Leading article

MMR vaccine—worries are not justified

The advocates of Vaccination have exalted in the prospect of exterminating the Small Pox from the face of the earth; while its opponents have framed their tales of horror, replete with stories of novel diseases and unheard-of plagues. ... When I consider the many evidences in favour of Vaccination, which the public documents of almost every nation afford, I am at a loss to conceive from what cause such doubts can have arisen; for I think, if an unprejudiced mind will fairly consider the question, it must be convinced that Vaccination has answered the promised end.

(from a letter to The Gentleman’s Magazine, March 1808, by “Cosmopoliton”)

Since the introduction of the measles vaccine in 1968 and then the measles, mumps, and rubella (MMR) vaccine in 1988, measles, mumps, and rubella have become rare diseases. However, on the basis of research, primarily from one unit, some parents and health professionals have become concerned about the safety of MMR vaccine. This has led to a decline in uptake and fears of impending outbreaks. In this paper we review the background to these concerns and examine the evidence to date.

In the early 1990s the Inflammatory Bowel Disease Study Group (IBDSG) at the Royal Free Hospital in London suggested that measles disease in children predisposed them to inflammatory bowel disease as adults. However, further research, including that by the IBDSG has shown this not to be so. Later, the IBDSG suggested that measles vaccination could lead to adult inflammatory bowel disease. This study was much criticised at the time and further work, including some by the IBDSG, has shown no link. More recently, Ghosh et al reviewed all the evidence surrounding the presence of measles virus in Crohn’s disease and concluded that measles virus is not found in the intestines of patients with the disease.

It is against this background that in 1998 the IBDSG published their paper in the Lancet. They described 12 children with bowel symptoms and pervasive developmental disorder. In eight children the symptomatology was recalled by the parent or general practitioner as starting soon after the child had received MMR vaccine. Although the authors clearly stated that they had not proven a link between the vaccine and the disorders, this was not the interpretation made in many quarters. In the media coverage that followed, one of the researchers said that he believed MMR vaccine overloaded the immune system and should be given to children separately at yearly intervals. He is yet to produce any sound scientific evidence to support this view. In contrast, three of the paediatricians on the research team said, “We emphatically endorse current vaccination policy until further data are available.”

Since 1998 several studies have been published which specifically set out to investigate the link between MMR vaccine, autism, and bowel disease and have found no association between the vaccine and the conditions.

More recent events

In January 2001, Wakefield and Montgomery published another paper in which they claimed to show that the safety studies carried out before MMR vaccine was licensed were inadequate to pick up longer term side effects. They also looked at some of the studies that have been carried out since MMR was licensed. The paper contains no new information; it has many errors, and is highly selective in the studies it includes. In particular no mention is made of an important, well-conducted study among twins. In this Finnish study only a very low rate of side effects was reported and in particular, there was no increased incidence of bowel problems after MMR.

In the original paper from the IBDSG in which the case histories of the 12 children with pervasive developmental disorder and bowel disease were described, the interval between receipt of MMR vaccine and onset of behavioural symptoms was said to be short (mean 6.3 days, range 1–14). Taylor et al looked specifically to see if there was any excess risk of autism up to a year after MMR vaccine and found none. However, more recently it has been suggested that in most cases there is a much longer interval to the onset of autism. To explore this hypothesis Farrington et al reanalysed their data to include a time period for onset of parental concern up to three years after vaccination in children subsequently diagnosed as autistic. They again found no link.

Two recent extensive reviews of published and unpublished evidence have been conducted. At a conference...
convened by the American Academy of Pediatrics (AAP), it was concluded that the “available evidence does not support the hypothesis that MMR vaccine causes autism or associated disorders or IBD”22. An independent committee of the Institute of Medicine reached a similar conclusion.23 The AAP has subsequently endorsed the continued use of combined MMR vaccine and said that the use of separate vaccines has no place.24 At a hearing of the House of Representatives Committee of Government Reform on 25 April 2001, a range of experts testified. Among them was Dr Gershon who pointed out that the leaky bowel hypothesis was inherently implausible in that the liver would filter out any toxins before they reached the general circulation.25 He also reported that samples of gut containing measles virus had been sent to a virology department which had been performing tests for the presence of measles virus for the IBDSG. The results were inconsistent and he suggested that any conclusions based on results from this laboratory would have to be confirmed independently.

Use of single antigen vaccines

In the light of all this evidence, there is no case for the use of single vaccines. However, some parents are requesting them and we suggest including the following points when discussing the issue.

- There is a large body of evidence to show that MMR vaccine is highly effective and only rarely causes serious side effects. This is from research studies26-28 as well as from years of experience using MMR vaccine. It has been used in the USA for nearly 30 years, in Scandinavia for nearly 20 years, and in the UK since 1988.

In contrast, a regimen of giving single measles, mumps, and rubella vaccine separately to preschool children has never been used anywhere in the world. We therefore have no research evidence about the safety and effectiveness of the single vaccines used in this way as well as no experience. This means there are a number of important unanswered questions: is this regimen safe, what are the side effects, does it provide children with adequate protection against the diseases, in what order should the single vaccines be given, and what is the optimum time interval between doses?

Although there is no reason to suspect there may be a link between the single vaccines and autism and bowel disease, this has never been investigated.

- In the past, before the introduction of MMR vaccine:
  - From 1968 single measles vaccine was used in the second year of life.
  - From 1970 rubella vaccine was given to schoolgirls and susceptible adult women. As not all women were vaccinated, and a very small number who had been immunised lost their immunity, children with rubella passed it on to their pregnant mothers, friends, teachers, etc and cases of congenital rubella syndrome (CRS) continued to occur. It became apparent that the most effective strategy for preventing congenital rubella infection is to eliminate rubella from the childhood population. Since the introduction of the policy of MMR vaccination in early childhood there are now fewer than 10 babies born a year with CRS.
  - Mumps vaccine only became available in this country with the introduction of MMR vaccine.

- Giving the vaccines separately at intervals means that children are not protected against all three diseases as easily as possible. They are therefore at risk of catching one of the diseases while they wait to complete the course. This will allow continued circulation of the infections.

- Two doses of MMR are recommended to ensure full protection against all three diseases, and so children would need to have six injections rather than two.

- Currently, although in the UK there are four licences for measles vaccine and one for mumps vaccine, there are no longer any products produced which meet the specifications of these licences. Therefore, by definition, all single measles and mumps vaccines are unlicensed in the UK.

- Since the separate vaccines are not licensed in this country, there is less control over what children are getting.
  - A few years after MMR was introduced, several vaccines were in use from different vaccine manufacturers. It became clear that two MMR vaccines containing a particular type of mumps virus, Urabe, were causing a small increased risk of meningitis.29 This was carefully investigated and these MMR vaccines were withdrawn. However, some children having the separate vaccines have been given the Urabe single mumps vaccine.
  - Another mumps vaccine, Rubini, has very poor effectiveness.30 Some children have received this vaccine and are now not adequately protected against mumps.

- In Japan, there were similar problems with the MMR vaccine containing the Urabe, or similar, mumps virus. Unfortunately the Japanese did not have an alternative MMR vaccine and so they have continued to use single measles and rubella vaccines given on the same day.

- No country in the world recommends the use of single measles, mumps, and rubella vaccines as an alternative to the combined MMR vaccine.

- In France, single measles vaccine is available. This is because there is a recommendation that children under the age of 1 year who attend nursery have a single measles vaccine at 9 months of age. This is to prevent outbreaks of measles in the nursery setting. All these infants, as well as all other French children, still have two doses of MMR vaccine at similar ages to British children.

Conclusion

There is no good scientific evidence to support a link between MMR vaccine and autism or inflammatory bowel disease; indeed there is mounting evidence that shows no link. There is considerable evidence of the effectiveness and safety of MMR vaccine. Using separate vaccines is an untried and untested policy and, as far as protecting children from infectious disease is concerned, a backward step.

While the final decision rests with the parents, the evidence of the safety and efficacy of MMR vaccine is so overwhelmingly conclusive that health professionals should have no hesitation in recommending its use.

USEFUL WEBSITES

Health Promotion England: http://www.hpe.org.uk
Department of Health: http://www.doh.gov.uk
Public Health Laboratory Service: http://www.phls.co.uk
Centers for Disease Control, USA: http://www.cdc.gov
World Health Organization: http://www.who.int

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CJD has also fuelled concerns of some parents that the uncertainty among the experts is going to appear in the media, leading some parents, and possibly mending the use of this vaccine. Yet scare stories continue to be published as a risk factor for inflammatory bowel disease. Lancet 1995;345:1071–4.


the literature in detail, should be reassured by the opinion of those who have undertaken this task on their behalf.

Questions relating to vaccine safety will inevitably continue to arise and it is important that these are investigated with rigour and speed. The current investigations into the possible effects of thiomersal, a mercury based preservative in some vaccines, are a good example of this. However, while it should not be assumed that vaccines are necessarily beneficial in all individuals, the scientific criteria applied to the evidence of harm should be no less stringent than in other areas of medical science. These criteria have recently been reviewed by the World Health Organisation through its Global Vaccine Safety Advisory Committee. Publication in respectable medical journals of papers that in no way meet these criteria is a disservice to patients and health professionals alike.

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4. MRC. Ad hoc meeting to examine evidence relating to measles or measles vaccine to chronic gastrointestinal inflammation or autism. Final Report, 23 March 1988.
5. Wakefield AJ. Testimony to the Congress of the United States of America House Committee on Government Reform. 25 April 2001.

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