

## Scientific Studies on MMR and Autism

Publication	Study	Lead Researcher	Objective	Method/Design	Conclusion*	Funding
<i>Pediatrics</i> October 2001	No Evidence for a New Variant of Measles-Mumps-Rubella-Induced Autism	Eric Fombonne, FRCPsych	If "autistic enterocolitis" had some validity, then 1 or several of the following 6 predictions should be supported by empirical data: 1) childhood disintegrative disorder has become more frequent, 2) the mean age of first parental concern for autistic children who are exposed to MMR is closer to the mean immunization age than in children who are not exposed to MMR, 3) regression in the development of children with autism has become more common in MMR-vaccinated children, 4) the age of onset for autistic children with regression clusters around the MMR immunization date and is different from that of autistic children without regression, 5) children with regressive autism have distinct symptom and severity profiles, and 6) regressive autism is associated with gastrointestinal symptoms and/or inflammatory bowel disorder.	Three samples were used. Epidemiologic data on 96 children (95 immunized with MMR at a median age of 13.5 months) who were born between 1992 and 1995 and had a pervasive developmental disorder diagnosis as reported in a recent UK survey (post-MMR sample) were compared with data from 2 previous clinical samples (1 pre-MMR [n = 98] and 1 post-MMR [n = 68]) of autistic patients. All patients were assessed with the standardized Autism Diagnostic Interview (ADI), allowing rigorous comparison of age at first parental concerns and rates of regression across samples. Reliability was excellent on ADI scores, age of parental concern, and developmental regression. Furthermore, data on bowel symptoms and disorders were available in the epidemiologic survey from both pediatric and parental sources, and immunization dates were obtained from computerized records.	No evidence was found to support a distinct syndrome of MMR-induced autism or of "autistic enterocolitis." These results add to the recent accumulation of large-scale epidemiologic studies that all failed to support an association between MMR and autism at population level. When combined, the current findings do not argue for changes in current immunization programs and recommendations.	
<i>Pediatrics</i> November 2002	Neurologic Disorders After Measles-Mumps-Rubella Vaccination	Annamari Makela, MD	The aim of this study was to assess whether an association prevails between MMR vaccination and encephalitis, aseptic meningitis, and autism.	A retrospective study based on linkage of individual MMR vaccination data with a hospital discharge register was conducted among 535,544 1- to 7-year-old children who were vaccinated between November 1982 and June 1986 in Finland. Changes in the overall number of hospitalizations for autism after vaccination throughout the study period were searched for. In addition, hospitalizations because of inflammatory bowel diseases were checked for the children with autism.	We did not identify any association between MMR vaccination and encephalitis, aseptic meningitis, or autism.	Partial funding from Merck

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<i>Archives of Pediatrics &amp; Adolescent Medicine</i> July 2003	Association of Autistic Spectrum Disorder and the Measles, Mumps, and Rubella Vaccine	Kumanan Wilson, MD, MSc, FRCP	To systematically review the evidence for and against the existence of an association between autistic spectrum disorder (ASD) and the measles, mumps, and rubella (MMR) vaccine.	A systematic review of the medical literature to identify all controlled epidemiological articles examining for an association between ASD and the MMR vaccine. Extracted data from the articles on the characteristics and objectives of the study as well as evidence of an association.	The current literature does not suggest an association between ASD and the MMR vaccine; however, limited epidemiological evidence exists to rule out a link between a rare variant form of ASD and the MMR vaccine. Given the real risks of not vaccinating and that the risks and existence of variant ASD remain theoretical, current policies should continue to advocate the use of the MMR vaccine.	Grant from the Canadian Institutes for Health Research, Ottawa, Ontario
<i>The Lancet</i> September 2004	MMR Vaccination and Pervasive Developmental Disorders: A Case-Control Study	Liam Smeeth, MRCP	To investigate whether MMR vaccination is associated with an increased risk of autism or other pervasive developmental disorders.	Matched case-control study using the UK General Practice Research Database. Cases were 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 were matched on age, sex, and general practice.	Findings suggest that MMR vaccination is not associated with an increased risk of pervasive developmental disorders.	
<i>Pediatrics</i> July 2006	Pervasive Developmental Disorders in Montreal, Quebec, Canada: Prevalence and Links With Immunizations	Eric Fombonne, MD	The purpose of this work was to estimate the pervasive developmental disorder prevalence in Montreal, Canada, in cohorts born from 1987 to 1998 and evaluate the relationship of trends in pervasive developmental disorder rates with: (1) changes in cumulative exposure to ethylmercury (thimerosal) occurring through modifications in the immunization schedule of young children and (2) trends in measles-mumps-rubella vaccination use rates and the introduction of a 2-measles-mumps-rubella dosing schedule during the study period.	Surveyed 27749 children born from 1987 to 1998 attending 55 schools from the largest Anglophone school board. Children with pervasive developmental disorders were identified by a special needs team. The cumulative exposure by age 2 years to thimerosal was calculated for 1987-1998 birth cohorts. Ethylmercury exposure ranged from medium (100-125 microg) from 1987 to 1991 to high (200-225 microg) from 1992 to 1995 to nil from 1996 onwards when thimerosal was entirely discontinued. Measles-mumps-rubella coverage for each birth cohort was estimated through surveys of vaccination rates. The immunization schedule included a measles-mumps-rubella single dose at 12 months of age up to 1995, and a second measles-mumps-rubella dose at 18 months of age was added on after 1996.	The prevalence of pervasive developmental disorder in Montreal was high, increasing in recent birth cohorts as found in most countries. Factors accounting for the increase include a broadening of diagnostic concepts and criteria, increased awareness and, therefore, better identification of children with pervasive developmental disorders in communities and epidemiologic surveys, and improved access to services. The findings ruled out an association between pervasive developmental disorder and either high levels of ethylmercury exposure comparable with those experienced in the United States in the 1990s or 1- or 2-dose measles-mumps-rubella vaccinations.	Partially funded through the Canada Research Chair Canadian Institutes for Health Research

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<i>Archives of Disease in Childhood</i> February 2008	Measles Vaccination and Antibody Response in Autism Spectrum Disorders	Gillian Baird, F.R.C.Paed.	To test the hypothesis that measles vaccination was involved in the pathogenesis of ASD as evidenced by signs of a persistent measles infection or abnormally persistent immune response shown by circulating measles virus or raised antibody titres in MMR vaccinated children with ASD compared with controls.	A community sample of vaccinated children aged 10-12 years in the UK with ASD (N=98) and two control groups of similar age, one with special educational needs but no ASD (N=52) and one typically developing group (N=90), were tested for measles virus and antibody response to measles in serum.	No difference was found between cases and controls for measles antibody response. There was no dose response relationship between autism symptoms and antibody levels. There was no evidence of a differential response to measles virus or the measles component of the MMR in children with ASD, with or without regression, and controls who had either one or two doses of MMR. Only one child from the control group had clinical symptoms of a possible enterocolitis.	
<i>PLoS One</i> September 2008	Lack of Association Between Measles Virus Vaccine and Autism with Enteropathy: A Case-Control Study	Mady Hornig	The objective of this case-control study was to determine whether children with GI disturbances and autism are more likely than children with GI disturbances alone to have MV RNA and/or inflammation in bowel tissues and if autism and/or GI episode onset relate temporally to receipt of MMR.	The sample was an age-matched group of US children undergoing clinically-indicated ileocolonoscopy. Ileal and cecal tissues from 25 children with autism and GI disturbances and 13 children with GI disturbances alone (controls) were evaluated by real-time reverse transcription (RT)-PCR for presence of MV RNA in three laboratories blinded to diagnosis, including one wherein the original findings suggesting a link between MV and ASD were reported. The temporal order of onset of GI episodes and autism relative to timing of MMR administration was examined.	This study provides strong evidence against association of autism with persistent MV RNA in the GI tract or MMR exposure. Autism with GI disturbances is associated with elevated rates of regression in language or other skills and may represent an endophenotype distinct from other ASD.	CDC grant U50 CCU522351 to AAP and by National Institutes of Health awards AI57158 (Northeast Biodefense Center-Lipkin), HL083850, and NS47537

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