Vaccine Studies: Examine the Evidence

The safety and efficacy of vaccines are under constant study and scrutiny. Since vaccines are designed to be given routinely during well child care visits, they must be extraordinarily safe. Safety testing begins as soon as a new vaccine is contemplated and continues until it is licensed and indefinitely after licensure. The Committee on Infectious Diseases of the American Academy of Pediatrics works closely with the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention to make recommendations for vaccine use.

Over the past decade, questions have been raised regarding a relationship between autism and vaccines, specifically the measles, mumps, rubella combination vaccine (MMR) and the preservative thimerosal, which while not present in MMR, was present in several vaccines used in the 1990s. In 1999, vaccine manufacturers began to remove thimerosal from their products. Currently thimerosal is present some of the inactivated influenza vaccines. The concerns regarding vaccine safety have received a great deal of attention by parents, doctors, vaccine manufacturers and the media. Dozens of studies have been performed in the United States and elsewhere. The purpose of this document is to list those studies and provide links to the publications to allow parents and all those who administer or recommend vaccines to read the evidence for themselves. The studies provided have been published in peer-reviewed medical journals. This is not an exhaustive list and it will need to be updated frequently since vaccine safety studies are ongoing.

It is not surprising that these studies do not show any link between vaccines and autism. Natural measles virus causes a respiratory infection but can cause infection of the brain and subsequent brain damage; however, autism has not been reported as a complication of wild measles. The measles vaccine is a weakened strain of the wild measles virus. Thimerosal is a mercury-containing preservative which does not stay in the body. Mercury itself can cause brain damage when present in excessive amounts. The amount and type of mercury in vaccines was not enough to cause damage.

Please examine the evidence for yourself.

Studies looking at measles, mumps and rubella (MMR) vaccine

**Lack of Association between Measles Virus Vaccine and Autism with Enteropathy: A Case-Control Study**

Researchers looked for measles virus in the guts of 25 children with both autism and gastrointestinal disorders, and another 13 children with the same gastrointestinal disorders but no autism. The virus was detected in one child from each group.

AUTHOR CONCLUSION: This study provides strong evidence against association of autism with persistent measles virus RNA in the gastrointestinal tract or with measles, mumps and rubella (MMR) vaccine exposure.

**Measles Vaccination and Antibody Response in Autism Spectrum Disorders**
Baird G et al., *Archives of Disease in Childhood* 2008; 93(10):832-7

Case-control study of 98 vaccinated children aged 10-12 years in the UK with autism spectrum disorder (ASD) and two control groups of similar age: 52 children with special educational needs but no ASD and 90 children in the typically developing group. No difference was found between cases and controls for
measles antibody response. There was no dose-response relationship between autism symptoms and antibody concentrations.

AUTHOR CONCLUSION: No association between measles vaccination and ASD was shown.

**MMR-Vaccine and Regression in Autism Spectrum Disorders: Negative Results Presented from Japan**  

Study of 904 patients with Autism Spectrum Disorders (ASD). During the period of measles, mumps and rubella vaccine (MMR) usage, no significant difference was found in the incidence of regression between MMR-vaccinated children and non-vaccinated children. Among the proportion and incidence of regression across the three MMR-program-related periods (before, during and after MMR usage), no significant difference was found between those who had received MMR and those who had not. Moreover, the incidence of regression did not change significantly across the three periods.

AUTHOR CONCLUSION: The data do not support an association between MMR and autism.

**No Evidence of Persisting Measles Virus in Peripheral Blood Mononuclear Cells from Children with Autism Spectrum Disorder**  
D’Souza Y et al. *Pediatrics* 2006; 118(4):1664-75

Peripheral blood mononuclear cells were isolated from 54 children with Autism Spectrum Disorders (ASD) and 34 developmentally normal children, and up to 4 real-time polymerase chain reaction assays and 2 nested polymerase chain reaction assays were performed. No sample from either ASD or control groups was found to contain nucleic acids from any measles virus gene. In the nested polymerase chain reaction and in-house assays, none of the samples yielded positive results. Furthermore, there was no difference in anti-measles antibody titers between the autism and control groups.

AUTHOR CONCLUSION: There is no evidence of measles virus persistence in the peripheral blood mononuclear cells of children with ASD.

**Immunizations and Autism: A Review of the Literature**  

Literature review found very few studies supporting an association between vaccines and autism, with the overwhelming majority showing no causal association between the measles, mumps and rubella (MMR) vaccine and autism. The vaccine preservative thimerosal has alternatively been hypothesized to have a possible causal role in autism. No convincing evidence was found to support an association between the vaccine preservative thimerosal and autism, nor for the use of chelation therapy in autism.

AUTHOR CONCLUSION: With decreasing uptake of immunizations in children and the inevitable occurrence of measles outbreaks, it is important that clinicians be aware of the literature concerning vaccinations and autism so that they may have informed discussions with parents and caregivers.

**Pervasive Developmental Disorders in Montreal and Quebec, Canada: Prevalence and Links with Immunizations**  

Study of thimerosal and measles, mumps and rubella (MMR) vaccine uptake in 28,000 Canadian children born between 1987 and 1998, of whom 180 were identified with a pervasive developmental disorder.
AUTHOR CONCLUSION: The data rule out an association between pervasive developmental disorder and either high levels of ethyl mercury exposure comparable with those experienced in the United States in the 1990s or 1- or 2-dose MMR vaccinations.

*Is there a ‘regressive phenotype’ of Autism Spectrum Disorder associated with the measles-mumps-rubella vaccine? A CPEA Study*  

A multi-site study of 351 children with Autism Spectrum Disorders (ASD) and 31 typically developing children used caregiver interviews to describe the children's early acquisition and loss of social-communication milestones. For the majority of children with ASD who had experienced a regression, pre-loss development was clearly atypical.

AUTHOR CONCLUSION: No evidence that onset of autistic symptoms or of regression was related to measles, mumps and rubella vaccination.

*Relationship between MMR Vaccine and Autism*  

Ten articles that specifically evaluated the possible relationship between the measles, mumps and rubella (MMR) vaccine and autism were identified. Review articles, commentaries, and evaluations of a link between gastrointestinal symptoms in autistic children and MMR immunization were excluded.

AUTHOR CONCLUSION: Based upon the current literature, it appears that there is no relationship between MMR vaccination and the development of autism.

*Immunization Safety Review: Vaccines and Autism*  
Institute of Medicine, The National Academies Press: 2004

The IOM's Committee on Immunization Safety Review was convened in the fall of 2000 to provide an independent review of increasingly prominent vaccine safety concerns. The 15 committee members with expertise in pediatrics, internal medicine, immunology, neurology, infectious diseases, epidemiology, biostatistics, public health, risk perception, decision analysis, nursing, genetics, ethics and health communications analyzed over 200 relevant studies.

AUTHOR CONCLUSION: The committee rejected a causal relationship between the MMR vaccine and autism as well as a causal relationship between thimerosal-containing vaccines and autism.

*No effect of MMR withdrawal on the incidence of autism: a total population study*  

Study examined incidence of Autism Spectrum Disorders (ASD) to age 7 for children born between 1988 and 1996 in Yokohama, Japan. The measles, mumps and rubella (MMR) vaccination rate in Yokohama declined significantly in the birth cohorts of years 1988-92, and no MMR vaccines were administered in 1993 or thereafter. In contrast, cumulative incidence of ASD up to age 7 increased significantly in the birth cohorts of years 1988 through 1996 and most notably rose dramatically beginning with the birth cohort of 1993.

AUTHOR CONCLUSION: MMR vaccination is not likely to be a main cause of ASD, and cannot explain the rise over time in the incidence of ASD. Withdrawal of MMR in countries where it is still being used cannot be expected to lead to a reduction in the incidence of ASD.
**No evidence for links between autism, MMR and measles virus**


AUTHOR CONCLUSION: No increased risk of autism was found following exposures to wild measles and vaccinations with monovalent measles, and Urabe or Jeryl-Lynn variants of measles, mumps and rubella (MMR) vaccine.

**Age at First Measles-Mumps-Rubella Vaccination in Children with Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta**
DeStefano F et al. *Pediatrics* 2004; 113(2): 259-66

Study compared ages at first measles, mumps and rubella (MMR) vaccination between children with autism and children who did not have autism in the total population and in selected subgroups, including children with regression in development.

AUTHOR CONCLUSION: Similar proportions of case and control children were vaccinated by the recommended age or shortly after (i.e., before 18 months) and before the age by which atypical development is usually recognized in children with autism (i.e., 24 months).

**MMR Vaccination and Pervasive Developmental Disorders: A Case-Control Study**

Matched case-control of 1,295 people born in 1973 or later who had first recorded diagnosis of pervasive developmental disorder while registered with a contributing general practice between 1987 and 2001. Controls (4,469) were matched on age, sex and general practice. 1,010 cases (78.1%) had measles, mumps and rubella (MMR) vaccination recorded before diagnosis, compared with 3,671 controls (82.1%) before the age at which their matched case was diagnosed.

AUTHOR CONCLUSION: Data suggest that MMR vaccination is not associated with an increased risk of pervasive developmental disorders.

**Prevalence of Autism and Parentally Reported Triggers in a North East London Population**
Lingam R et al. *Archives of Disease in Childhood.* 2003; 88(8):666-70

Study of reported age of onset of Autism Spectrum Disorder (ASD) among 567 children in northeast London born between 1979 and 1998. The age at diagnosis of ASD was estimated to have decreased per five-year period since 1983, by 8.7% for childhood autism and by 11.0% for atypical autism. There was some evidence that measles, mumps and rubella (MMR) vaccine was more likely to be mentioned as a trigger after August 1997 than before.

AUTHOR CONCLUSION: The data suggest that a rise in autism prevalence was likely due to factors such as increased recognition, a greater willingness on the part of educators and families to accept the diagnostic label, and better recording systems. The proportion of parents attributing their child's autism to MMR appears to have increased since August 1997.

**A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism**

Compared relative risk of Autism Spectrum Disorder (ASD) in children vaccinated with measles, mumps and rubella (MMR) vaccine and unvaccinated children born in Denmark between 1991 and 1998. Of the
537,303 children in the cohort, 82% had received the MMR vaccine. Researchers identified 316 children with a diagnosis of autism and 422 with a diagnosis of other ASDs. There was no association between the age at the time of vaccination, the time since vaccination, or the date of vaccination and the development of autism.

AUTHOR CONCLUSION: This study provides strong evidence against the hypothesis that MMR vaccination causes autism.

**Neurologic Disorders after Measles-Mumps-Rubella Vaccination**

1- to 7-year-old children who were vaccinated between November 1982 and June 1986 in Finland.

AUTHOR CONCLUSION: Data do not support an association between measles, mumps and rubella (MMR) vaccination and encephalitis, aseptic meningitis or autism.

**Relation of Childhood Gastrointestinal Disorders to Autism: Nested Case Control Study Using Data from the UK General Practice Research Database**
Black C et al. *British Medical Journal*. 2002; 325:419-21

Nested case control study of 96 children diagnosed with autism and 449 controls. The estimated odds ratio for a history of gastrointestinal disorders among children with autism compared with children without autism was 1.0 (95% confidence interval 0.5 to 2.2).

AUTHOR CONCLUSION: No evidence was found that children with autism were more likely than children without autism to have had defined gastrointestinal disorders at any time before their diagnosis of autism.

**Measles, Mumps, and Rubella Vaccination and Bowel Problems or Developmental Regression in Children with Autism: Population Study**

Population study of 278 children with core autism and 195 with atypical autism, born between 1979 and 1998. The proportion of children with developmental regression (25% overall) or bowel symptoms (17%) did not change significantly during the 20 years from 1979, a period which included the introduction of measles, mumps and rubella (MMR) vaccination in October 1988.

AUTHOR CONCLUSION: Data provide no support for an MMR associated “new variant” form of autism with developmental regression and bowel problems, and further evidence against involvement of MMR vaccine in the initiation of autism.

**No Evidence for a New Variant of Measles-Mumps-Rubella-Induced Autism**

Study compared 96 children with a pervasive developmental disorder (PDD) born between 1992 and 1995 and who had received the measles, mumps and rubella (MMR) vaccine, to PDD patients who did not receive MMR.

AUTHOR CONCLUSION: No evidence was found to support a distinct syndrome of MMR-induced autism or of “autistic enterocolitis.” These results add to the large-scale epidemiologic studies that all failed to support an association between MMR and autism at population level. These findings do not argue for changes in current immunization programs and recommendations.
Measles-Mumps-Rubella and Other Measles-Containing Vaccines Do Not Increase the Risk for Inflammatory Bowel Disease: A Case-Control Study from the Vaccine Safety Datalink Project

A case control study of 155 persons with inflammatory bowel disease with up to five controls each. Neither past vaccination nor age at vaccination with other MCV was associated with increased risk for Crohn’s disease, ulcerative colitis, or IBD. Risk for Crohn’s disease, ulcerative colitis, or IBD was not elevated in the time immediately following vaccination with either vaccine.

AUTHOR CONCLUSION: Vaccination with MMR or other MCV, or the timing of vaccination early in life, did not increase the risk for IBD.

Time Trends in Autism and in MMR Immunization Coverage in California

Scientists looked for correlation between increases in the rate of autism diagnoses and increases in the rate of measles, mumps and rubella (MMR) vaccination in children born between 1980 and 1994.

AUTHOR CONCLUSION: These data do not suggest an association between MMR immunization among young children and an increase in autism occurrence.

MMR and autism: further evidence against a causal association

Data from an earlier measles, mumps and rubella (MMR) vaccine study (Taylor et al, 2000) were reanalyzed to test a second hypothesis.

AUTHOR CONCLUSION: Results provide further evidence against a causal association between MMR vaccination and autism.

Mumps, Measles, and Rubella Vaccine and the Incidence of Autism Recorded by General Practitioners: A Time Trend Analysis

Study compared prevalence of measles, mumps and rubella (MMR) vaccination among children in the United Kingdom to rising prevalence of autism diagnoses for children.

AUTHOR CONCLUSION: The data provide evidence that no correlation exists between the prevalence of MMR vaccination and the rapid increase in the risk of autism over time.

Further Evidence of the Absence of Measles Virus Genome Sequence in Full Thickness Intestinal Specimens from Patients with Crohn’s Disease

Study of specimens of macroscopically inflamed and normal intestine along with mesenteric lymph nodes from patients with Crohn’s disease. None of the samples examined gave any evidence of the persistence of measles virus in the intestine of Crohn’s disease patients.

AUTHOR CONCLUSION: The study supports previous findings produced by this laboratory and others using highly sensitive measles virus specific PCR diagnostic technology.
Absence of Detectable Measles Virus Genome Sequence in Inflammatory Bowel Disease Tissues and Peripheral Blood Lymphocytes

Study looked for measles virus in 93 colonoscopic biopsies and 31 peripheral blood lymphocyte preparations, examined and obtained from patients with inflammatory bowel disease (IBD) and noninflammatory controls.

AUTHOR CONCLUSION: Measles virus was not detected using this method.

Autism and Measles, Mumps, and Rubella Vaccine: No Epidemiological Evidence for a Causal Association

Researchers looked for a change in trend in incidence or age at diagnosis associated with the introduction of measles, mumps and rubella (MMR) vaccination to the United Kingdom in 1988. The study identified 498 cases of autism (261 of core autism, 166 of atypical autism, and 71 of Asperger syndrome) in children born in the UK since 1979. There was a steady increase in cases by year of birth with no sudden "step-up" or change in the trend line after the introduction of MMR vaccination. There was no difference in age at diagnosis between the cases vaccinated before or after 18 months of age and those never vaccinated. There was no temporal association between onset of autism within 1 or 2 years after vaccination with MMR. Developmental regression was not clustered in the months after vaccination.

AUTHOR CONCLUSION: Data do not support a causal association between MMR vaccine and autism. If such an association occurs, it is so rare that it could not be identified in this large regional sample.

No Evidence for Measles, Mumps, and Rubella Vaccine-Associated Inflammatory Bowel Disease or Autism in a 14-year Prospective Study

Prospective study of 3 million adverse events in temporal relation to MMR vaccine. A form was filled and posted to the data collectors, followed by another form with further information 2-3 weeks later. Researchers traced subjects who developed gastrointestinal symptoms or signs lasting 24 hours or more at any time after MMR vaccination (apart from within the first hour). Researchers also checked hospital and health center records or interviewed the local public-health nurses.

AUTHOR CONCLUSION: Over a decade’s effort to detect all severe adverse events associated with MMR vaccine could find no data supporting the hypothesis that it would cause pervasive developmental disorder or inflammatory bowel disease.

Exposure to Measles in Utero and Crohn’s Disease: Danish Register Study

Investigators identified 472 women aged 15 to 43 years who had been admitted with measles between 1915 and 1966. Thirty-three were pregnant: 11 developed measles during the first trimester, 9 during the second, 6 during the third, and 9 had exanthema less than 14 days after delivery. Of the 26 offspring identified (including one set of twins), four died, one in infancy. The diagnoses of the other three, who died as adults, did not suggest inflammatory bowel disease. Among individuals still alive (median age 51.4 (36-79) years) none were registered as having Crohn’s disease or inflammatory bowel disease.

AUTHOR CONCLUSION: Exposure to measles in utero does not seem to be strongly associated with the development of Crohn’s disease later in life.
On Feb. 12, 2009, the “vaccine court” ruled in three test cases on the theory that MMR vaccine and the vaccine preservative thimerosal are linked to autism. The court found the scientific evidence is overwhelmingly contrary to this theory.

Studies looking at thimerosal

Continuing increases in autism reported to California's developmental services system: mercury in retrograde

Study analyzed autism client data from the California Department of Developmental Services between 1995 and 2007. Even though thimerosal was absent from scheduled childhood vaccines after 2002, cases of autism continued to climb quarter by quarter.

AUTHOR CONCLUSION: The California DDS data do not show any recent decrease in autism in California despite the exclusion of more than trace levels of thimerosal from nearly all childhood vaccines. The data do not support the hypothesis that exposure to thimerosal during childhood is a primary cause of autism.

Mercury Levels in Newborns and Infants After Receipt of Thimerosal-Containing Vaccines

Study assessed blood mercury levels of 216 healthy children prior to immunization with thimerosal-containing vaccines, and 12 hours to 30 days after. The blood mercury half-life was calculated to be 3.7 days and returned to prevaccination levels by day 30.

AUTHOR CONCLUSION: The blood half-life of intramuscular ethyl mercury from thimerosal in vaccines in infants is substantially shorter than that of oral methyl mercury in adults. Increased mercury levels were detected in stools after vaccination, suggesting that the gastrointestinal tract is involved in ethyl mercury elimination. Because of the differing pharmacokinetics of ethyl and methyl mercury, exposure guidelines based on oral methyl mercury in adults may not be accurate for risk assessments in children who receive thimerosal-containing vaccines.

Early Thimerosal Exposure and Neuropsychological Outcomes at 7 to 10 Years

Study compared early exposure to thimerosal-containing vaccines to 42 neuropsychological outcomes in 1,047 children between the ages of 7 and 10 years. Exposure to mercury from thimerosal was determined from computerized immunization records, medical records, personal immunization records and parent interviews.

AUTHOR CONCLUSION: The study does not support a causal association between early exposure to mercury from thimerosal-containing vaccines and immune globulins and deficits in neuropsychological functioning at the age of 7 to 10 years.

Pervasive Developmental Disorders in Montreal, Quebec, Canada: Prevalence and Links With Immunizations
Quantified thimerosal and measles, mumps rubella (MMR) vaccine uptake in 28,000 Canadian children born between 1987 and 1998, of whom 180 were identified with a pervasive developmental disorder.

AUTHOR CONCLUSION: The data rule out an association between pervasive developmental disorder and either high levels of ethyl mercury exposure comparable with those experienced in the United States in the 1990s or 1- or 2-dose measles-mumps-rubella vaccinations.

**Immunization Safety Review: Vaccines and Autism**
Institute of Medicine, The National Academies Press: 2004

The IOM's Committee on Immunization Safety Review was convened in the fall of 2000 to provide an independent review of increasingly prominent vaccine safety concerns. The 15 committee members with expertise in pediatrics, internal medicine, immunology, neurology, infectious diseases, epidemiology, biostatistics, public health, risk perception, decision analysis, nursing, genetics, ethics and health communications analyzed over 200 relevant studies.

AUTHOR CONCLUSION: The committee rejected a causal relationship between the MMR vaccine and autism as well as a causal relationship between thimerosal-containing vaccines and autism.

**Thimerosal Exposure in Infants and Developmental Disorders: A Retrospective Cohort Study in the United Kingdom Does Not Support a Causal Association**

Study analyzed thimerosal exposure and possible development delays in 109,863 children born in the United Kingdom from 1988-97. Exposure was defined according to the number of DTP/DT doses received by 3 and 4 months of age and also the cumulative age-specific DTP/DT exposure by 6 months.

AUTHOR CONCLUSION: With the possible exception of tics, there was no evidence that thimerosal exposure via DTP/DT vaccines causes neurodevelopmental disorders.

**Autism and thimerosal-containing vaccines: Lack of consistent evidence for an association**

Study compared the prevalence/incidence of autism in California, Sweden and Denmark from the mid-80s to the late 90s with average exposures to thimerosal-containing vaccines. In all three countries, the incidence and prevalence of Autism Spectrum Disorders began to rise in the 1985-1989 period, and the rate of increase accelerated in the early 1990s.

AUTHOR CONCLUSION: The data is not consistent with the hypothesis that increased exposure to thimerosal-containing vaccines is responsible for the apparent increase in the rates of autism in young children being observed worldwide.

**Thimerosal and the Occurrence of Autism: Negative Ecological Evidence From Danish Population-Based Data**

Analyzed data from the Danish Psychiatric Central Research Register recording all psychiatric admissions since 1971, and all outpatient contacts in psychiatric departments in Denmark since 1995. There was no trend toward an increase in the incidence of autism during that period when thimerosal was used in Denmark, up through 1990. From 1991 until 2000 the incidence increased and continued to rise after the removal of thimerosal from vaccines, including increases among children born after the discontinuation of thimerosal.
AUTHOR CONCLUSION: The discontinuation of thimerosal-containing vaccines in Denmark in 1992 was followed by an increase in the incidence of autism. The data do not support a correlation between thimerosal-containing vaccines and the incidence of autism.

**Association Between Thimerosal-Containing Vaccine and Autism**
Hviid et al., *Journal of the American Medical Association*, 2003; 290(13):1763-6

Study of 467,000 children born in Denmark between 1990 and 1996 compared children who were vaccinated with a thimerosal-containing vaccine to children who received a thimerosal-free formulation of the same vaccine. The risk of autism and other autism spectrum disorders did not differ significantly between children vaccinated with thimerosal-containing vaccine and children vaccinated with thimerosal-free vaccine.

AUTHOR CONCLUSION: The results do not support a causal relationship between childhood vaccination with thimerosal-containing vaccines and development of autistic-spectrum disorders.

**Thimerosal Exposure in Infants and Developmental Disorders: A Prospective Cohort Study in the United Kingdom Does Not Support a Causal Association**

The researchers monitored the thimerosal exposure of more than 14,000 children born in the United Kingdom between 1991 and 1992. The age at which doses of thimerosal-containing vaccines were administered was recorded, and measures of mercury exposure by 3, 4 and 6 months of age were calculated and compared with a number of measures of childhood cognitive and behavioral development covering the period from 6 to 91 months of age.

AUTHOR CONCLUSION: No convincing evidence was found that early exposure to thimerosal had any deleterious effect on neurologic or psychological outcome.