



MMR and Autism

by Prof. Bruce Tonge & Dr Avril Brereton

What is MMR?

The MMR vaccine is a 3 in 1 vaccine that protects against measles, mumps and rubella. The MMR is one of the recommended early childhood immunizations. Proof of MMR vaccination is generally required for school entry. The first MMR shot is recommended at 12 -15 months. A second MMR is recommended prior to school entry at 4-6 years of age.

Measles is a virus which causes a rash, cough, runny nose, eye irritation and fever in most people, but can also lead to pneumonia, seizures, brain damage and death in some cases.

Mumps is a virus that causes fever, headache, and swollen glands. It can also lead to deafness, meningitis, swollen testicle or ovaries and death in some cases.

Rubella also known as German measles, is generally a mild disease but can cause serious birth defects in the child of a woman who becomes infected whilst pregnant.

Is there a link between MMR and autism?

(From National Autistic Society www.nas.org.uk)

Despite considerable publicity, to date, there is no conclusive scientific evidence to prove a link between MMR and autism. The possible link was first raised by Dr Andrew Wakefield's team at the Royal Free Hospital in February 1998 (1). Their study noted that in 12 children seen by the research team the symptoms of their developmental disorder became apparent within six days of them receiving the MMR vaccine. This was a very small-scale study and it concludes:

"We did not prove a link between measles, mumps, and rubella vaccine and the syndrome described [autistic enterocolitis]. Virological studies are underway that may help to resolve

this issue." They also state that if there was a connection between autism and MMR then: "... a rising incidence might be anticipated after the introduction of this vaccine in the UK in 1988."

After the publication of this research this possibility was quickly examined. A major retrospective study was carried out in Finland where MMR has been used for a number of years (2). More than 1.5 million children were immunised against MMR between 1982 and 1996 and the researchers claimed that no link with an increased prevalence of autism could be established. However, the methodology of this research was heavily criticised by a number of experts, including Dr Lorna Wing. Of the records examined, it was only those of the 31 children who had shown signs of gastro-intestinal problems, which had also been followed up for autism.

This was followed by two further studies that examined the prevalence of autism since the introduction of MMR. Both state that such a link does not exist. The first report, published in *Current Problems in Pharmacovigilance* (3), describes an analysis of 92 cases of autism and 15 cases of Crohn's disease where the parents felt that vaccines had caused the problems. They found no evidence of extraordinary features in these cases that would suggest a new or novel type of autism. However, they did stress that: "It was impossible to prove or refute the suggested associations between the MMR vaccine and autism or inflammatory bowel disease because of the nature, the self-selection of the cases and the lack of comparators. Nevertheless, the Working Party found that the information available did not support the suggested causal associations or give cause for concern about the safety of MMR or MR vaccines."

The second study (4) was specifically commissioned by the Department of Health to examine the concerns raised about MMR and autism. The researchers who conducted the study were based at the Royal Free Hospital and examined the medical records of 498 children with autistic spectrum disorders (ASDs) living within the North Thames Health Authority region. They found clear evidence that there has been a significant rise in the prevalence of autism since the introduction of MMR in 1988. However, they also found that countries that have not used the MMR vaccine experienced this increase and concluded:

"Our results do not support the hypothesis that MMR vaccination is causally related to autism, either its initiation or to the onset of regression - the main symptom mentioned in the paper by Wakefield and others. This study does not rule out the possibility of a rare idiosyncratic response to MMR. However, if such an association occurs it is so rare it could not be identified in this large regional sample."

In 2001 the Medical Research Council (MRC) commissioned an Autism Review (5). An expert group of scientists and doctors, brought together by the MRC looked at MMR, amongst other factors, as a possible cause of ASDs. It concluded that the current epidemiological evidence does not support the proposed link of MMR to ASDs. Their conclusions are consistent with the previous MRC reviews and with the findings of other expert groups that have reviewed this question.

This review was followed by another study funded by the MRC at the London School of Hygiene and Tropical Medicine in 2004 (6). The research team analysed the medical records

of children registered with general practices across England and Wales. They compared the vaccination histories of children who had been diagnosed with a pervasive developmental disorder (PDD) or autism with those that had not received a diagnosis. This included 1,294 children who had received a diagnosis between 1987 and 2001 with 4,469 children of the same sex and similar age who had not received a diagnosis. The team was unable to establish a link between MMR and autism or PDD. Because many ASDs are not diagnosed before the age of three, the researchers then only studied children who had received the MMR vaccine before their third birthday. They were still unable to establish a link between MMR and autism.

More recently, the debate over the MMR vaccine and autism has resurfaced with two new studies being published receiving media attention. In 2005 a Japanese study (7), carried out jointly with Michael Rutter at the Institute of Psychiatry, London, concluded that there was no causal link between the MMR vaccine and autism. They studied over 30,000 children in the city of Yokohama in Japan. The MMR was withdrawn from Japan in April 1993 over concerns that the anti-mumps component was causing meningitis. Since then, single vaccinations have been administered, though the government is planning to introduce another version of the MMR vaccine. Despite this, they found that the number of children with autism continued to rise. They studied 31,426 children born in one district of Yokohama between 1988 and 1996. They found the cases of autism continued to rise after the MMR was withdrawn. 48 to 68 cases per 10,000 children were recorded before the withdrawal compared with 97 to 161 cases per 10,000 after the withdrawal. The same pattern of results was also seen in the incidence of a particular form of autism in which children appear to develop normally and then regress which was linked to the MMR in Dr Wakefield's study. However, the study could not rule out the possibility that MMR triggers autism in a tiny number of children which is what some have claimed. However, Hideo Honda of the Yokohama Rehabilitation Centre concluded that the vaccine 'cannot have caused autism in the many children with autistic spectrum disorders in Japan who were born and grew up in the era when MMR was not available'.

Michael Rutter has also said that the findings 'rubbished' the link between MMR and the general rise in autism. However, critics have said they would like more conclusive proof from UK-based studies before being convinced of the MMR's safety.

The second study was the Cochrane Review also in 2005 (8). Researchers searched international databases and found 139 studies assessing the effects of MMR in children. Thirty-one studies from the original 139 were included in the review, the others were discarded due to possible bias or error. No evidence was found linking MMR with either autism or Crohn's disease. The lead author, Dr Demicheli, concluded that 'all the major unintended events, such as triggering Crohn's disease or autism, were suspected on the basis of unreliable evidence.' However, critics of the study have pointed to the fact that in the abstract of this report, 'The design and reporting of safety outcomes in MMR vaccine studies, both pre and post marketing, are largely inadequate.' Some critics have also argued that the studies that were reviews lacked sufficient statistical power to detect an association between MMR causing regressive autism in a small percentage of children (9).

What about the MMR booster?

An MMR booster is given to children again just before they start school. Some parents are concerned about this second vaccination, especially families who have had a child recently diagnosed with autism. They are often concerned about giving their child or a sibling a second booster. To our knowledge, there is no research looking at the second booster and how this may affect a child with a autism or a family member. The research so far has focused on the first dose's possible links with a regressive form of autism.

Are there alternatives to the MMR vaccine?

The alternatives to MMR at present are either not to vaccinate or to have the vaccines administered singly at annual intervals. However, there is no research into the efficacy or timing of single monovalent vaccines against the triple MMR vaccination. For this reason parents cannot assume that following one route would be safer than the other. If parents choose not to vaccinate their children then they are currently placing them at great risk. Uptake of the MMR vaccine has dropped. In the UK, in 2005 73.3% of children under the age of five were given the vaccination. This is below the 95 per cent level recommended by the World Health Organization to prevent outbreaks of disease.

References

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Also see Australian websites:

http://www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/Immunisation_and_autism?OpenDocument

http://www.ncirs.usyd.edu.au/decisionaid/faq_01.html