

# Comment

## MMR vaccine

There is a serious decline in the vaccination of young children against measles, mumps and rubella due to concerns about safety and possible links between the triple vaccine and bowel disease and autism. Drs Afzal and Minor explore the scientific background to this important issue.

Measles, mumps and rubella (MMR) vaccine was introduced to the UK National Immunization Schedule in October 1988 and now about 600,000 doses are distributed annually. The vaccine is licensed by the government through the Medicines Control Agency (MCA) and contains three live viruses (measles, mumps and rubella). Their ability to cause disease has been reduced by growing each virus in a series of embryonated hen's egg and chicken embryo fibroblast (CEF) cells. Each vial of the finished triplet formulation contains a well defined amount of each component virus that is known to be sufficient to provoke effective immunity in the vaccine recipients. Only batches meeting the required specifications for potency, identity and thermostability after laboratory testing are released for use.

In Britain MMR vaccine is administered under a two-dose vaccination schedule in which the first dose (primary immunization) is given at or around 12 months of age while the second dose (booster immunization) is given between 5 and 7 years. Two doses are needed to raise immunity in the population to 95%, the level required to break the transmission of measles, mumps or rubella virus circulating in the community. A single immunization, at best, confers immunity in only 80–90% of vaccine recipients, since about 20% of the target population either fails to receive the primary dose altogether or fails to respond to the vaccine.

### ● Adverse events following immunization

MMR vaccine is highly efficacious and has no undesirable effects in most recipients. However, some children following vaccination may have symptoms of fever, skin rash or burning/stinging at the site of injection or other mild local reactions. Other rare reactions include sore throat, malaise, swollen glands, nausea, diarrhoea, low numbers of blood platelets, livid spots, and febrile and afebrile convulsions. Aseptic meningitis following MMR vaccination has been mainly associated with a specific brand of vaccine that contained the Urabe strain as a mumps virus component; this was withdrawn from the UK immunization programme in 1992. MMR vaccines currently licensed in the USA, UK and most other European countries contain the Jeryl Lynn strain as the mumps component which has not been linked to post-vaccinal meningitis.

However, in 1993 Dr Andrew Wakefield's group at the Royal Free Hospital, London, proposed that early measles infection could be linked to the onset of Crohn's disease later in life. Independent attempts to detect any genes of the measles virus in tissues as reported by this group failed and epidemiological studies concluded no link.

Subsequently, it was suggested that measles vaccine given as MMR was also linked with a specific gut syndrome, termed 'Ileal-lymphoid-nodular-hyperplasia' which was associated with Autistic Spectrum Disorder (ASD).

### ● MMR vaccine safety reviews

The alleged link between MMR vaccination and bowel inflammation leading to autism has raised serious concerns over the clinical safety of MMR vaccine. This has been extensively debated in scientific fora worldwide. In the UK between 1998 and 2001 bodies such as the Medical Research Council (MRC), the Medicine Control Agency (MCA), the Committee on Safety of Medicine (CSM) and the Joint Committee on Vaccination and Immunization (JCVI) conducted scientific reviews of its safety. Experts concluded that there was no evidence to support any association between MMR vaccine and inflammation of the bowel and autism. Following each review it was recommended that vaccination with MMR should be continued in line with the National Immunization Programme. More recently, the UK Department of Health commissioned the MRC to conduct a full review of all aspects of autism research. Although the report failed to identify any causal association between MMR vaccination and autism, it highlighted several key factors, including the environment, genetic predisposition, physiological and dietary aspects and other psychological abnormalities that require further investigation.

The issue of MMR vaccine in relation to juvenile autism has also been extensively discussed in the USA, including in a congressional hearings committee meeting and in expert panels formulated by the Institute of Medicine (IOM) and by the American Academy of Pediatrics. The review panel of the IOM committee rejected the claims of the causal relationship between MMR vaccine and autism. However, it warned that the possibility that MMR vaccine might contribute to ASDs in a subset of recipients could not be ruled out. One of their recommendations was the need to conduct further research on the possible occurrence of ASD in a small number of children following MMR vaccination and that the intestine of children with ASD should be tested for the possible presence of measles vaccine strain. A recent report from Professor John O'Leary's group, in collaboration with Andrew Wakefield's group, of the presence of measles virus fragments in the gut of autistic enterocolitis patients is thus of considerable interest. It is not yet known whether the virus sequences amplified were identical to the sequence of the vaccine strain or to any wild-type measles strain. These findings have not been verified independently, and in our opinion that must be done before any firm conclusion of the possible links between measles, MMR, and bowel inflammation and autism can be drawn.

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