MEASLES, MUMPS & RUBELLA

Frequently Asked Questions

NATIONAL IMMUNISATION ADVISORY COMMITTEE

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

MARCH 2002

WHAT ARE THESE DISEASES?

Measles is an acute viral illness characterised by a cough, runny nose, sore throat, red eyes, a rash that begins behind the ears and a high temperature. One in 15 children who contract measles develop serious complications which can include bronchitis, pneumonia, convulsions and encephalitis.

Mumps is an acute viral illness characterised by swelling of the salivary glands on one or both sides of the face. Complications of mumps include deafness, meningitis, encephalitis, pancreatitis and orchitis which can rarely lead to sterility. Before the introduction of the combination measles, mumps and rubella (MMR) vaccine, mumps was the commonest cause of viral meningitis and permanent unilateral deafness.

Rubella is a mild infectious disease most common in children aged 4-9 years. It causes a transient rash, enlargement of the lymph glands and occasional joint pain in adults. Rubella is often asymptomatic. The principal concern about rubella is that if it is contracted during early pregnancy it can result in major damage to the foetus. Features of the congenital rubella syndrome include mental handicap, visual and hearing defects and congenital heart lesions.

HOW COMMON ARE THESE DISEASES?

Measles:

Prior to the introduction of the measles vaccine, by the age of 25 years almost everyone had suffered from measles infection. In Ireland the number of cases of measles reported annually has dropped significantly since the introduction of the measles vaccine in 1985 and the MMR vaccine in 1988 as shown in Figure 1. In the 1950s in Ireland an average of 8,500 cases of measles were reported each year. In the 1970s an average of 7 children died in Ireland every year from measles. In 1985 there were almost 10,000 cases of measles notified. By 1991 this had dropped to 135.

Outbreaks of measles, however, continue to occur in Ireland. In 1993 over 4,328 cases of measles were reported. In 2000 over 1,600 cases of measles were reported to the National Disease Surveillance Centre (NDSC). Most of these cases were in the Eastern Regional Health Authority area and there were three associated deaths. The uptake of MMR vaccine in Ireland is currently not high enough to prevent outbreaks from occurring.

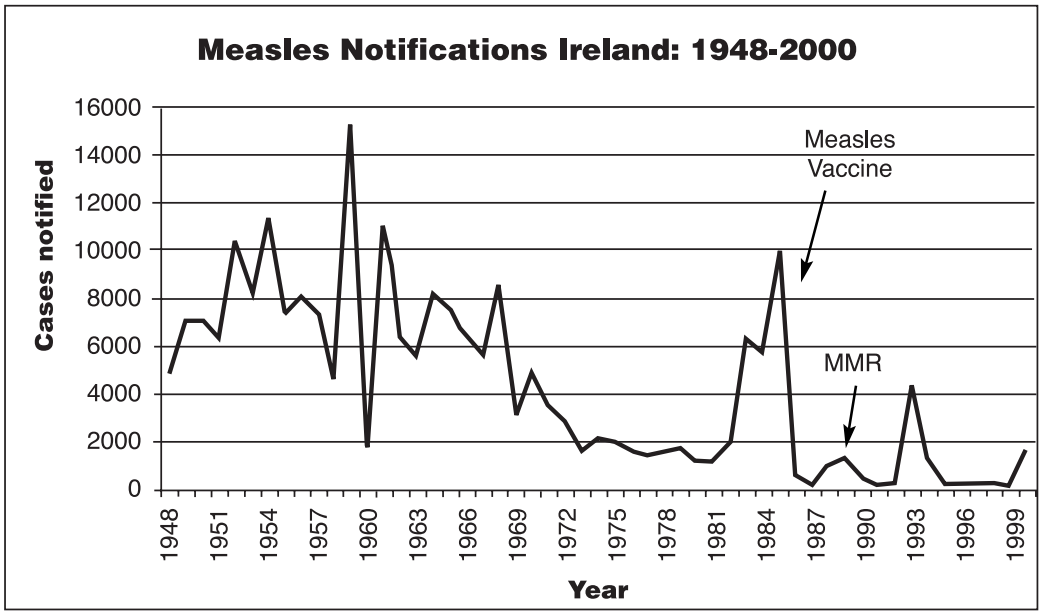


Figure 1: Measles notifications in Ireland, 1948-2000

Mumps:

Protection against mumps was first offered in 1988, with the introduction of the MMR vaccine, the same year that mumps became a notifiable disease.

In 1992, a second dose of MMR vaccine was recommended for both boys and girls aged 10-14 years. In 1999 the age of the second dose was lowered to 4-5 years. The number of cases of mumps notified in Ireland in recent years has been low. An increase in notifications was seen in 1996/7. Mumps outbreaks will continue to occur if vaccine uptake rates do not improve.

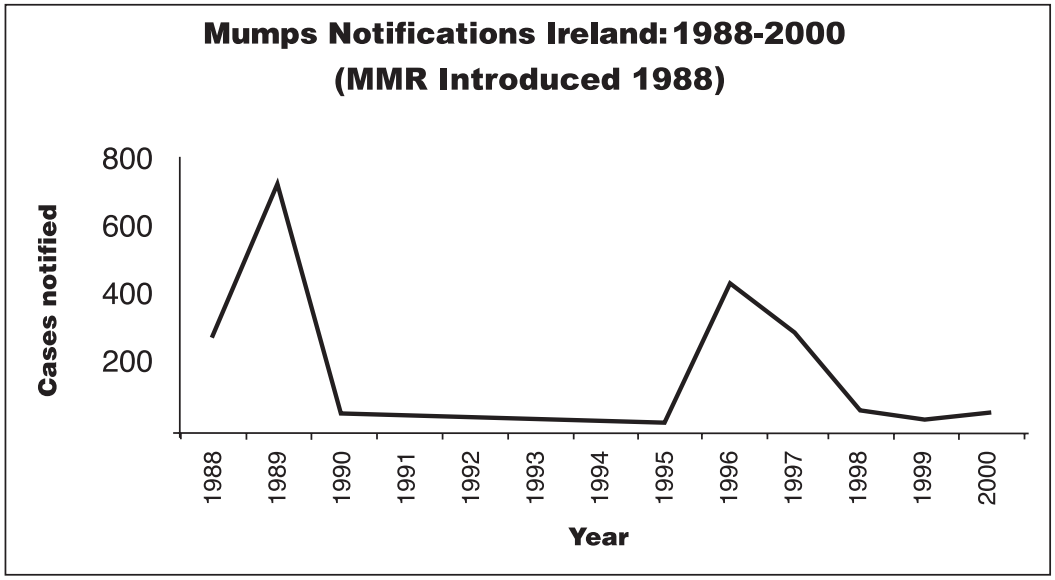


Figure 2: Mumps notifications in Ireland, 1988-2000

Rubella:

Rubella vaccine for pre-pubertal girls was introduced in 1971. The rubella virus continued to circulate among younger children and older boys, however, and pregnant women continued to be exposed to rubella. The vaccination policy was changed in 1988 and now both boys and girls are vaccinated with the MMR vaccine.

The incidence of rubella declined in the 1990s following the introduction of MMR vaccine in 1988. The number of cases of rubella reported in Ireland in recent years has remained largely unchanged apart from an increase in 1996 which was predominantly seen in teenage boys and young male adults who had never been vaccinated.

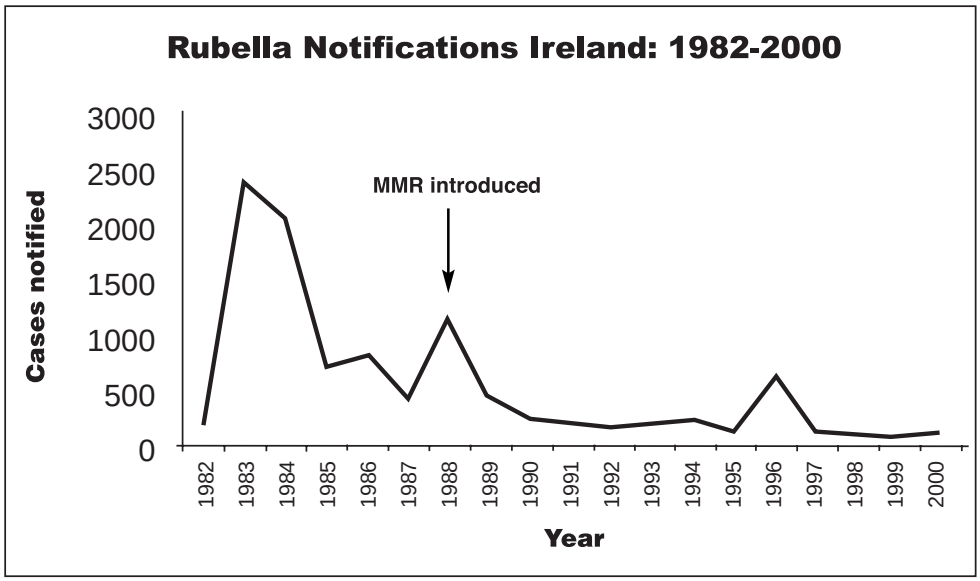


Figure 3: Rubella notifications in Ireland, 1982-2000

CAN CHILDREN DIE FROM MEASLES?

About one million children worldwide die from measles each year making it the eighth commonest killer disease of children. Death rates for measles vary depending on age. On average, between 1 in 2,500 and 1 in 5,000 cases die from measles. However, in recent years, deaths from measles have been reported as approximately 1-2 per 1,000 reported cases in the United States. This has also been the experience in several recent outbreaks in Europe due to low vaccine uptake, where there have been fatal cases of measles. In Ireland eight deaths from measles were reported to the Central Statistics Office between 1990 and 1999. There were three deaths and over 1,600 reported cases in Ireland in 2000 and three deaths in 2,961 reported cases (1 in 1,000) in the Netherlands during an outbreak in 1999/ 2000.

The risk of death is significantly higher in children developing measles under one year of age. This group are not currently offered the vaccine as they are too young and can only be protected through the 'population protection' of high vaccine uptake. Young adults who acquire measles at an older age also have a higher rate of encephalitis.

A serious complication of measles in children is subacute sclerosing panencephalitis (SSPE). This is a rare degenerative neurological condition that can develop some years after natural measles infection and causes gradual loss of function and death within a few years. The risk is greatest in those who were infected at a young age. The average interval from measles infection to the onset of SSPE is around eight years. Measles vaccine directly protects against SSPE.

WHY IS THE MMR VACCINE SO IMPORTANT?

The MMR vaccine is very important because it protects children against contracting measles, mumps and rubella, which are all diseases that can have serious consequences as described above. An example of what can happen if MMR immunisation rates are low was highlighted by the measles outbreak seen in Ireland in 2000.

The MMR vaccine can protect children in three ways:

- individual protection
- population protection
- potential eradication of diseases.

- **Individual protection**:

One dose of MMR vaccine will provide immunity against measles and mumps in at least 90% of those vaccinated and against rubella in at least 95%. A second dose of vaccine has been shown to increase protection significantly to 99%.

- **Population protection** (also known as 'herd immunity'):

This means that if someone incubating measles (or mumps or rubella) has contact with others in the community, the disease will not spread if immunisation uptake rates are high as the chance of being in contact with someone who is not immune is so small if most people have immunity. Children who cannot be immunised (e.g. those with leukaemia, cancer or on immunosuppressive treatment) depend on high population levels for their personal protection as do children under one year of age. Women who have not been immunised against rubella depend on high 'population protection' to prevent them from catching rubella and their babies being damaged.

- **Potential eradication of disease**:

The World Health Organisation concluded in 1996 that measles eradication is feasible through immunisation. This will only occur, however, if uptake of the vaccine is high. Smallpox has already been eradicated by vaccination and rapid progress is being made towards eradication of poliomyelitis through immunisation. Many countries have already virtually eliminated measles (e.g.) Finland, Sweden, Spain and United States.

HOW DOES THE MMR VACCINE WORK?

MMR vaccine is a live virus vaccine. This means that it contains measles, mumps and rubella viruses that have been modified (or attenuated) so that they are extremely unlikely to cause disease symptoms in humans. The vaccine has been developed to produce an immune response sufficient to protect children against the real disease, with no illness at all or only a very mild version of the illness.

A child is injected with the vaccine and this causes the immune system to respond and make antibodies against the viruses in the vaccine. These antibodies then destroy the vaccine viruses but special cells of the immune system 'remember' the virus so that there is a prompt response if exposure occurs again. Because the viruses in the vaccine and the wild viruses are very similar, the immune system responds to both. This means that if a child is later infected with the wild viruses, these are very quickly recognised by the immune system and large numbers of antibodies are produced rapidly to halt the infection.

The immune response to vaccination is very similar to natural infection. The immunity to the measles and other antigens in the MMR vaccine occurs at different times; measles after 6-11 days, rubella after 10-15 days and mumps after 15-21 days. Unlike a wild virus, the vaccine virus cannot be spread to others, so there is no risk of infection from people who have been recently vaccinated with MMR. Studies show that when vaccine viruses are combined, the same high levels of protection are achieved as when the same component vaccine viruses are given individually.

The MMR vaccine is routinely given in Ireland as follows:

- first dose: by injection at 12-15 months, usually on its own
- second dose: by injection as part of the school entry vaccination programme at age 4-5 years.

WHAT IS THE DIFFERENCE BETWEEN CATCHING MEASLES AND HAVING THE LIVE VIRUS VACCINE INJECTED INTO THE BODY?

The difference between catching measles and receiving the vaccine relate to the fact that the measles virus is in an attenuated form in the vaccine. As a result the vaccine strain can stimulate the child's immune system to protect them from future infection with the wild virus, without the complications associated with wild virus infection. On the other hand infection with the wild measles virus weakens the immune system, often leading to a secondary infection such as pneumonia or middle ear infection.

Like all vaccines, side effects can occur with MMR. However these are almost always trivial and, as can be seen from the table below, the small risks from the vaccine are far outweighed by the substantial risks associated with wild measles infection.

Measles		**MMR vaccine**	
Ear infection:	1 in 20	Ear infection:	1 in 2,000
Hospitalised:	1 in 5	Hospitalised:	1 in 1,000
Encephalitis:	1 in 1,000	Encephalitis:	1 in 1,000,000
Pneumonia:	1 in 20	Pneumonia:	None
Death:	1 in 2,500 to 1 in 5,000	Death:	None

Table 1: Complications of measles versus MMR vaccine.

IF THE MMR VACCINE IS SO EFFECTIVE, WHY DO CHILDREN NEED A SECOND VACCINATION?

Very few vaccines provide full protection against the disease concerned after only one dose. Over 90% of children vaccinated with the MMR vaccine will have full protection after a single dose. A second dose increases protection to 99%. Compared to most vaccines this is a very effective response.

IS IT NOT TRUE THAT THE MAJORITY OF PEOPLE WHO DEVELOP MEASLES HAVE BEEN VACCINATED AGAINST MEASLES?

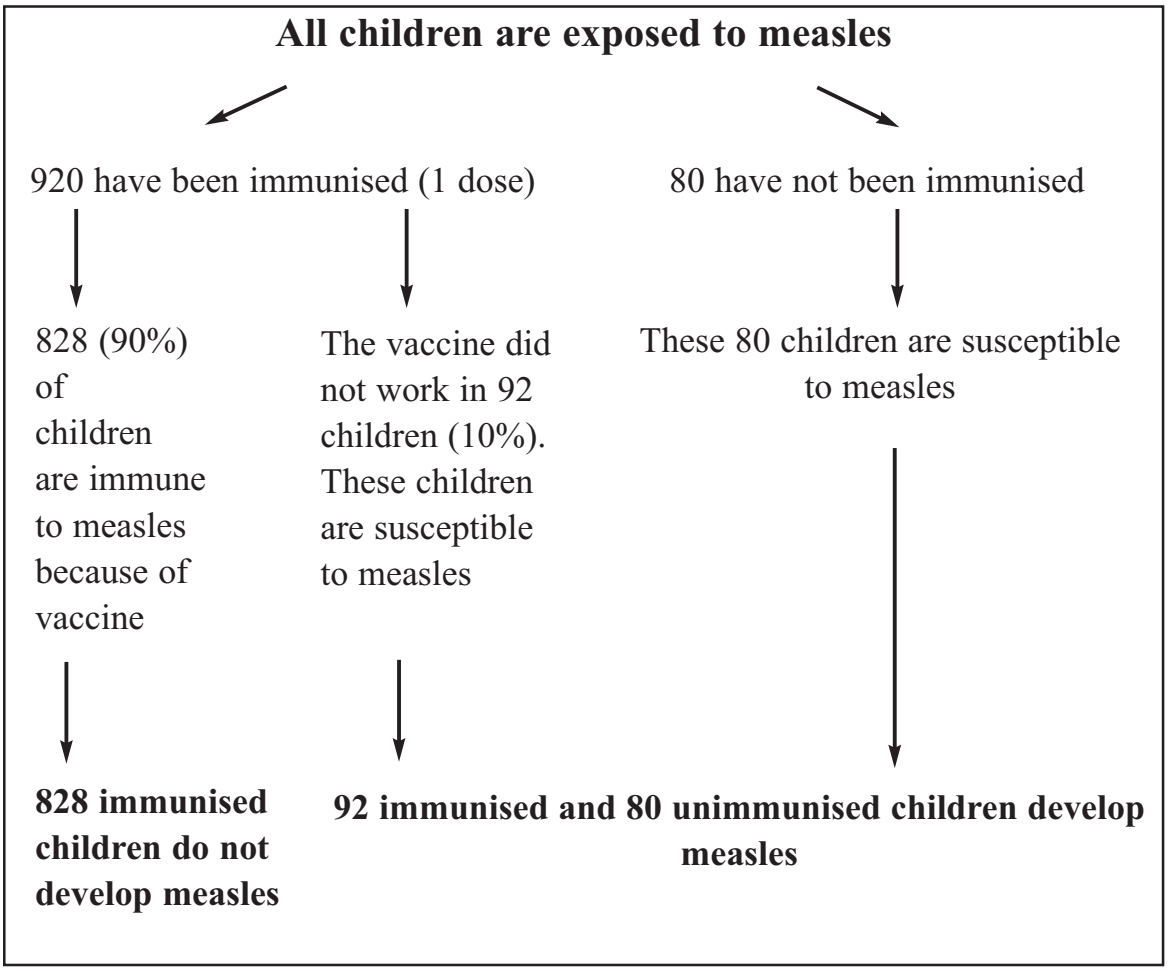
This is an argument frequently found in anti-vaccine literature – the implication being that this proves that vaccines are not effective. In fact it is true that in an outbreak those who have been vaccinated often outnumber those who have not – even with vaccines such as measles which are 99% effective when used as recommended.

This apparent paradox or contradiction is explained by two factors:

- Firstly no vaccine is 100% effective. For reasons related to the individual not all vaccinated persons develop immunity. The MMR vaccine is very effective with up to 99% of those receiving two doses developing immunity and 90% after one dose.
- Secondly in countries such as Ireland the people who have been vaccinated outnumber the people who have not.

How these two factors work together to result in outbreaks in which the majority of children have been vaccinated is explained below.

Example 1: In a school with 1000 students none have ever had measles.
920 children are immunised and 80 are not immunised.



It is important to note in this example that 828 children were protected against the disease and did not develop measles. All of those who were not immunised developed measles.

DOES THE MMR VACCINE CAUSE SERIOUS DISEASES?
(e.g. Autism, Crohn's disease)

Many researchers have actively investigated an alleged association between the MMR vaccine and autism or inflammatory bowel disease (Crohn's disease). The body of scientific evidence does not support the suggestion.

All of the scientific evidence has been assessed by the following expert groups who have all concluded that there is no link between the MMR vaccine and autism or bowel disease.

- National Immunisation Advisory Committee, Royal College of Physicians of Ireland
- Committee on Safety of Medicines (CSM)
- Joint Committee on Vaccination and Immunisation (JCVI)
- Medical Research Council (MRC) Expert Group
- United States Institute of Medicine
- American Academy of Pediatrics.

This is endorsed by the World Health Organisation (WHO) and the following professional organisations:

- Irish College of General Practitioners
- Faculty of Paediatrics, Royal College of Physicians of Ireland
- Faculty of Public Health Medicine, Royal College of Physicians of Ireland
- Irish Medical Organisation.

The Oireachtas Joint Committee on Health and Children in their Report on Childhood Immunisation (2001) concluded that:

- There is no evidence of a proven link between MMR and autism
- There is no evidence to show that the separate vaccines are any safer that the combined MMR vaccine
- Giving separate measles, mumps and rubella vaccines would leave children unnecessarily exposed and vulnerable.

AUTISM

Autism is a condition that involves delayed speech and communication. The first signs of autism tend to show at around 1-2 years of age. The MMR vaccine is also given around this age, so it is not surprising that some parents have linked the two events. **However, there is no evidence that MMR causes autism**.

The suggestion of a link between the MMR vaccine and autism was first made in a Danish TV programme in 1993, by a mother of twins, one of whom had autism, which the mother believed was caused by the MMR vaccine. At that time, no scientist had ever suggested a link.

In 1998, Dr Andrew Wakefield and colleagues in London published a paper in the Lancet describing 12 children with developmental and bowel problems. Eight of the children had autism, which the parents reported began soon after vaccination with MMR. The hypothesis put forward was that the MMR vaccine caused a leaky bowel. This allowed a toxin to enter which affected the brain and caused autism. This hypothesis is not proven, and the researchers themselves stated that they had not proven a link with MMR vaccine.

A number of studies have failed to demonstrate any link between MMR and autism. A UK study published in the Lancet in June 1999 by Taylor et al. looked at the immunisation records of 498 cases of autism, born between 1979 and 1998. They found no change in trends in autism after the introduction of MMR, no difference in the age at diagnosis between vaccinated and unvaccinated children and no clustering of developmental regression in the months after vaccination.

A Finnish study by Patja et al. that reviewed adverse drug reactions reported, after 1.8 million individuals were immunised with 3 million doses of MMR, that no case of inflammatory bowel disease or autism was linked to the vaccine during a long follow up period (1982-1996). An earlier paper by Peltola et al., using the same Finnish dataset, identified those vaccinees for whom gastro-intestinal (GI) symptoms were reported and traced them to check the prevalence of autism. Out of 31 children with GI symptoms none developed autism.

In February 2001, a UK study was published in the British Medical Journal by Kaye et al. The study reported a notable rise from 1988 to 1999 in the diagnosis of autism as recorded by UK general practitioners. Over that same time period there was no change in the proportion of children who had been vaccinated with MMR. The study authors concluded that these data provided no evidence to support a causal association between MMR vaccination and the risk of autism.

A paper in the Journal of the American Medical Association in March 2001 by Dales et al. compared trends over time in autism and in MMR immunisation coverage in California. The paper concluded that ‘these data do not suggest an association between MMR immunisation among young children and an increase in autism occurrence’.

In March 2001 the British Journal of General Practice published a paper by De Wilde et al. The authors looked at whether children who go on to be diagnosed as autistic are more likely to see their GP in the six months after MMR vaccination than other non-autistic children. The authors concluded that there is no change in consultation behaviour in autistic children and matched controls in the six months after MMR.

Further evidence supporting the absence of a causal link between MMR and autism was recently published in the British Medical Journal. The investigators (Taylor et al.) identified 278 children with autism and 197 with atypical autism born between 1979 and 1998 in London. The proportion of children with developmental regression or bowel symptoms did not change significantly during the study period, a period which included the introduction of MMR vaccination in October 1988. The authors concluded that the findings provide no support for an MMR associated 'new variant' form of autism with developmental regression and bowel problems.

CROHN'S DISEASE

The alleged link between the measles virus and Crohn's disease was first suggested in 1993, by Dr Andrew Wakefield and other researchers working at the Royal Free Hospital in London. However, since 1993, the body of scientific evidence has not supported the allegation.

The measles virus is not found in the gut affected by Crohn's disease, as was the original claim. This is based on work done by Afzal et al. using more sensitive tests than were used in the original research. Dr Wakefield has repeated his original work using more sensitive tests which confirmed that measles virus is not present in Crohn's disease.

A study to be published in Molecular Pathology in April 2002 by Uhlmann et al. investigated the presence of persistent measles virus in the gut of children with developmental disorders and inflammatory bowel disease. Although persistence of measles virus was found in 75 of 91 patients with bowel disease the lead author commented that 'the research did not set out to investigate the role of MMR in the development of bowel disease or developmental disorder, and no conclusions about such a role could, or should be, drawn from our findings'. An editorial by Morris accompanying the article also states that it would be entirely wrong to jump to the conclusion that the measles component of MMR 'causes' the colitis or the developmental disorder. The measles virus persistence could reflect the inability of patients with a developmental disorder to clear the virus.

The children of women who catch measles during pregnancy are not more likely to develop Crohn's disease, as was originally suggested by a study by Ekbom et al. of Crohn's disease in children born after measles epidemics in Sweden. A similar study in the UK by Thompson et al. found no such association. Two larger and more recent studies looked at a total of 73 individuals whose mothers had measles during pregnancy and showed that none of them developed Crohn's disease. (Jones et al., Nielson et al.)

Several large studies have not shown an increased risk of Crohn's disease after measles vaccination or MMR vaccination, i.e. individuals with Crohn's disease were no more likely to have had measles or MMR vaccine than individuals without Crohn's disease.

WHY HAS THE INCIDENCE OF AUTISM INCREASED IN RECENT YEARS?

An increase in autism has been commented on in recent years in many different countries. In the UK, one study reported a marked increase in the incidence of autism between 1988 and 1999, with no increase seen in the uptake of MMR. Thus MMR could not explain the rapid increase in the incidence of autism seen in the UK.

An American study compared the number of cases of autism reported during the years 1980 to 1994 in California with MMR immunisation rates over that time period. There was a sharp increase in the incidence of autism over these 14 years with only a small increase in MMR uptake over the same time period. They also found that the rapid increase in cases of autism began *before* the small increase in MMR rates and that the increase in autism continued even after MMR immunisation rates had stabilised.

It has been suggested that the reported increase in autism may be explained by changes in how autism is defined, with children with mild forms of disability now recognised as falling within the autistic spectrum, coupled with an increased awareness and diagnosis of the disease. There may, however, be other factors that are causing a real increase in the incidence of autism, particularly in its more severe form.

In summary although we don't know at present whether the increase in autism is due to factors such as increased awareness, changes in case definition or other environmental factors, we do know that it is not linked to the MMR vaccine.

WHAT DO WE REALLY KNOW ABOUT THE SAFETY AND SIDE EFFECTS OF THE MMR VACCINE?

No one claims that medicines and vaccines are without side-effects, but vaccines are among the safest treatments available today. The MMR vaccine has been used for 30 years with an excellent safety record. The MMR vaccine underwent extensive pre-market trials and has been through a licensing process which requires safety, quality and effectiveness to be carefully reviewed before a license is granted. Worldwide, over 500 million doses of the MMR vaccine have been given since the mid-1970s. The US has used over 200 million doses of the MMR vaccine routinely since the mid-1970s and the UK has given around 13 million doses since its

introduction in 1988. Post marketing surveillance is conducted globally to ensure that any potential problems with vaccines are detected. Side effects of the MMR vaccine are carefully researched and findings are published in professional journals. The safety of vaccines is regularly reviewed by independent expert groups who assess any new evidence. In Ireland these include the National Immunisation Advisory Committee of the Royal College of Physicians of Ireland and the Irish Medicines Board.

In Ireland there is continued surveillance of potential adverse effects by the Irish Medicines Board. Established adverse effects are fully described in the Immunisation Guidelines for Ireland, produced by the National Immunisation Advisory Committee of the Royal College of Physicians of Ireland, and distributed to all relevant health professionals.

Very rarely, MMR can cause serious adverse effects, but these adverse effects are significantly more common following the natural disease, as described above.

HOW DO THOSE WHO ARE UNVACCINATED PUT OTHER CHILDREN AT RISK OF DEVELOPING DISEASE?

After two doses of MMR vaccine 99% of children will be completely protected (i.e.) will have no risk of contracting measles, mumps or rubella. However 1 in 100 are not protected and could potentially contract these diseases. Thus, although vaccinated children are far less likely to contract the diseases, a small risk remains. This is why we try to ensure that at least 95% of children in the community are vaccinated. This produces what is known as “herd immunity” or population immunity, so that the 1 in 100 children who are not protected have little or no chance of coming in contact with a case of measles, mumps or rubella.

IF THESE DISEASES ARE SO RARE NOW WHY SHOULD CHILDREN BE IMMUNISED?

Immunisation has enabled us to reduce most vaccine preventable diseases to very low levels in Ireland. However some of these diseases are very prevalent in other parts of the world. Travellers can unknowingly bring these diseases into Ireland and they could quickly spread throughout the population causing outbreaks here if we were not protected by vaccination. Similarly the relatively small number of cases we currently get in Ireland would increase quickly without the protection that we get from vaccines. We should, therefore, continue to immunise our children to protect the children themselves and to protect those around us who cannot be vaccinated or who don’t respond to vaccines.

WHAT IS THE EVIDENCE THAT GIVING THE THREE COMPONENTS OF MMR AS SEPARATE VACCINES IS SAFER?

There is no evidence that doing this is safer. Nothing has been published that even suggests that giving the three vaccines separately would be any safer than giving the MMR combination. One of the authors of the Lancet paper of 1998 speculated to the press that giving the vaccines separately might be safer. No trials have been done to support this theory and no country in the world advocates the use of the three separate vaccines rather than the MMR vaccine. The World Health Organisation recommends the use of the combination MMR vaccine rather than the single vaccines.

WOULD THERE BE RISKS IF THE THREE COMPONENTS OF THE MMR VACCINE WERE GIVEN SEPARATELY?

The main risk associated with giving the vaccines separately is that it leaves children unprotected against these diseases for longer. It also means that children must return for six injections instead of two which can lead to reduced uptake. The use of three separate vaccines for measles, mumps and rubella has never been recommended in preference to MMR in any country in the world. There have been no studies done to determine whether or not this approach is safe or effective. Likewise there is no experience with using this approach. This raises a number of unanswered questions: Is this approach safe? Will it protect children against these diseases? In what order should the vaccines be given? How much time should be left between vaccine doses?

Some of the single mumps vaccines contain a strain of mumps virus known as the Urabe strain which has been shown to be associated with an increased number of cases of viral meningitis. Others use the Rubini strain which is of questionable efficacy. The MMR vaccine in current use does not contain either of these strains of mumps virus.

WHY DO OTHER COUNTRIES OFFER THREE SEPARATE VACCINES?

No country in the world recommends that MMR vaccine is divided into three separate injections or recommends that parents should have the choice of getting the three vaccines separately for their children.

Japan is often quoted as using single vaccines. They withdrew a strain of MMR in the early 1990s and have not licensed another strain yet. They offer single measles and rubella vaccines

to be given at the same time and they do not give mumps vaccine at all. Japan has seen 75 deaths from measles in recent years.

SHOULD SOME CHILDREN NOT BE GIVEN THE MMR VACCINE?

A small number of children should not be given the MMR vaccine:

- Those who have had an anaphylactic reaction to a previous dose of MMR vaccine or one of its components (gelatin, neomycin etc).
- Those with severe immune deficiency except selective IgA and complement deficiencies.
- Those with certain cancers (Hodgkin's disease, lymphoma etc.).
- Those on treatment causing suppression of their immune system.

The vaccine should be postponed in the following cases:

- Moderate or severe illness - postpone until recovery.
- Pregnancy - postpone for three months after delivery.
- Recent administration of blood or immunoglobulin – postpone for three months.
- Injection with another live vaccine within the previous three weeks.

GLOSSARY OF TERMS

Anaphylactic reaction: a severe life-threatening allergic reaction

Antigens: the chemicals that stimulate the immune system to produce immunity to viruses and other foreign substances

Attenuated: this means that the viruses in a vaccine have been modified so that they are extremely unlikely to cause disease symptoms in humans

Encephalitis: inflammation of the brain

Eradication: permanent elimination to zero

Immunisation: the process of inducing or providing immunity artificially

Neurological: affecting the nervous system

Notifiable disease: a disease which the diagnosing clinician is obliged by law to report to the local Medical Officer of Health

MMR: combination measles, mumps and rubella vaccine

Orchitis: inflammation of the testicles

Pancreatitis: inflammation of the pancreas

Rubella: German measles

Vaccination: the administration of any vaccine

Wild virus: non-vaccine strain

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