed autism. In this study, no association was found between MMR and pervasive developmental disorder or inflammatory bowel disease. (Peltola et al, 1998)

Epidemiological Studies

Numerous epidemiologic studies have been done to see if there is an association between MMR and autism. Taylor, et al (1999) did a chart review of cases of autism diagnosed in a region in England, in children born between 1979-1992. They identified 498 cases of ASDs in the population, of which only 293 could be confirmed according to ICD-10 criteria. They analyzed the data in different ways to test if autism was related to the MMR vaccination. Data they collected included the age at which the children were diagnosed, the age of first parental concern, and age when regression became obvious. The trend of autism was examined to see whether or not there had been a sudden step-up in autism diagnoses in children who received the MMR vaccine after it was introduced in England in 1988. They found that the prevalence rates of autism began an exponential rise starting with children born a couple of years before the introduction of the MMR vaccine, and that there had been no sudden step-up after 1988. They concluded that this refuted a temporal relationship.

A study done in California collected data regarding MMR coverage rates and age at the time of immunization for children born between the years 1980-1994 from school immunization records in California Kindergartens. The number of cases of autism diagnosed during those years were retrieved from the California Department of Developmental Services where they were enrolled. The results did not show a correlation between rates of autism and number of immunizations given. As can be seen by Figure 1, autism cases increased from 44 cases per 100,000 live births in the 1980 cohort to 208 cases per 100,000 live birth in the 1994 cohort, a 393% increase. In contrast, MMR immunization rates by the age of 24 months increased from 72% to 82%, only a 10% increase. Since the rate of increasing autism cases does not compare with the only small rise in MMR coverage, a correlation was not observed between the two. (Dales, et al, 2001)

Figure 1



Percentage of Children Receiving Measles-Mumps-Rubella (MMR) Immunization in Second Year of Life and Caseload of Children With Autism, by Year of Birth, California, 1980-1994 (Dales, et al, 2001)

A population study was done in Japan by Honda, et al (2005). It examined incidence of ASD in children born from 1988-1996. Japan's MMR immunization program was launched in 1989 but ended in 1993, due to suspected side effects of the mumps vaccine. This allowed for an opportunity to research the effect of removing the MMR vaccine which was believed to cause a rise in autism. If it was really the cause of the increased autism caseloads when it was introduced, autism would drop after the risk factor (MMR vaccine) was withdrawn. All children who had been diagnosed with ASD were selected from a patient list of the YRC Developmental Psychiatry Unit, which offers diagnostic and intervention services to all those with ASD. The annual trends for both typical autism and all other categories of ASD were examined. According to the statistics, MMR vaccination rates were 69.8%, 42.9%, 33.6%, 24.0%, and 1.8% respectively in the years 1989-1993. As can be seen by this data, the rate decreased significantly during these years, with only a bare minimum of 1.8% of children vaccinated with MMR in the year 1993. The annual trends of ASD were compiled for the years 1988-1996. The ASD incidence rates ranged from 47.6 per 10000 in 1988 to 117.2 per 10000 in those that were born in 1996. The rate of autism incidences continued to rise even after the MMR vaccination program was terminated. This provides evidence that it is highly unlikely that MMR is linked to greater autism incidences. (Table 1) (Honda, et al, 2005)

Table 1

Number and cumulative incidence up to age seven of ASD with developmental regression and total ASD for each year from 1988 to 1996

Year of birth	Birth cohort	ASD with regression: Definite only N	ASD with regression: Definite only Incidence per 10,000 (95% CI)	ASD with regression: Definite + probable N	ASD with regression: Definite + probable Incidence per 10,000 (95% CI)	All ASD N	All ASD Incidence per 10000 (95% CI)
1988	3571	4	11.2 (.2–22.2)	4	11.2 (.2–22.2)	17	47.6 (25.0–70.2)
1989	3246	5	15.4 (1.9–28.9)	5	15.4 (1.9–28.9)	17	52.4 (27.5–77.2)
1990	3492	9	25.8 (9.0–42.6)	10	28.6 (10.9–46.4)	30	85.9 (55.3–116.5)
1991	3763	5	13.3 (1.6–24.9)	8	21.3 (6.5–36.0)	21	55.8 (32.0–79.6)
1992	3632	6	16.5 (3.3–29.7)	8	22.0 (6.8–37.3)	23	63.3 (37.5–89.1)
1993	3618	6	16.6 (3.3–29.8)	8	22.1 (6.8–37.4)	35	96.7 (64.8–128.6)
1994	3905	16	41.0 (20.9–61.0)	16	41.0 (20.9–61.0)	63	161.3 (121.8–200.8)
1995	3128	4	12.8 (.3–25.3)	5	16.0 (2.0–30.0)	36	115.1 (77.7–152.5)
1996	3071	5	16.3 (2.0–30.5)	8	26.1 (8.0–44.1)	36	117.2 (79.2–155.3)
Total	31426	60	19.1 (14.3–23.9)	72	22.9 (17.6–28.2)	278	88.5 (78.1–98.8)

Thimerosal

Since the 1930s, thimerosal, a mercury-containing preservative has been used in many biological and drug products, including multi-dose vaccines, to prevent bacterial and fungal contamination Thimerosal is not found in live vaccines, such as MMR because of the damaging interaction they can have with the active substance. Before 1991, diphtheria-tetanus-pertussis (DTaP) vaccination was the only common vaccine that contained thimerosal. Recently though, more vaccines have been introduced that consist of thimerosal like Hepatitis B and HIB. (Nelson, Bauman, 2003) Too much mercury can have toxic effects especially in little children, where the brain is still developing. As can be seen by Table 2, the FDA estimated that 6-month old babies could have received doses of mercury as high as 187.5 µg in their vaccines and 2 year olds as much as 237.5 µg. (Freed, et al, 2002)

Table 2

Vaccines	1999 Maximum Mercury Dose (µg)	2004 Maximum Mercury Dose (µg)
3 doses of DTaP[†]	75.0	<0.9
3 doses of Hep B[‡]	37.5	<1.5
3 doses of HIB	75.0	0
TOTAL	**187.5**	**<2.4**
Estimated Exposure to Mercury from Vaccines in 1999 and in 2004 (< 2 years of age)		
Vaccines	1999 Maximum Mercury Dose (µg)	2004 Maximum Mercury Dose (µg)
4 doses of DTaP[†]	100	<1.2
3 doses of Hep B	37.5	<1.5
4 doses of HIB	100	0
3 doses of influenza[*]	[**][37.5]	[**]37.5
TOTAL	**237.5 [275]**	**< 40.2**

Because of the increasing amount of this chemical that babies were being exposed to, there was a growing concern that the ethylmercury which is found in thimerosal can cause brain damage and contribute to autism. Fearing this, the FDA removed thimerosal from all vaccines in 1999 even though direct evidence of harm was not found. Since not much was not known about ethylmercury at that point in time, assumptions were made based on knowledge of methylmercury. Methylmercury was known to have toxic effects and many assumed that ethylmercury has similar consequences. Since ethylmercury had not been extensively studied, researchers began to experiment with ethylmercury to see if it can really have those damaging effects in vaccines. (Straton, 2001)

Research was done by analyzing the VAERS database, a database maintained by the CDC which holds a record of all adverse reactions. The VAERS database was used to compare the neurodevelopmental disorders that were found following the administration of thimerosal-containing DTaP vaccines in contrast to thimerosal-free DTaP vaccines. A close linear correlation was found between increasing mercury due to thimerosal vaccines and an increase in the odds ratio of neurodevelopmental disorders. According to the results in the baseline year of 1984, the odds ratio of autism increased by 0.029 per mg of mercury, personality disorders by 0.012 per mg of mercury, and mental retardation by 0.048 per mg of mercury. The total odds of developing autism increased in those immunized with thimerosal-containing vaccines vs those who received thimerosal-free vaccines. This study showed that more research had to be done to see if there is indeed a correlation between mercury levels and higher risks of autism and other developmental disorders. (Geier et al, 2003)

A study done used hair and urine analysis to detect heavy metal exposure in those with autism compared to those who did not have autism. It consisted of 25 autistic children and 25 controls. Metal testing was performed via ICP-MS spectroscopy utilizing cell technique to detect levels of different metals in the hair. The mean mercury level in the hair of autistic children was 0.47±0.42 while the levels in the control children was a lower mean of 0.30±0.3. A similar observation was found of the mercury levels in the urine of autistic children compared to control children, with means of 2.48±2, and 1.10±0, respectively. These results seem to show an association between higher levels of mercury in those with autism. Limitations in the amount of mercury they ingest seems to be important for the safety of these children. However, a larger sample size should be studied on in order to validate these findings. (Blaurock-Busch, 2011)

A study was done by Pichichero et al, (2002) to measure the concentration of mercury found in infants' stool, blood, and urine after they received vaccines. If high levels were found, it would show that thimerosal can be potentially harmful in vaccines. In this experiment, 40 infants who were 6 months or younger received thimerosal containing vaccines while 21 controls received thimerosal free vaccines. Samples of the infants' stool, blood, and urine were obtained 3-28 days after and were

tested for mercury levels. Blood samples contained low levels of mercury with a range of 4.50-20.55 nmol/L. Fourteen out of 15 controls did not have quantifiable levels of mercury. Those with the highest levels of mercury were infants who were measured soon after they were vaccinated. There was no mercury found in urine samples, besides for one of the 2-month olds and three of the 6-month olds who had received thimerosal in their vaccines. The highest amount of mercury in the urine was 6.45 nmol/L. No mercury was found in any of the control infants. Detectable amounts of mercury were found in stool samples in those who were exposed to thimerosal containing vaccines. Those who did received thimerosal free vaccines were not measured for mercury levels in their stool. (Table 3)

Table 3

	Infants aged 2 months		Infants aged 6 months	
	Thiomersal-exposed (n=20)	Controls (n=11)	Thiomersal-exposed (n=20)	Controls (n=10)
Bodyweight (kg)				
Mean (range)	5·3 (4·0–6·4)	NR	8·1 (6·7–10·6)	NR
Total mercury exposure (μg)*				
Mean (range)	45·6 (37·5–62·5)	0	111·3 (87·5–175·0)	0
Blood mercury (nmol/L)				
Number of samples tested	17	8	16	7
Number with mercury in range	12	1	9	0
Mean (SD)†	8·20 (4·85)	4·90	5·15 (1·20)	..
Median (IQR)†	6·15 (4·60–10·85)	4·90	5·30 (4·55–6·10)	..
Range†	4·50–20·55	..	2·85–6·90	..
Urinary mercury (nmol/L)				
Number of samples tested	12	6	15	8
Number with mercury in range	1	0	3	0
Mean (SD)†	3·8‡	..	5·75 (1·05)	..
Median (range)†	3·8‡	..	6·2 (4·55–6·45)	..
Stool mercury (ng/g dry weight)				
Number of samples tested	12	NT	10	NT
Number with mercury in range	12	..	10	..
Mean (SD)†	81·8 (40·3)	..	58·3 (21·2)	..
Median (IQR)†	83·5 (47·0–121·3)	..	58·0 (42·0–68·5)	..
Range†	23·0–141·0	..	29·0–102·0	..

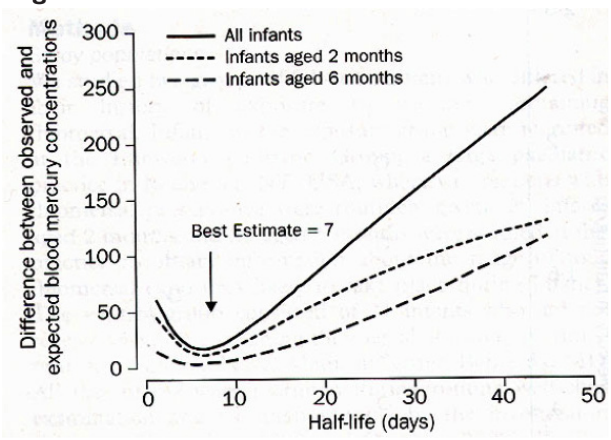
NR=Not recorded. NT=not tested. *Via vaccination. †All calculations done only with samples within range of accurate quantitation. ‡Only one value so SD and range are not applicable.

Concentrations of mercury in blood, urine, and stool of infants who received vaccines containing thiomersal and those who did not

To determine if dietary intake could contribute to mercury levels in the stool, samples were obtained from 9 infants who were age-matched to those who received thimerosal containing vaccines but were not exposed to thimerosal themselves. The mean levels of mercury in these samples was 22 ng/g which was considerably lower than those exposed to thimerosal. Out of all these samples, however, no concentration exceeded 29 nmol/L which is known to be an accepted safe value. The results did show an increased amount of mercury in those who were vaccinated compared to those who did not receive thimerosal, but the quantity was still below the harmful level. Before the samples were measured, a prediction model was made of the expected measurements of mercury corresponding to the possible half-life days ranging from 1-45. The best estimate of the half-life of ethylmercury would be the difference between the predicted value and the observed value.

The concentration of mercury in the blood not long after vaccination suggests that the half-life of ethylmercury is not nearly as long as the half-life of methylmercury. As we can see from Figure 2, the estimated half-life for ethylmercury was 7 days. This contrasts with the half-life of around 40-50 days in methylmercury. The long half-life of methylmercury can allow the organic-mercury to cross over the blood brain barrier where it

Figure 2



can accumulate and get converted to inorganic mercury which can cause neurodevelopmental damage. Ethylmercury, however, which is found in thimerosal is rapidly eliminated through the stool which prevents toxicity from accumulating that could be detrimental to parts of the body including the brain. (Pichichero, et al, 2002)

Since creating controlled experiments is not possible in an existing vaccination program, determining if there is an association between thimerosal and autism is not so simple. Several epidemiological studies have been done to see if there is a causal relationship between receiving thimerosal containing vaccines and an increase in autism cases. A population cohort study of children in Denmark who were born in the years 1990-1996 was done to compare children who received thimerosal in their vaccines and those who did not. Doses that were administered before 1992 were considered to be vaccines containing thimerosal and those doses given after 1992 were thimerosal free vaccines. Information regarding vaccine administrations was obtained from the Danish Board of Health and data regarding autism diagnoses was retrieved from the Danish Psychiatric Central Register. Follow ups were done from one year of age till the year 2000 to see if there would be possible cases of autism disorders in those children. During these years, 440 cases of autism and 787 cases of other autistic-spectrum disorders were diagnosed among those children (table 4).

Table 4

Table. Rate Ratio of Autism and Other Autistic-Spectrum Disorders Comparing Children Vaccinated With a Thimerosal-Containing Vaccine to Children Vaccinated With a Thimerosal-Free Formulation of the Same Vaccine

		Autism			Other Autistic-Spectrum Disorders		
	Person-Years at Risk	No. of Cases	RR (95% CI)*	RR (95% CI)†	No. of Cases	RR (95% CI)*	RR (95% CI)†
Vaccinations							
All thimerosal-free	1 660 159	303	1.00	1.00	430	1.00	1.00
Any containing thimerosal	1 220 006	104	0.85 (0.60-1.20)	0.85 (0.60-1.20)	321	1.12 (0.88-1.43)	1.12 (0.88-1.43)
Doses of thimerosal-containing vaccine							
None	1 660 159	303	1.00	1.00	430	1.00	1.00
1 dose (25 μg eHg)	189 920	18	0.99 (0.59-1.68)	1.01 (0.60-1.71)	40	0.96 (0.67-1.39)	0.95 (0.66-1.37)
2 doses (75 μg eHg)	447 973	33	0.71 (0.46-1.09)	0.70 (0.46-1.09)	130	1.20 (0.92-1.56)	1.20 (0.92-1.56)
3 doses (125 μg eHg)	602 113	53	0.96 (0.63-1.46)	0.96 (0.63-1.47)	151	1.11 (0.83-1.48)	1.13 (0.84-1.51)
Trend (increase in RR per 25 μg eHg)			0.98 (0.90-1.06)	0.98 (0.90-1.06)		1.03 (0.97-1.09)	1.03 (0.98-1.09)

Abbreviations: CI, confidence interval; eHg, ethylmercury; RR, rate ratio.
*Adjusted for confounders: age and calendar period.
†Fully adjusted: age, calendar period, child's sex, child's place of birth, birth weight, 5-minute Apgar score, gestational age, mother's age at birth of child, and mother's country of birth.

We can see from the results shown in table 4, that when comparing those who received at least one dose of thimerosal-containing vaccine and those who only received thimerosal-free vaccinations there was a rate ratio of 0.85% for autism and 1.12% for other autistic spectrum disorders. Also, there was no association between a higher dose of thimerosal-containing vaccine and a higher rate of autism disorders. The increase in rate ratio per 25 ug of mercury was 0.98% in autism and 1.03% in other autistic spectrum disorders. In order to rule out the possibility that some thimerosal-containing vaccines were administered soon after 1992, the vaccinations between June and December of 1992 were omitted from the data and similar results were found. This study showed no association between thimerosal intake and increased autism rates. (Hviid, et al, 2003)

In the United Kingdom, the only thimerosal containing vaccines that have been administered in the past few decades is DTaP and DT. The total amount of thimerosal per dose in these vaccines is 50 ug (25 ug of ethylmercury). In the United Kingdom, the schedule for vaccination called for 3 doses by the age of 4 months, totaling 150 ug of thimerosal at that age. Data regarding date of birth and vaccination dates were obtained for 109,863 children who were born from 1988 to 1997. Some children were excluded from the study including those who had certain medical conditions before the age of 6 months and those who had received the Hep B or flu vaccination before 6 months of age. Hg exposure was calculated based on the number of vaccine doses the children received. A number of developmental disorders were investigated and the number of cases diagnosed, the mean age of diagnoses, and the percentage that was male was assessed. When these children were linked to the dates of their vaccination and any of the neurodevelopmental disorders they had, no evidence of increasing neurodevelopmental disorder rate was found with an increasing dose of ethylmercury. The only disorder that showed a possible link to thimerosal was tics, which had a hazard rate of 1.50 in 4 months of age. The rest of the disorders had a Hazard rate close to 1, showing no link to thimerosal. (Andrews, et al, 2004)

Another study was done in Sweden and Denmark to compare the prevalence of autism cases with the exposure of thimerosal-containing vaccines during the 1980s and 1990s. Data regarding vaccine coverage and autism cases were collected in these countries. The total amount of ethylmercury exposure was calculated by multiplying the amount of thimerosal in vaccines by the number of vaccines with thimerosal administered during that time period. The rate of autism was calculated by dividing the total number of autism cases diagnosed in those years by the number of person-years accumulated during those years.

As shown in figure 3a, the incidences of autism in Sweden began

Figure 3a

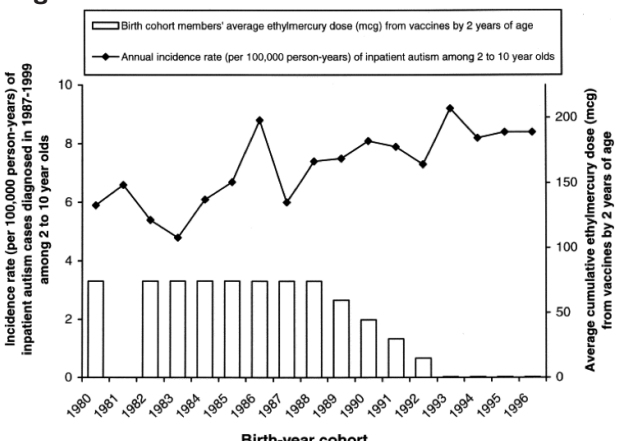
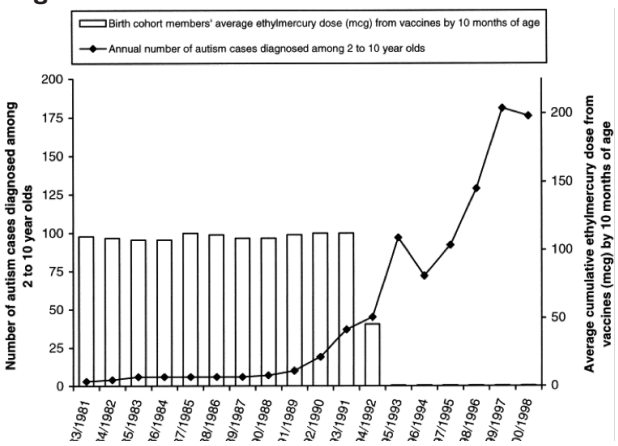


Figure 3b



to rise in the year 1985 to a rate of around 6 per 100,000 person-years and peaked in the year 1993 to a rate of 9.2 per 100,000 person-years. The coverage of thimerosal-containing vaccines, however, have remained steady over most of those years, decreasing over time and eventually being completely removed in 1993. A similar explanation goes for Denmark, shown in figure 3b. Thimerosal-containing vaccination coverage remained constant throughout the years 1981-1991 and ended in 1992, but autism rates continued to increase sharply in the years after that. We can see from these studies that the rise of autism needs a better explanation than the exposure of thimerosal to children.

Conclusion

From the studies that have been done so far, no evidence has been found to show a link between vaccines and autism. Increasing autism rates need to have another explanation. It has been suggested that the broadening of the diagnosis, and the greater awareness of autism and other ASDs have contributed to more diagnoses of autism. The claim that MMR is associated

with a regressive form of autism has been proven to be highly unlikely. The fact that MMR vaccination withdrawal did not lead to a decrease in autism cases indicated that there is not any correlation between the two. The concern that thimerosal-containing vaccines cause autism has also not been validated. However, despite the shorter half-life and less damage that ethylmercury can have in comparison to other mercury compounds like methylmercury, the current literature does not rule out a role for thimerosal in neurodevelopmental damage other than autism to children. Therefore, it is best that thimerosal continue to remain excluded from vaccines.

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