

Q&A VACCINES AND AUTISM: WHAT YOU SHOULD KNOW

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Some parents are concerned that vaccines can cause autism. Their concerns center on three areas: the combination measles-mumps-rubella (MMR) vaccine; thimerosal, a mercury-containing preservative previously contained in several vaccines; and the notion that babies receive too many vaccines too soon.

Q. What are the symptoms of autism?

A. Symptoms of autism, which typically appear during the first few years of life, include difficulties with behavior, social skills and communication. Specifically, children with autism may have difficulty interacting socially with parents, siblings and other people; have difficulty with transitions and need routine; engage in repetitive behaviors such as hand flapping or rocking; display a preoccupation with activities or toys; and suffer a heightened sensitivity to noise and sounds. Autism spectrum disorders vary in the type and severity of the symptoms they cause, so two children with autism may not be affected in quite the same way.

Q. What causes autism?

A. The specific cause or causes of autism in all children are not known. But one thing is clear: Autism spectrum disorders are highly genetic. Researchers figured this out by studying twins. They found that when one identical twin had autism, the chance that the second twin had autism was greater than 90 percent. But when one fraternal twin had autism, the chance that the second twin had autism was less than 10 percent. Because identical twins have identical genes and fraternal twins don't, these studies proved the genetic basis of autism. Researchers have successfully identified some of the specific genes that cause autism.

Some parents wonder whether environmental factors — defined as anything other than genetic factors — can cause autism. It's possible. For example, researchers found that thalidomide, a sedative, can cause autism if used during early pregnancy. Also, if pregnant women are infected with the rubella virus (German measles) during early pregnancy, their babies are more likely to have autism.

Q. Does the MMR vaccine cause autism?

A. No. In 1998, a British researcher named Andrew Wakefield raised the notion that the MMR vaccine might cause autism. In the medical journal *The Lancet*, he reported the stories of eight children who developed autism and intestinal problems soon after receiving the MMR vaccine. To determine whether Wakefield's suspicion was correct, researchers performed a series of studies comparing hundreds of thousands of children who had received the MMR vaccine with hundreds of thousands who had never received the vaccine. They found that the risk of autism was the same in both groups. The MMR vaccine didn't cause autism.

Some parents wary of the safety of the MMR vaccine stopped getting their children immunized. As immunization rates dropped, particularly in the United Kingdom and, to some extent, the United States, outbreaks of measles and mumps led to hospitalizations and deaths that could have been prevented.

Q. Does thimerosal cause autism?

A. No. Multiple studies have shown that thimerosal in vaccines does not cause autism. Thimerosal is a mercury-containing preservative that was used in vaccines to prevent contamination. In 1999, professional groups called for thimerosal to be removed from vaccines as a precaution. Unfortunately, the precipitous removal of thimerosal from all but some multi-dose preparations of influenza vaccine scared some parents. Clinicians were also confused by the recommendation.

Since the removal of thimerosal, several studies have been performed to determine whether thimerosal causes autism. Hundreds of thousands of children who received thimerosal-containing vaccines were compared to hundreds of thousands of children who received the same vaccines free of thimerosal. The results were clear: The risk of autism was the same in both groups; thimerosal in vaccines did not cause autism.

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Q. Is autism caused by children receiving too many vaccines too soon?

A. Several facts make it very unlikely that babies are overwhelmed by too many vaccines given too early in life.

First, before they are licensed, new vaccines are always tested alone and in combination with existing vaccines. These studies determine whether new vaccines alter the safety and efficacy of existing vaccines and, conversely, whether existing vaccines affect the new vaccine. These studies, called concomitant use studies, are performed every time a new vaccine is added to the existing vaccination schedule.

Second, although the number of vaccines has increased dramatically during the past century, the number of immunological components in vaccines has actually decreased. One hundred years ago, children received just one vaccine, for smallpox. The smallpox vaccine contained about 200 immunological components. Today, with advances in protein purification and recombinant DNA technology, the 14 vaccines given to young children contain only about 150 immunological components.

Third, the immunological challenge from vaccines is minuscule compared to what babies typically encounter every day. The womb is sterile, containing no bacteria, viruses, parasites or fungi. But when babies leave the womb and enter the world, they are immediately colonized by trillions of bacteria that live on the linings of their nose, throat, skin and intestines. Each bacterium contains between 2,000 and 6,000 immunological components. And babies often make an immune response to these bacteria to prevent them from entering the bloodstream and causing harm. The challenge that vaccines present is tiny in comparison to that from the environment.

Fourth, children have an enormous capacity to respond to immunological challenges. Susumu Tonegawa, a molecular biologist who won a Nobel Prize for his work, showed that people have the capacity to make between 1 billion and 100 billion different types of antibodies. Given the number of immunological components contained in modern vaccines, a conservative estimate would be that babies have the capacity to respond to about 10,000 different vaccines at once. Although this sounds like a huge number, when you consider the number of challenges that babies face from bacteria in their environment, it's not.

Here's another way to understand the difference in scale between immunological challenges from vaccines and natural challenges from the environment. The quantity of bacteria that live on body surfaces is measured in grams (a gram is the weight of about one-fifth of a teaspoon of water). The quantity of immunological components contained in vaccines is measured in micrograms or nanograms (millionths or billionths of a gram).

Q. Are the studies showing that neither the MMR vaccine nor thimerosal causes autism sensitive enough to detect the problem in small numbers of children?

A. The studies showing that neither the MMR vaccine nor thimerosal causes autism, called epidemiological studies, are very sensitive. For example, epidemiological studies have shown that a rotavirus vaccine used between 1998 and 1999 in the United States caused intestinal blockage in one out of every 10,000 vaccine recipients; that measles vaccine caused a reduction in the number of cells needed to stop bleeding (platelets) in one out of every 25,000 recipients; and that an influenza (swine flu) vaccine used in the United States in 1976 caused a type of paralysis called Guillain-Barré syndrome in one out of every 100,000 recipients.

About one out of every 59 children in the United States is diagnosed with an autism spectrum disorder. Even if vaccines caused autism in only 1 percent of autistic children, the problem would have easily been detected by epidemiological studies.

Q. If I am concerned that vaccines cause autism, what is the harm in delaying or withholding vaccines for my baby?

A. A study by Michael Smith and Charles Woods found that children who were fully vaccinated in the first year of life were not more likely to develop autism than those whose parents had chosen to delay vaccines. Further, all of the evidence shows that vaccines don't cause autism, so delaying or withholding vaccines will not lessen the risk of autism; it will only increase the period of time during which children are at risk for vaccine-preventable diseases. Several of these diseases, like chickenpox, pertussis (whooping cough) and pneumococcus (which causes bloodstream infections, pneumonia and meningitis) are still fairly common. Delaying or withholding vaccines only increases the time during which children are at unnecessary risk for severe and occasionally fatal infections.

AUTISM REFERENCES

Because autism research is continually evolving, a great way to stay up-to-date is to visit the Autism Science Foundation's research pages at:

www.autismsciencefoundation.org/research-year

Alarcon M, Abrahams BS, Stone JL, et al. Linkage, association, and gene-expression analyses identify CNTNAP2 as an autism-susceptibility gene. *Am J Hum Genet.* 2008;82(1):150-159.

Arking DE, Cutler DJ, Brune CW, et al. A common genetic variant in the neurexin superfamily member CNTNAP2 increases familial risk of autism. *Am J Hum Genet.* 2008;82(1):160-164.

Bailey A, LeCouteur A, Gottesman I, et al. Autism as a strongly genetic disorder: evidence from a British twin study. *Psychol Med.* 1995;25:63-77.

Bauman M. Autism: clinical features and neurological observations. In: Tager-Flusberg H, ed. *Neurodevelopmental Disorders.* Cambridge, MA: The MIT Press;1999;383-399.

Chess S, Fernandez P, Korn S. Behavioral consequences of congenital rubella. *J Pediatr.* 1978;93:699-703.

Folstein S, Rutter M. Infantile autism: a genetic study of 21 twin pairs. *J Child Psychol Psychiatry.* 1977;18:297-321.

Gai X, Xie HM, Perin JC, et al. Rare structural variation of synapse and neurotransmission genes in autism. *Mol Psych.* 2011; 1-10.

Glessner JT, Wang K, Cai G, Korvatska O, et al. Autism genomewide copy number variation reveals ubiquitin and neuronal genes. *Nature.* 2009;459:569-573.

International Molecular Genetic Study of Autism Consortium (IMGSAC). A genomewide screen for autism: strong evidence for linkage to chromosomes 2q, 7q, and 16p. *Am J Hum Genet.* 2001;69:570-581.

Moessner R, Marshall CR, Sutcliffe JS, et al. Contribution of SHANK-3 mutations to autism spectrum disorder. *Am J Hum Genet.* 2007;81: 1289-1297.

Rodier PM. The early origins of autism. *Sci Am.* 2000;282:56-63.

Smith MJ and Woods CR. On-time vaccine receipt in the first year does not adversely affect neuropsychological outcomes. *Pediatrics.* 2010;125(6): 1134-1141.

Strömmland K, Nordin V, Miller M, Akerström B, Gillberg C. Autism in thalidomide embryopathy: a population study. *Dev Med and Child Neurol.* 1994;36:351-356.

Wang K, Zhang H, Ma D, Bucan M, et al. Common genetic variants on 5p14.1 associate with autism spectrum disorders. *Nature.* 2009;459: 528-533.

Wassink TH, Piven J, Vieland VJ, et al. Evidence supporting WNT2 as an autism susceptibility gene. *Am J Med Genet.* 2001;105:406-413.

AUTISM AND VACCINES REFERENCES

Afzal MA, Ozoemena LC, O'Hare A, et al. Absence of detectable measles virus genome sequence in blood of autistic children who have had their MMR vaccination during the routine childhood immunization schedule of UK. *J Med Virol* 2006;78:623-630.

Dales L, Hammer SJ, Smith NJ. Time trends in autism and in MMR immunization coverage in California. *JAMA.* 2001;285:1183-1185.

Davis RL, Kramarz P, Bohlke K, et al. 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. *Arch Pediatr Adolesc Med.* 2001;155:354-359.

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. *Pediatrics.* 2004;113:259-266.

DeStefano F, Chen RT. Negative association between MMR and autism. *Lancet.* 1999;353:1986-1987.

Farrington CP, Miller E, Taylor B. MMR and autism: further evidence against a causal association. *Vaccine.* 2001;19:3632-3635.

Fombonne E, Chakrabarti S. No evidence for a new variant of measles-mumps-rubella-induced autism. *Pediatrics.* 2001;108:E58.

Fombonne E, Cook EH Jr. MMR and autistic enterocolitis: consistent epidemiological failure to find an association. *Mol Psychiatry.* 2003;8: 133-134.

Honda H, Shimizu Y, Rutter M. No effect of MMR withdrawal on the incidence of autism: a total population study. *J Child Psychol Psychiatry.* 2005;46(6):572-579.

Hornig M, Briese T, Buie T, et al. Lack of association between measles virus vaccine and autism with enteropathy: a case-control study. *PLoS ONE* 2008;3(9):e3140.

Kaye JA, del Mar Melero-Montes M, Jick H. Mumps, measles, and rubella vaccine and the incidence of autism recorded by general practitioners: a time trend analysis. *BMJ.* 2001;322:460-463.

Madsen KM, Hviid A, Vestergaard M, et al. A population-based study of measles, mumps and rubella vaccination and autism. *N Engl J Med.* 2002;347:1477-1482.

Marshall JA, Buikema A, et al. Autism occurrence by MMR vaccine status among US children with older siblings with and without autism. *JAMA.* 2015;313(15):1534-1540.

Peltola H, Patja A, Leinikki P, Valle M, Davidkin I, Paunio M. No evidence for measles, mumps and rubella vaccine associated inflammatory bowel disease or autism in a 14-year prospective study. *Lancet.* 1998;351: 1327-1328.

Smeeth L, Cook C, Fombonne E, et al. MMR vaccination and pervasive developmental disorders: a case-control study. *Lancet* 2004;364:963-969.

Taylor B, Miller E, Farrington CP, et al. Autism and measles, mumps and rubella vaccine: no epidemiological evidence for a causal association. *Lancet.* 1999;353:2026-2029.

Taylor LE, Swerdfeger AL, Eslick GD. Vaccines are not associated with autism: an evidence-based meta-analysis of case-control and cohort studies. *Vaccine* 2014;32:3623-3629.

Uchiyama T, Kurosawa M, Inaba Y. MMR-vaccine and regression in autism spectrum disorders: negative results presented from Japan. *J Autism Dev Disord* 2007;37:210-217.

Wilson K, Mills E, Ross C, McGowan J, Jadad A. Association of autistic spectrum disorder and the measles, mumps and rubella vaccine: a systematic review of current epidemiological evidence. *Arch Pediatr Adolesc Med.* 2003;157:628-634.

IMMUNOLOGICAL CAPACITY AND TOO MANY VACCINES REFERENCES

DeStefano F, Price CS, Weintraub ES. Increasing exposure to antibody-stimulating proteins and polysaccharides in vaccines is not associated with risk of autism. *J Pediatr* 2013;163:561-567.

Glanz JM, Newcomer SR, Daley MF, DeStefano F, et al. Association between estimated cumulative vaccine antigen exposure through the first 23 months of life and non-vaccine-targeted infections from 24 to 47 months of age. *JAMA* 2018;319(9):906-913.

Hviid A, Wohlfahrt J, Stellfeld M, et al. Childhood vaccination and nontargeted infectious disease hospitalization. *JAMA* 2005;294(6):699-705.

Iqbal S, Barile JP, Thompson WW, and DeStefano F. Number of antigens in early childhood vaccines and neuropsychological outcomes at age 7-10 years. *Pharmacoepidemiol Drug Saf* 2013;22:1263-1270.

Offit PA, Quarles J, Gerber MA, et al. Addressing parents' concerns: do multiple vaccines overwhelm or weaken the infant's immune system? *Pediatrics.* 2002;109:124-129.

Sherrid AM, Ruck CE, Sutherland D, et al. Lack of broad functional differences in immunity in fully vaccinated vs. unvaccinated children. *Pediatr Res* 2017;81(4):601-608.

Smith MJ and Woods CR. On-time vaccine receipt in the first year does not adversely affect neuropsychological outcomes. *Pediatrics* 2010;125:1134-1141.

THIMEROSAL REFERENCES

Andrews N, Miller E, Grant A, Stowe J, Osborne V, Taylor B. Thimerosal exposure in infants and developmental disorders: a retrospective cohort study in the United Kingdom does not support a causal association. *Pediatrics.* 2004;114:584-591.

Christensen DL, Baio J, Van Naarden Braun K, Charles J, Constantino JN, et al. Prevalence and characteristics of autism spectrum disorder among children age 8 years – Autism Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012. *MMWR* 2016;65(3):1-23.

Fombonne E, Zakarian R, Bennett A, Meng L, McLean-Heywood D. Pervasive developmental disorders in Montreal, Quebec, Canada: prevalence and links with immunizations. *Pediatrics.* 2006;118:E139-150.

Heron J, Golding J. Thimerosal exposure in infants and developmental disorders: a prospective cohort study in the United Kingdom does not support a causal association. *Pediatrics.* 2004;114:577-583.

Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. Association between thimerosal-containing vaccines and autism. *JAMA.* 2003;290:1763-1766.

Madsen KM, Lauritsen MB, Pedersen CB, et al. Thimerosal and the occurrence of autism: negative ecological evidence from Danish population-based data. *Pediatrics.* 2003;112:604-606.

Picciozzo IH, Green PG, Delwiche L, et al. Blood mercury concentrations in CHARGE study children with and without autism. *Environ Health Perspect.* 2010;118(1):161-166.

Price CS, Thompson WW, Goodson B, et al. Prenatal and infant exposure to thimerosal from vaccines and immunoglobulins and risk of autism. *Pediatrics.* 2010;126:656-664.

Schechter R, Grether J. Continuing increases in autism reported to California's developmental services system: mercury in retrograde. *Arch Gen Psychiatry.* 2008;65:19-24.

Stehr-Green P, Tull P, Stellfeld M, Mortenson PB, Simpson D. Autism and thimerosal-containing vaccines: lack of consistent evidence for an association. *Am J Prev Med.* 2003;25:101-106.

Thompson WW, Price C, Goodson B, et al. Early thimerosal exposure and neuropsychological outcomes at 7 to 10 years. *N Engl J Med* 2007;357(13):1281-1292.

Tozzi AE, Bisiacchi P, Tarantino V, et al. Neuropsychological performance 10 years after immunization in infancy with thimerosal-containing vaccines. *Pediatrics.* 2009;123(2):475-482.

Verstraeten T, Davis RL, DeStefano F, et al. Study of thimerosal-containing vaccines: a two-phased study of computerized health maintenance organization databases. *Pediatrics.* 2003;112:1039-1048.

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