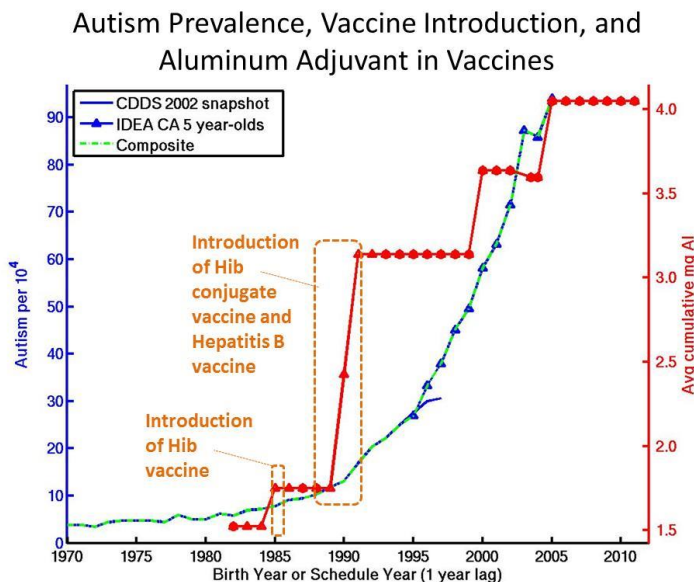




## Review of Epidemiological Studies on Hib & Hepatitis B Vaccines and Autism The Foundation For Pediatric Health, 4/30/2015

The Hib and Hepatitis B vaccines were introduced in 1985-1991. The phase-in of these vaccines in the subsequent years after introduction closely aligns with the rapid increase in autism prevalence, per this graph from *Nevison* [1]. It is hypothesized that the increase in abnormal immune activation in infancy from these two vaccines, potentially amplified by the increased use of aluminum adjuvant in vaccines [2], contributed to the autism epidemic. Have there been any epidemiological studies that have studied this question?



*Used with permission from author; vaccine introductions superimposed by Foundation For Pediatric Health*

The scientific approach to answer such a question is to compare autism rates in children who received the Hib or Hepatitis B vaccine series to children who did not receive the vaccines. Autism rates are not studied in pre-licensing studies for any vaccines, so the question is whether post-licensing epidemiological studies have investigated a possible link to autism with the Hib or Hepatitis B vaccines. The Foundation For Pediatric Health (FFPH) conducted a review of epidemiological studies to identify studies which meet these criteria for the Hepatitis B Vaccine (HBV) or Hib Conjugate Vaccine (HCV):

- As part of the study design, autism prevalence in children who received the HBV or HCV vaccine series as recommended by the CDC was compared to autism prevalence in children who did not receive any of the HBV or HCV vaccine series
- Study found a statistically significant association between the HBV or HCV vaccine series and autism, or resulted in a statistically significant finding of 'no association'

Studies referenced by the CDC website as well as other potentially relevant studies were reviewed. The review concluded that there are zero studies meeting these criteria which resulted in a finding of 'no association'. The review identified one independent study which found a 3x increased risk of autism associated with the HBV vaccine. In summary, there were no studies on the Hib Conjugate Vaccine and the only study which was performed found a link between the Hepatitis B vaccine and autism. The details of the review are included in the following tables.

Table 1a: Review of “Vaccines and Autism: A Summary of CDC Conducted or Sponsored Studies:” [3]

Study Citation and CDC Summary	FFPH Review: Does this meet criteria to study HBV or HCV for possible autism link?
<p>DeStefano F, Price CS, Weintraub ES. Increasing exposure to antibody-stimulating proteins and polysaccharides in vaccines is not associated with risk of autism. <i>J Pediatr.</i> 2013 Aug;163(2):561-7. Epub 2013 Mar 30.</p> <p>Per CDC [3]: This study looked at the number of antigens (substances in vaccines that cause the body’s immune system to produce disease-fighting antibodies) from vaccines during the first two years of life. Researchers compared children with ASD to children without ASD. The results showed that the total amount of antigen from vaccines received was the same between children with and without ASD.</p>	<p><b>No.</b> This study compared groups that received more or less antigens, primarily due to a change from the DPT to DTaP vaccine in the 1990s. Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Price CS, Thompson WW, Goodson B, Weintraub ES, Croen LA, et al. Prenatal and Infant Exposure to Thimerosal From Vaccines and Immunoglobulins and Risk of Autism. <i>Pediatrics.</i> Epub 2010 Sep 13.</p> <p>Per CDC [3]: Exposure to thimerosal, a vaccine preservative, has been said to be associated with the increased risk of ASD. This study compared children with ASD to those without, and looked at prenatal and infant exposure to thimerosal from vaccines. This study found no difference in exposure to thimerosal between children with and without ASD.</p>	<p><b>No.</b> This study compared groups that received more or less of one ingredient, thimerosal (a mercury-based preservative). Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Stehr-Green P, Tull P, Stellfeld M, Mortenson PB, Simpson D. Autism and thimerosal-containing vaccines: lack of consistent evidence for an association. <i>Am J Prev Med.</i> 2003 Aug;25(2):101-6.</p> <p>Per CDC [3]: In 1992, Denmark and Sweden stopped using thimerosal in vaccines. This study compared the rate of ASD in these countries before and after thimerosal was removed. In both countries, ASD rates increased between 1987 and 1999. If thimerosal exposure was related to ASD, one would expect that ASD rates would decrease after 1992 when children were no longer being exposed.</p>	<p><b>No.</b> This study compared groups that received more or less of one ingredient, thimerosal (a mercury-based preservative). Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Verstraeten T, Davis RL, DeStefano F, Lieu TA, Rhodes PH, et al. Safety of thimerosal-containing vaccines: a two-phased study of computerized health maintenance organization databases. <i>Pediatrics.</i> 2003 Nov;112(5):1039-48.</p> <p>Per CDC [3]: CDC used the Vaccine Safety Datalink (VSD) to look for possible links between thimerosal-containing vaccines and a variety of health problems. CDC and VSD researchers found statistically significant associations between thimerosal and language delays and tics. However, the associations were weak and were not consistent between study populations. The study found no link between thimerosal and ASD.</p>	<p><b>No.</b> This study compared groups that received more or less of one ingredient, thimerosal (a mercury-based preservative). Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Thompson WW, Price C, Goodson B, Shay DK, Benson P, et al. Early Thimerosal Exposure and Neuropsychological Outcomes at 7 to 10 Years. <i>N Engl J Med</i> 2007; 357:1281-1292.</p> <p>Per CDC [3]: This study measured neurodevelopmental disorders in children. The study found only a few statistically significant associations between exposure from thimerosal and neuropsychological functioning. Results of this study show no link between thimerosal-containing vaccines and neurodevelopmental disorders in children.</p>	<p><b>No.</b> This study compared groups that received more or less of one ingredient, thimerosal (a mercury-based preservative). Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>

Table 1b: Review of “Vaccines and Autism: A Summary of CDC Conducted or Sponsored Studies:” [3]

Study Citation and CDC Summary	FFPH Review: Does this meet criteria to study HBV or HCV for possible autism link?
<p>Tozzi AE, Bisiacchi P, Tarantino V, De Mei B, D'Elia L, et al. Neuropsychological Performance 10 Years After Immunization in Infancy With Thimerosal-Containing Vaccines. <i>Pediatrics</i> 2009;123(2):475 -482.</p> <p>Per CDC [3]: CDC funded this follow-up study in Italy that compared neuropsychological outcomes of children who were randomly assigned to receive one of two forms of diphtheria-tetanus-acellular pertussis vaccine (DTaP) in the first year of life: one containing thimerosal and the other containing 2-phenoxyethanol. Ten years after vaccination, the two groups were tested on 24 neuropsychological outcomes. This study adds to the body of scientific evidence that thimerosal in vaccines is not harmful to children.</p>	<p><b>No.</b> This study compared groups that received or did not receive one ingredient, thimerosal (a mercury-based preservative). Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Madsen KM, Hviid A, Vestergaard M, Schendel D, Wohlfahrt J, et al. A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism. <i>N Engl J Med</i> 2002; 347:1477-1482.</p> <p>Per CDC [3]: CDC has an ongoing cooperative agreement with the Danish Medical Research Council which supports a collaborative research program with Danish researchers and provides opportunities for CDC to study causes of developmental disabilities through Denmark's unique public health infrastructure. This study, which followed more than 500,000 children over 7 years, found no association between the MMR vaccine and ASD.</p>	<p><b>No.</b> This study compared the MMR vaccine and autism. Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>DeStefano F, Bhasin TK, Thompson WW, Yeargin-Allsopp M, Boyle C. Age at First Measles-Mumps-Rubella Vaccination in Children With Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta. <i>Pediatrics</i> 2004;113(2):259 -266</p> <p>Per CDC [3]: CDC conducted this study using data collected through the Metropolitan Atlanta Developmental Disabilities Surveillance Program. This study looked at MMR vaccination and ASD by comparing children who had been diagnosed with ASD to those who had not. The study included children vaccinated by the age of 18 months, 24 months, and 36 months. The findings revealed that vaccination between 24 and 36 months was slightly more common among children with ASD, and that association was strongest among children 3-5 years of age. This finding was most likely a result of immunization requirements for preschool special education program attendance in children with ASD. .</p>	<p><b>No.</b> This study compared the MMR vaccine and autism. Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Hornig M, Briese T, Buie T, Bauman ML, Lauwers G, et al. Lack of Association between Measles Virus Vaccine and Autism with Enteropathy: A Case-Control Study. <i>PLoS ONE</i> 2008; 3(9): e3140.</p> <p>Per CDC [3]: CDC supported a study to investigate the association between MMR vaccine, gastrointestinal tract (GI) disorders, and ASD. Researchers studied MMR vaccine timing and evaluated bowel tissue samples from 25 children with ASD and GI disorders and 13 children with GI disturbances alone, looking for a difference in the presence of measles vaccine virus in the samples between children with and without ASD. The study's results showed that MMR vaccine does not trigger or exacerbate GI disorders or ASD.</p>	<p><b>No.</b> This study compared the MMR vaccine and autism. Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Richler J, Luyster R, Risi S, Hsu WL, Dawson G. Is there a 'regressive phenotype' of Autism Spectrum Disorder associated with the measles-mumps-rubella vaccine? A CPEA Study. <i>J Autism Dev Disord.</i> 2006 Apr;36(3):299-316.</p> <p>Per CDC [3]: The National Institute of Child Health and Human Development (NICHD) and CDC collaborated to study regressive autism and measles-mumps-rubella (MMR) vaccination. This study used data from children with regressive autism and children without autism. The results showed no evidence of a link between regression in ASD and MMR vaccination.</p>	<p><b>No.</b> This study compared the MMR vaccine and autism. Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>

Table 2: Review of other studies referenced at the CDC “Vaccine Safety – Autism” website 4/30/2015 [4]

Study Citation and Summary	FFPH Review: Does this meet criteria to study HBV or HCV for possible autism link?
<p>IOM report, 2011: Adverse Effects of Vaccines: Evidence and Causality</p> <p>Per the study: The committee finds that evidence convincingly supports a causal relationship between some vaccines and some adverse events—such as MMR, varicella zoster, influenza, hepatitis B, meningococcal, and tetanus-containing vaccines linked to anaphylaxis. Additionally, evidence favors rejection of five vaccine-adverse event relationships, including MMR vaccine and autism and inactivated influenza vaccine and asthma episodes. However, for the majority of cases (135 vaccine-adverse event pairs), the evidence was inadequate to accept or reject a causal relationship.</p>	<p><b>No.</b> This study did not analyze HBV for a possible autism link. This study did not analyze HCV for links to any adverse events.</p>
<p>IOM review, 2004. Immunization Safety Review: Vaccines and Autism.</p> <p>Per the study: The committee concludes that the body of epidemiological evidence favors rejection of a causal relationship between the MMR vaccine and autism. The committee also concludes that the body of epidemiological evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism.</p>	<p><b>No.</b> This review addressed a possible autism link with one ingredient (thimerosal) and one vaccine (MMR). This review did not address a possible link between the HBV or HCV vaccines and autism.</p>
<p>Taylor LE, Swerdfeger AL, Eslick GD. Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies. <i>Vaccine</i>. 2014 June;32(29):3623–3629.</p> <p>This study is a meta-analysis of five cohort studies and five case-control studies on either MMR and thimerosal studies.</p>	<p><b>No.</b> This meta-analysis review of other studies addressed a possible autism link with one ingredient (thimerosal) and one vaccine (MMR). This review did not address a possible link between the HBV or HCV vaccines and autism.</p>
<p>Schechter R, Grether JK. Continuing increases in autism reported to California’s developmental services system: mercury in retrograde. <i>Arch Gen Psychiatry</i>. 2008;65:19-24.</p>	<p><b>No.</b> This study addressed a possible autism link with one ingredient (thimerosal). This review did not address a possible link between the HBV or HCV vaccines and autism.</p>
<p>Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. Association between thimerosal-containing vaccine and autism. <i>JAMA</i>. 2003;290:1763–6.</p>	<p><b>No.</b> This study addressed a possible autism link with one ingredient (thimerosal). This review did not address a possible link between the HBV or HCV vaccines and autism.</p>
<p>Ball L, Ball R, Pratt RD. An assessment of thimerosal in childhood vaccines. <i>Pediatrics</i>. 2001;107:1147–1154.</p>	<p><b>No.</b> This assessment addressed a possible autism link with one ingredient (thimerosal). This review did not address a possible link between the HBV or HCV vaccines and autism.</p>

**FFPH Review of whether research has studied HBV or HCV for a link to autism**  
**Table 3: Studies not referenced at the CDC “Vaccine Safety – Autism” website 4/30/2015 [4]**

Study Citation and Summary	FFPH Review: Does this meet criteria to study HBV or HCV for possible autism link?
<p>Kuwaik GA et al. Immunization uptake in younger siblings of children with autism spectrum disorder. <i>Autism</i>. 2014, Vol. 18(2) 148-155.</p> <p>Study design and procedures: Data were collected regarding diphtheria, pertussis, tetanus, and polio (DPTP) and MMR immunizations between 2005 and 2009.</p> <p>Study Results: One or more immunizations in 59/98 younger sibs were delayed (47/98; 48%) or declined (12/98; 12.2%); immunizations were delayed in 16/98 probands (16.3%) and declined in only one. All controls were fully immunized, with only 6 (9.2%) delayed. Within the "younger sibs" group, 25/98 received an autism spectrum disorder diagnosis; 7 of whom (28%) were fully immunized. The rates of autism spectrum disorder diagnosis did not differ between immunized and nonimmunized younger sib groups, although small sample size limits interpretability of this result.</p>	<p><b>No.</b> This study did not analyze the HBV or HCV vaccines, per the study design.</p>
<p>Jain A, Marshall J, Buikema A, Bancroft T, Kelly J, Newschaffer C. Autism occurrence by MMR vaccine status among US children with older siblings with and without autism. <i>JAMA</i>. April 21, 2015. Volume 313, Number 15.</p> <p>Study conclusion: receipt of the MMR vaccine was not associated with increased risk of ASD.</p>	<p><b>No.</b> This study compared the MMR vaccine and autism. Study did not compare autism rates in children who received vs did not receive the HBV or HCV vaccines.</p>
<p>Gallagher, C and Goodman M. Hepatitis B vaccination of male neonates and autism diagnosis, NHIS 1997-2002. <i>Journal of Toxicology and Environmental Health, Part A</i>, 73:1665–1677, 2010.</p> <p>Per the study: <b>Findings suggest that U.S. male neonates vaccinated with the hepatitis B vaccine prior to 1999 (from vaccination record) had a threefold higher risk for parental report of autism diagnosis compared to boys not vaccinated as neonates during that same time period.</b></p>	<p><b>Yes, and this study found a 3x increased risk of autism associated with the HBV.</b></p>

**References:**

- [1] Nevison, CD. A comparison of temporal trends in United States autism prevalence to trends in suspected environmental factors. *Environ Health*. 2014 Sep 5;13:73. doi: 10.1186/1476-069X-13-73.
- [2] Shoenfeld, Y. Autoimmune/inflammatory Syndrome Induced by Adjuvants (Schoenfeld’s syndrome): clinical and immunological spectrum. *Expert Rev. Clin. Immunol*. 9(4), 361–373 (2013).
- [3] Vaccines and Autism: A Summary of CDC Conducted or Sponsored Studies. [http://www.cdc.gov/vaccinesafety/00\\_pdf/CDCStudiesonVaccinesandAutism.pdf](http://www.cdc.gov/vaccinesafety/00_pdf/CDCStudiesonVaccinesandAutism.pdf)
- [4] CDC website, Vaccine Safety – Autism page, 4/30/20125. <http://www.cdc.gov/vaccinesafety/concerns/autism/>