

## MMR, Bowel disease and Autism

Sense has taken advice from a number of specialists about the alleged links between MMR and autism. This is our interpretation of the theory linking MMR to autism and the evidence against it. It is not an exhaustive account.

Initially, around 1995 questions were raised about possible links between a persistent measles infection and bowel disease. One paper looked at the role of wild measles infection and its links to Crohn's disease. No evidence to support this has been found by a number of papers:

- Thompson et al. *EU J Gastro & Hepatol* 1995
- Jones et al. *Lancet* 1997
- Nielsen et al. *BMJ* 1998
- Pardi et al. *Inflammatory Bowel Diseases* 1999
- Haslam et al. *Gut* 2000

A further paper looked at the role of measles vaccination in relation to Crohn's and ulcerative colitis. Again no evidence for a link was found in a number of papers:

- Feeney et al. *Lancet* 1997
- Pebody et al. *Lancet* 1998
- Morris et al. *Am J Gastroenterology* 2000
- Davies R L. *Arch Ped Adol Med* 2001

In 1998 Dr Wakefield and colleagues published a paper<sup>1</sup> claiming to have identified a new condition describing particular bowel disease in children with pervasive developmental disorder (autism). The paper focused on 12 children who had behavioural symptoms and bowel problems. It suggested that something causes the bowel to be inflamed, that peptides leak from the bowel into the blood stream, that this has a direct effect on the brain and causes autism. The paper speculated whether MMR could be the cause of the bowel inflammation, based on parents of the children linking the onset of the symptoms to the timing of the MMR vaccine.

The paper itself concluded that the researchers did not prove an association between the MMR vaccine and the syndrome they described. This did not stop Dr Wakefield, at a press conference and in a video briefing he had prepared for journalists, claiming that there was sufficient doubt in his own mind about the role of MMR for a case to be made to give the vaccines individually with at least a year interval. Others involved in the research, such as Dr S Murch emphasised that the link was unproven and that MMR vaccination should continue.

Once the question had been raised, significant research has taken place to look at the theory. This has taken two forms: epidemiological studies to look at the impact of the vaccination on populations who have received it; virological studies trying to identify persistent measles infection in children with bowel disease and autism.

Observations in individuals, such as the 1998 Lancet paper can generate theories and leave in the care of individuals but not cause. Epidemiological studies investigate suggested associations between vaccines and rare events, and they have a successful history of having done this in the past. Epidemiological studies have consistently shown no link between MMR vaccines and autism, and there remain no studies to support the suggestion of a link. Numerous studies have looked back at children who received the MMR vaccine and they have found no rise in referrals to autistic clinics following the introduction of MMR, no link between MMR and autism and regressive autism, and no difference in rates of autism between those children who had and had not received MMR. These studies, partly because of their retrospective nature, do have limitations but it is unlikely they would have all failed to find a link that was there. Indeed a Cochrane review<sup>2</sup> of all the literature that only included the most robust studies, concluded that "no credible evidence of an involvement of MMR with either autism or Crohn's disease was found". Virological studies have tried to look at the evidence for persistent measles virus in children with autism, particularly those with bowel disease, either by looking at blood, gut biopsies or cerebral fluids. No evidence that has been reproduced independently has found evidence of a persistent measles virus link in children with a development disorder. A study in 2002<sup>3</sup> found evidence of the measles virus in children with bowel disease and autism. Recent evidence to the Autism Omnibus hearings in the US has cast doubt on these findings and the ability of the research methods used to accurately identify measles. Several researchers linked to Dr Wakefield have claimed to find evidence of measles virus in subsequent studies, often unpublished. However several independent researchers have not been able to replicate the findings<sup>4</sup>.

From the advice Sense has received we have concluded that the evidence is open as to whether a new condition of bowel disease in children with regressive autism has been identified. There is no evidence linking measles or measles vaccine to Crohn's or bowel disease. There is a large body of evidence suggesting there is no casual link between MMR vaccines and autism, and there remain no studies to support the suggestion of a link. There is no peer reviewed, reproducible evidence of persistent measles virus in children with development disorder. The questions asked about the MMR vaccine have been answered and it remains the best way to protect children in the UK against measles, mumps and rubella.

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<sup>1</sup> Wakfield et al. Ileal-lymphoid nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998;351:1327-8

<sup>2</sup> Demicheli V, Jefferson T, Rivetti A, et al. Vaccines for measles, mumps and rubella in children. *Cochrane Database Syst Rev* 2005;4:CD004407.

<sup>3</sup> Uhlmann V, Martin CM, Sheils O, et al.. Potential viral pathogenic mechanism for new variant inflammatory bowel disease. *Mol Pathol* 2002;55:84-90. Correction in O'Leary JJ. Potential viral pathogenic mechanism for new variant inflammatory bowel disease. *Mol Pathol* 2002;56:248.

<sup>4</sup> 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 immunisation schedule of UK. *J Med Virol* 2006;78:623-30.

D'Souza Y, Fombonne E, Ward BJ. No evidence of persisting measles virus in peripheral blood mononuclear cells from children with autism spectrum disorder. *Pediatrics* 2006;118:1664-75. Erratum in: *Pediatrics*. 2006 Dec;118:2608.

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