

# Measles, Mumps, Rubella (MMR) Vaccine discussion pack

an information guide for health professionals and parents



The Health Boards Executive  
*Working Together for Health*



# The MMR discussion pack

## an information guide for health professionals and parents

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Further copies of the leaflet *MMR your questions answered* may be obtained from local health board health promotion departments. Further copies of the pack contents may be downloaded from the Health Boards Executive, Health Boards, or NDSC websites. Website addresses are given at the back of the pack.

This information pack has been endorsed by the following organisations:  
Royal College of Physicians of Ireland, Irish College of General Practitioners, Department of Health and Children.





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## Introduction

Some parents may feel that the issues around immunisation, in general, and MMR in particular pose a real dilemma for them about what is best for their child. The sustained negative media coverage and high-profile public debates over the last few years have also left many health professionals asking searching questions about MMR. These concerns have contributed to a decrease in the uptake of MMR vaccine and the re-emergence of these diseases in our population.

*The MMR discussion pack* will help professionals and parents review the evidence around MMR and will help to provide the basis for informed decision-making. It sets out the facts about the most common concerns about MMR vaccine in a way that helps health professionals and parents to explore these concerns together.

Nine main questions are covered and each question outlines the basic facts plus *Key Notes* for parents, together with *Additional Notes* for health professionals, which are fully referenced. Whilst the *Additional Notes* are essentially for health professionals, the information is presented in such a way as to allow full discussion between health professionals and parents, on each issue.

The format allows for exploration of all the issues in any order and as much, or as little, of the information can be photocopied to take away, as desired.



How serious are measles,  
mumps and rubella?





# How serious are measles, mumps and rubella?

## Question 1

### Complications of measles:

- ear infection (1 in 20)
- pneumonia / bronchitis (1 in 25)
- convulsions (1 in 200)
- diarrhoea (1 in 6)
- meningitis / encephalitis (1 in 1000)
- conditions affecting blood clotting (1 in 6000)
- late onset subacute sclerosing panencephalitis (SSPE) (1 in 8000 children who get measles under 2 years)
- deaths (1–2 deaths in 1000 reported cases in recent years).

### Complications of mumps:

- viral meningitis (1 in 20)
- encephalitis (1 in 1000)
- inflammation of testicles (4 in 10 adult males)
- permanent hearing loss (1 in 20 000).

### Complications of rubella (German measles):

- encephalitis (1 in 6000)
- birth defects (90% chance baby will have birth defects if mother catches rubella early in pregnancy). Birth defects include blindness, deafness, learning difficulties and heart disease
- conditions affecting blood clotting (1 in 3000).



### Measles

- 1 Measles accounts for one million deaths every year worldwide in children under five years old.
- 2 Measles is difficult to diagnose accurately, as other viral infections can be mistaken for measles.
- 3 Measles is transmitted by coughs and sneezes and it is extremely infectious. Cases are highly infectious even before the appearance of a rash. Cases have a high temperature, cough, conjunctivitis and generally feel miserable for days.
- 4 Serious complications have been reported in 1 in 15 notified cases in the UK.
- 5 Conditions affecting blood clotting can occur in 1 in 6000 cases.
- 6 Complications are more common and severe in chronically ill children.
- 7 In recent years, 1-2 people in every 1000 with reported measles infection died from it. Death from measles is highest in children under one year - a group too young to receive the MMR vaccine- and in those who are immunosuppressed due to disease (e.g. leukaemia) or treatment (e.g. organ transplantation). These children can only be protected through the 'population protection' of high vaccine uptake.
- 8 The serious risks associated with measles are not always appreciated.

## Mumps

- ① Cases will have fever, headache, swelling of one or both cheeks or sides of the jaw and swollen glands, which can last up to 7-10 days.
- ② 4-6% of people with mumps will have viral meningitis.
- ③ 1 in 1000 cases will have encephalitis.
- ④ 4 in 10 adult males with mumps will have inflammation of the testicles.
- ⑤ Hearing loss, which may be permanent, may occur.
- ⑥ Death is very rare.

## Rubella

- ① This is generally a mild disease that causes a rash and fever for 2-3 days.
- ② 1 in 6000 cases will have encephalitis.
- ③ Major birth defects are highly likely to occur to the foetus of a pregnant woman who has the disease just before conception or early in pregnancy. These birth defects include blindness, deafness, learning difficulties and heart disease.

### Measles

- 1 Measles causes 10% of all deaths worldwide amongst children aged five years and under, which is the equivalent of one million deaths annually.<sup>1</sup>
- 2 The incidence of measles has fallen since the introduction of MMR. Although the uptake of vaccine has not been sufficient to eliminate measles, the size of epidemics has reduced and the interval between epidemics increased. In non-epidemic circumstances measles is difficult to diagnose accurately. Therefore, mild viral illnesses causing a rash may be labelled as measles.
- 3 Measles is an acute viral illness transmitted by respiratory droplets, and is extremely infectious. Clinical features include conjunctivitis, bronchiolitis, Koplik spots, rash and fever. The incubation period is about 10 days, with a further 2-4 days before the rash appears. Measles is highly infectious before, and up to four days after, the appearance of the rash.
- 4 Serious complications have been reported for 1 in 15 notified cases.<sup>2</sup>
- 5 Complications are more common and severe in chronically ill children. It is therefore particularly important that children with chronic conditions (such as cystic fibrosis, congenital heart or kidney disease and failure to thrive) and with Down's Syndrome are fully immunised, including vaccinations against measles, mumps and rubella. A serious complication of measles in children is subacute sclerosing panencephalitis (SSPE).<sup>3</sup> 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.

- 6 Case fatality rates for measles are age related and so rates vary depending on the particular age at infection. On average, between 1 in 2500 and 1 in 5000 cases die from measles.<sup>2,4</sup> However, in recent years, deaths from measles have been reported as approximately 1-2 per 1000 reported cases in the United States.<sup>5</sup> 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. There were three deaths in over 1600 reported cases in Ireland and three deaths in 2961 reported cases (1 in 1000) in The Netherlands.<sup>6,7</sup> Eight deaths from measles were reported to the Central Statistics Office in Ireland for the ten year period 1990 to 1999 (Source CSO).

The risk of death is significantly higher in children under one year of age (this group are not offered the vaccine as they are too young and can only be protected through the 'population protection' of high vaccine uptake). The figures are lowest in children aged 1-9 years and then rise again with increasing age.

In children receiving immunosuppressive treatment, e.g. for leukaemia or after organ transplantation, measles was a major cause of morbidity and mortality. Between 1970 and 1983, 19 children with acute lymphatic leukaemia died from measles in England and Wales.<sup>4</sup> A study conducted at four UK hospitals between 1974 and 1984 identified 1043 children with acute lymphoblastic leukaemia. Fifty one of these children died while in first remission and 15 of these deaths were due to measles or its complications (10 deaths from pneumonia and 5 from encephalitis). The study recommended that 'population protection' through high vaccine uptake in the community is vital to protect immunosuppressed children against measles with severe complications and possible death.<sup>8</sup>

- 7 Younger parents tend to have less knowledge and experience of measles.<sup>9</sup> Some view illnesses such as measles and mumps as mild diseases that benefit the child in the long run. This view ignores the complications and risks associated with measles in particular. Older people may have had personal experience of measles and may know a lot more about the risks associated with it.

## Mumps

- 1 Mumps is an acute viral disease transmitted by respiratory droplets. Clinical features include parotitis, fever and headache. The incubation period is about 12-25 days, with the fever usually lasting 1-6 days, and parotitis for up to 10 days or more.
- 2 Mumps can have serious complications, including viral (aseptic) meningitis, encephalitis, inflammation of the testes (orchitis), pancreatitis and permanent deafness.<sup>10</sup> Neurological involvement occurs in 10-20% of cases and may precede or follow parotitis, and can also occur in its absence.
- 3 Inflammation of the testes is the most common complication of mumps in adult males (4 out of 10 cases).<sup>11</sup> Approximately half of these cases may have some testicular atrophy. Reports of sterility are rare, but increased risk of testicular cancer has been reported.
- 4 Mumps can cause permanent deafness, usually unilateral, at any age and is one of the main causes of acquired sensorineural deafness in childhood. The incidence is estimated at 1 in 20 000 cases.<sup>12</sup>
- 5 Fulminant encephalitis is a rare, but potentially fatal complication of mumps. In the years 1971-1981, 13 deaths from mumps encephalitis were registered in England and Wales.<sup>10</sup>
- 6 Death is a rare outcome of mumps. A total of 93 deaths from mumps were registered for 1962-1981 in England and Wales, an average of five per year.<sup>10</sup> Inspection of death certificates of the 38 deaths registered in 1971-1981 showed that 16 were indeed probably due to mumps; in 13 the diagnosis was mumps encephalitis. There have been no recorded deaths from Mumps in Ireland in the years 1980-2000 (Source CSO).

## Rubella

- ① Rubella is generally a mild illness with a rash developing after a 14 to 21-day incubation period. Complications of arthritis and arthralgia can occur in adults especially women. Encephalitis occurs in approximately 1 in 6000 cases and can be fatal. Clinical diagnosis of rubella is often inaccurate.
- ② Rubella if acquired by mothers in early pregnancy, can have devastating effects on unborn children.<sup>13</sup> The virus affects all fetal organs and can lead to serious birth defects. These include learning difficulties, cataracts, deafness, cardiac abnormalities, retardation of intrauterine growth and inflammatory lesions of the brain, liver, lungs and bone marrow. Any combination of these defects may occur and when relatively mild, or a single organ is affected, the link with rubella may not be recognised.
- ③ The likely outcome of infection in pregnancy is related to the time of gestation.<sup>13</sup> Maternal rubella infection in the first 10 weeks of pregnancy results in foetal damage in up to 90% of infants and multiple defects are common (Congenital Rubella Syndrome). The risk of damage declines to about 10-20% by 16 weeks. Rubella between 16 and 20 weeks carries a minimal risk of deafness only.<sup>14</sup> Rubella after 20 weeks carries no documented risk.



How does the  
MMR vaccine work?



## How does the MMR vaccine work?

### Question 2

- The MMR vaccine contains weakened forms of the natural viruses to give protection against disease without the risks associated with natural infection.
- The vaccine causes the child's immune system to respond to and 'remember' the viruses in the vaccine. This means that if the child is later infected with the real viruses these are very quickly recognised by the immune system which reacts rapidly to halt the infection.
- MMR vaccination provides long lasting immunity.
- Vaccination can also provide 'population protection' if vaccination uptakes are sufficiently high.



- 1 The MMR vaccine contains weakened forms of the natural viruses to give protection against disease without the risks associated with natural infection. MMR vaccine contains measles, mumps and rubella viruses that have been modified so that they no longer 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 non-infectious version of the illness.
- 2 A child will be injected with the vaccine and this causes the immune system to respond and destroy the vaccine viruses. The immune system 'remembers' the virus so that there is a prompt response if exposure occurs again. The viruses in the vaccine and the natural viruses are very similar so the immune system responds to both. Therefore if a child is later infected with the real viruses these are very quickly recognised by the immune system which reacts rapidly to halt the infection.

MMR vaccine is routinely given as:

**first dose:** by injection at 12-15 months, usually on its own

**second dose:** by injection as part of the school entry programme at age 4-5 years or in 6th class in primary school if the child has not already had a second dose.

- 3 The level of effectiveness varies for the different components of the MMR vaccine:
  - 90-95% of people will be immune to measles after the first dose
  - 90-95% of people will be immune to mumps after the first dose
  - 97-99% of people will be immune to rubella after the first dose.
- 4 MMR can protect children in three ways:
  - individual protection
  - 'population protection'
  - potential eradication of diseases.



- 1 MMR is a live vaccine - it contains measles, mumps and rubella viruses that have been modified (or attenuated) so that they no longer 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. The viruses have been attenuated by growing successive generations of the virus under specially modified conditions that select for these mild strains.
- 2 A child will be 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 (lymphocytes) 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 natural viruses are very similar, the immune system responds to both. This means that if a child is later infected with the real viruses, these are very quickly recognised by the immune system and large numbers of antibodies are produced rapidly to halt the infection.
- 3 The immune response to vaccination is very similar to natural infection, with induction of both humoral and cell-mediated immunity. 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 natural 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.<sup>15</sup> 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.<sup>16</sup>

4 There are three methods of protection:

- (a) *individual protection*: one dose of MMR vaccine will provide immunity against measles and mumps in at least 90% of those vaccinated and against rubella for at least 95%.<sup>5,17</sup> A second dose of vaccine has been shown to increase protection significantly. Those who do not seroconvert after the first dose have a 90-95% chance of seroconverting after a second dose. If a child did not respond the first time, he or she remains susceptible to natural infection, and needs the second dose.
- (b) *population protection* (also known as 'herd immunity'): whereby if someone incubating measles (or mumps or rubella) has contact with others in the community, measles (or mumps or rubella) will not spread as the chances of being in contact with someone who is not immune is so small. Children who cannot be immunised (e.g. those with leukaemia, cancer or immunosuppressive treatment) depend on high 'population protection' for their personal protection,<sup>8</sup> as do children under one year of age. They are not offered MMR vaccination because the vaccine is less effective in children under one year old, due to interference from maternally derived transplacental antibodies.<sup>18</sup> Women who have not been immunised against rubella depend on high 'population protection' to prevent them from catching rubella and from their babies being damaged.
- (c) *potential eradication of disease*: The World Health Organization concluded in 1996, that measles eradication is feasible through immunisation.<sup>19</sup> Smallpox has already been eradicated by vaccination and rapid progress is being made towards eradication of poliomyelitis (polio), through immunisation.<sup>20</sup>

Has the MMR vaccine  
made a difference?

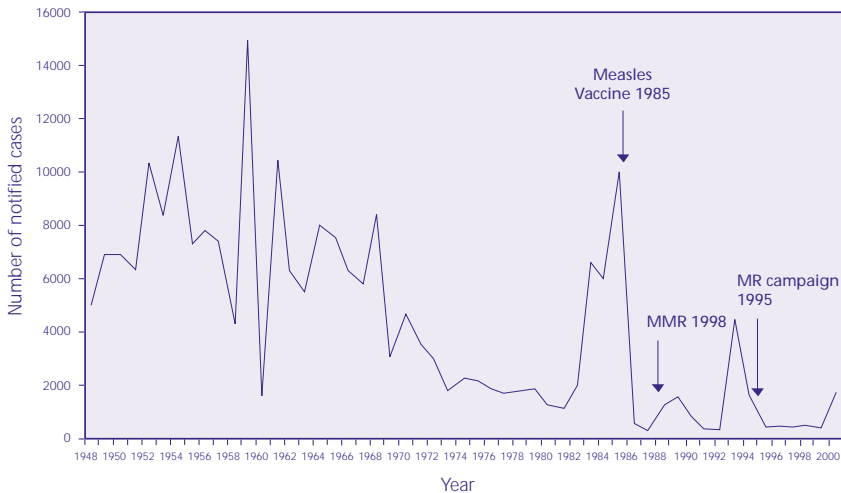




# Has the MMR vaccine made a difference?

## Question 3

**Graph 1:**  
Measles notifications and introduction of vaccine Ireland, 1948-2000

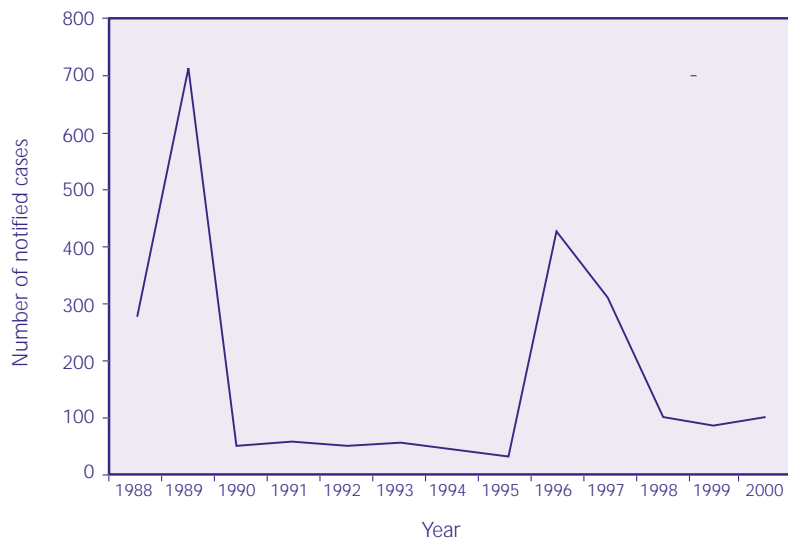


Measles vaccine was introduced in 1985. In 1988 the combined MMR vaccine was introduced.

In 1992, a second dose of MMR was recommended for both boys and girls aged 10-14 years. This replaced the previous selective rubella vaccination programme for prepubertal girls, which had been introduced in 1971. A measles and rubella (MR) vaccination campaign for primary school-age children was conducted in 1995. In 1999 the Immunisation Advisory Committee of the Royal College of Physicians of Ireland advised changing the age of the second dose of MMR to 4-5 years.

The introduction of measles vaccine and the MMR vaccine has led to a decrease in the number of measles notifications. However the uptake of MMR in Ireland is not high enough to prevent a build up of susceptible children with consequent outbreaks in 1993 and 2000.

**Graph 2:**  
Mumps notifications Ireland, 1988-2000

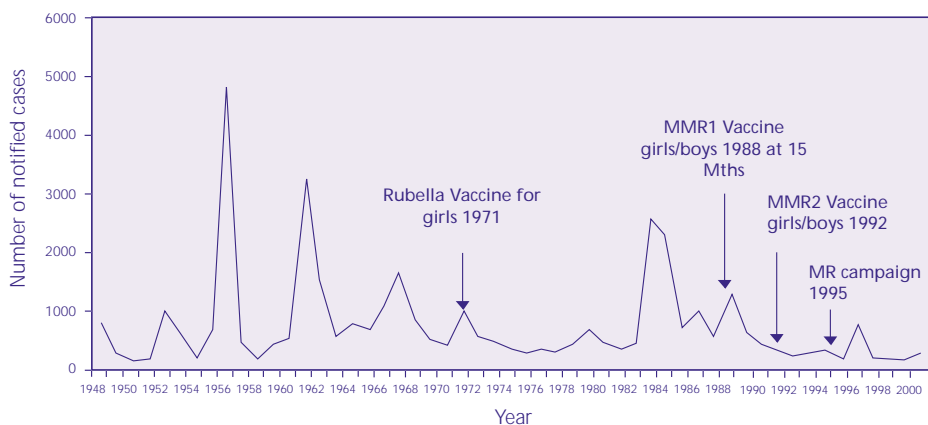


Protection against mumps was first offered in 1988, with the introduction of the MMR vaccine, the same year that mumps became a notifiable disease.

In 1992, a second dose of MMR 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 MMR vaccine has led to a decrease in the number of cases of mumps but outbreaks will continue to occur if vaccine uptake rates do not improve.

**Graph 3:**  
Rubella notifications Ireland, 1948-2000



Rubella vaccine for prepubertal girls was introduced in 1971. This policy allowed wild rubella virus to circulate among younger children and older boys. Because this policy did not totally prevent rubella in pregnant women, the policy was changed to vaccinate both boys and girls.

Rubella vaccine was first included in the infant immunisation programme with the introduction of the MMR vaccine in 1988. A measles and rubella (MR) vaccination campaign for primary school-age children was conducted in 1995. In 1992, a second dose of MMR was recommended at age 10-14 years.

Vaccination of both boys and girls against rubella at a young age has led to a decrease in rubella notifications.



### Measles (see Graph 1)

- 1 Before immunisation became widely available thousands of children caught measles each year in Ireland.
- 2 The introduction of measles vaccine and the MMR vaccine has led to a decrease in the number of measles notifications. However the uptake of MMR in Ireland is not high enough to prevent a build up of susceptible children with consequent outbreaks in 1993 and 2000.
- 3 Over 1600 cases of measles were notified in Ireland in 2000. This compares with less than 100 in the United States in 2000, where measles is close to elimination due to good uptake of MMR vaccine. Measles has also been eliminated or is close to elimination in Finland, Spain and other European countries where there is good uptake of vaccines. However measles remains a problem where vaccination rates are low. In Ireland 8 deaths from measles were reported to the CSO between 1990 and 1999. In the outbreak in 2000 three children in Dublin died (two died from pneumonia complicating measles and a third child died from post-infectious encephalitis)

### Mumps (see Graph 2)

Before the MMR vaccine introduction, mumps was a leading cause of viral meningitis in children.

## Rubella (see Graph 3)

- ① Since the MMR vaccine introduction in 1988, the MR campaign in 1995 and the introduction of a second dose of MMR in 1992, notifications of rubella have decreased. There is a longer interval between outbreaks and the size of outbreaks is less than half the size of the outbreaks before the vaccine. In order to prevent these outbreaks we need to have 95% uptake of two doses of MMR vaccine.
- ② Both girls and boys must be vaccinated against rubella at a young age to stop rubella virus spreading in the community and infecting pregnant women.
- ③ MMR has decreased congenital rubella births by stopping children spreading rubella to pregnant women.

Congenital rubella cases in Ireland -

*1975-1980: 76 cases of congenital rubella; an average of 13 cases per year.*

*1981-1990: 30 cases of congenital rubella; an average of 3 cases per year.*

*1991-2000: 2 cases of congenital rubella.*

### Measles

- 1 In the 1950s an average of 8,500 cases of measles were reported each year. In the 1970s an average of seven children died every year from measles in Ireland. Eight deaths from measles were reported to the CSO between 1990 and 1999. In the Dublin outbreak in 2000 three children died from complications of measles (two from pneumonia and a third from encephalitis).<sup>6</sup>
- 2 Measles vaccine was introduced in 1985 and MMR in 1988. The uptake of these vaccines however never reached the 95% target and outbreaks continued to occur in 1993, 1994 and again in 2000. Measles continued to claim the lives of eight people in Ireland in the 1990s.
- 3 When the MMR vaccine was introduced in 1988 in the United Kingdom, vaccination uptake quickly rose to above 90%. By 1992 there were less than 10,000 notifications and an average of one death each year in the UK. Following the MR campaign in 1994, and the introduction of the second MMR dose pre-school in 1996, measles became rare in the UK, mostly occurring as single cases or small outbreaks following importation of the disease from abroad.
- 4 Since the beginning of 1999 in Scotland, doctors notifying cases have been asked to collect a sample of saliva to check whether the individual genuinely has measles. Between 20 and 50% of all cases have been tested. In 1999 there were only two confirmed cases, and three in 2000.<sup>21</sup> Measles has therefore almost been eliminated in Scotland due to high MMR vaccine uptake.
- 5 The incidence of measles in different countries correlates with the level of vaccine uptake. In countries and regions where uptake is high, the incidence of measles is low, and vice versa.<sup>22</sup>
- 6 If MMR coverage drops, outbreaks of measles, mumps and rubella will occur. Low vaccine uptake has led to outbreaks of measles in Ireland <sup>6</sup> and The Netherlands,<sup>7</sup> and also in some UK communities with low vaccine uptake.<sup>23</sup>

## Mumps

- 1 Protection against mumps was first offered in October 1988 with the introduction of the MMR vaccine. Mumps then also became a notifiable disease. In 1989 there were 709 mumps notifications. A decade later, in 1999, there were only 38 notifications. However, the vaccine uptake never reached the target of 95% resulting in outbreaks, in 1996 (422 cases) and 1997 (285 cases), occurring in primary school children.

## Rubella

- 1 The incidence of rubella declined in the 1990s following the introduction of MMR vaccine in 1988 (8426 cases notified in the 1980s versus 1889 cases in the 1990s). An outbreak in 1996 occurred predominantly in teenage boys and young male adults who had never been vaccinated. In 1999 there were outbreaks at several British universities, including Aberdeen, and links with a concurrent outbreak in Greece have been proposed.<sup>24</sup> This reinforces the need to maintain high levels of vaccine uptake throughout the community, particularly in order to protect pregnant women and unborn children.
- 2 The main aim of rubella vaccination is to protect pregnant women against rubella, resultant congenital infection and fetal damage. This is why the rubella vaccine was introduced in 1971 for immunisation of schoolgirls and non-immune women of child-bearing age. However, this strategy had little impact on the circulation of rubella in the community. Therefore, both boys and girls were offered protection against rubella when the MMR vaccine was introduced in 1988.
- 3 In Ireland 106 cases of congenital rubella were recorded between 1975 and 1990. Seventy-six were reported from 1975-1980, compared with 30 from 1981-1990 <sup>25</sup>. There was a dramatic decrease in congenital rubella following the introduction of the MMR vaccine in 1988. In the interval 1991- 2000 only two cases were reported from Ireland to the British Paediatric Surveillance Unit (Provisional figures, personal communication).

Does the MMR vaccine  
cause serious diseases?  
(eg Autism, Crohn's disease)



## Does the MMR vaccine cause serious diseases (e.g. Autism, Crohn's disease)?

### Question 4

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

All 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.

- Department of Health and Children.
- National Immunisation Committee, Royal College of Physicians of Ireland.
- National Disease Surveillance Centre.
- Irish Medicines Board (IMB).
- UK Committee on Safety of Medicines (CSM).
- UK 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 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 than the combined MMR vaccine.
- Babies are very susceptible to measles, mumps and rubella, which are killer diseases, so they must be protected as soon as possible and this can only be done with the 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 with other intellectual impairment. 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.

A UK study of 498 autistic children did 'not support a causal association between MMR vaccine and autism'. It found that:

- there was no clustering of autistic regression after MMR.
- MMR did not affect the age at diagnosis of autism.
- reports of autism were increasing before MMR was introduced and there was no sudden 'step up' in autism or change in trend after introduction of MMR.
- MMR uptake was the same for autistic children as for the general population.

These findings are supported by other studies.

- No cases of autism or inflammatory bowel disease were linked to the MMR vaccine given to 1.8 million individuals in Finland from 1982 to 1996.
- There was no increase in cases of autism in the 10 years during which the MMR vaccine was introduced in Sweden.
- A study in England of 201 autistic children born after 1987 and likely to have had the MMR vaccine showed none to have had inflammatory bowel disease.
- Uptake of MMR was constant during an increase in the diagnosis of autism by a UK GP in 1988-1999.
- A Californian study has shown no correlation between MMR vaccine uptake and increasing numbers of children with autism.
- The UK Committee on Safety of Medicines (CSM) has evaluated over 100 cases of autism collected by solicitors. They concluded the information available did not support the suggested association between the MMR vaccine and autism.

## Crohn's disease

Crohn's disease (Crohn's) is a chronic inflammatory bowel disease that can affect any part of the gastro-intestinal tract. At least 30 or 40 different factors have been linked to this illness.

- The evidence used to support an alleged link between measles virus and Crohn's has now proved incorrect. Independent researchers have not been able to find evidence of measles virus in the gut affected by Crohn's.
- The children of women who catch measles during pregnancy are not more likely to develop Crohn's, as was originally suggested.
- Large studies do not show an increased risk of Crohn's after measles or MMR vaccination.
- In the UK the incidence of Crohn's started to rise before measles vaccine was introduced in 1968.

## Autism

- 1 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 at the Royal Free Hospital in London published a paper in the *Lancet* describing 12 children with developmental and bowel problems.<sup>26</sup> 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. Experts from the WHO concluded that the study 'fails at every level to make a causal association'.<sup>27</sup> The preliminary report was followed by a more extensive analysis of 60 children, including those from the first report, but did not investigate MMR vaccination.<sup>28</sup>
- 2 The first step in the hypothesis requires that MMR damages the bowel. As explained under Crohn's disease, there is good evidence that neither measles nor MMR causes bowel disease, and children with autism are not more likely than other children to develop Crohn's disease.<sup>29</sup> The bowel changes described in the cases are not unique, and are found in other children investigated for bowel problems who do not have autism.<sup>30</sup> The research group is well known for their interest in this area and it is therefore very likely that parents who believe in a vaccine link will be seen by the group (ascertainment bias). Also, the first symptoms of autism are extremely subtle and it is possible that the parents of the children studied had incorrectly recalled the time of onset of the first symptoms and linked it to the MMR vaccination, especially if they also believed the vaccine was to blame (recall bias).
- 3 Autism affects nearly 1/1000 children and usually starts at age one or two years, around the time MMR is given.<sup>31</sup> Over the eight years from which the 1998 *Lancet* study collected cases, there would have been around 400 children who develop autism completely by chance within two months of the MMR vaccination.<sup>32</sup> The eight cases reported in the *Lancet* study<sup>26</sup> therefore represents a small fraction of the cases of autism whose onset coincides with giving MMR vaccine.<sup>32</sup>
- 4 A 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.<sup>33</sup> They found no sudden 'step up' or change in trend after the introduction of MMR; no difference in the age at diagnosis between vaccinated and unvaccinated children; no association between the onset of autism within 18 months after MMR; and no clustering of developmental regression in the months after vaccination.

The researchers also looked at onset of parental concern in 12 time periods, between 1 and 12 months after vaccination. No clustering of parental concern was found, with the exception of the one time period,

within six months after vaccination. However, further analysis suggested this was an artefact, resulting from many MMR vaccinations being given at 13 months, and the selection of 18 months as an approximation for onset of concern. They concluded that their findings did not support a causal association between the MMR vaccine and autism. Furthermore, the authors later re-analysed the data in response to a change in hypothesis and found there to be no link between MMR and autism at any time period examined after vaccination.<sup>34</sup>

- 5 In December 2000, Patja et al published the results of a Finnish study that reviewed adverse drug reactions (ADRs) reported after 1.8 million individuals were immunised with 3 million doses of MMR, since 1982.<sup>35</sup> No case of inflammatory bowel disease or autism was linked to the vaccine during a long follow up (1982-1996) of those specific cases. An earlier paper by Peltola, 1998 in the *Lancet*, 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.<sup>36</sup>
- 6 A study in Sweden showed that over a decade when MMR was introduced around the mid point, the incidence of autism did not rise as a result of MMR.<sup>37</sup>
- 7 In February 2001, a study was published in the *British Medical Journal* by Kaye et al. The study reported that there was a notable rise from 1988 to 1999 in the diagnosis of autism 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, which remained at over 95% for the age groups and children in this study. The study authors concluded that these data provided no evidence to support a causal association between MMR vaccination and the risk of autism.<sup>38</sup>
- 8 A paper in the *Journal of the American Medical Association* in March 2001 by Dales et al. compared time trends in autism and in MMR immunisation coverage in California. The study reported no correlations between the trend of early childhood MMR immunisation rates and the trend in numbers of children with autism. For the 1980-1994 birth cohorts a marked and sustained increase in autism case numbers was noted, but changes in early childhood MMR immunisation coverage over the same period were much smaller and of shorter duration. The paper concluded that 'these data do not suggest an association between MMR immunisation among young children and an increase in autism occurrence'.<sup>39</sup>
- 9 In March 2001 the *British Journal of General Practice* published a paper by DeWilde 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.<sup>40</sup>

- 10 Further evidence supporting the absence of a causal link between MMR and autism was published in the *British Medical Journal* in February 2002.<sup>41</sup> The investigators identified 278 children with core autism and 197 with atypical autism born between 1979 and 1998 in northeast London. Information was abstracted from clinical notes and then linked to independent computerised vaccination records. The proportion of children with developmental regression (25% overall) or bowel symptoms (17%) did not change significantly during the 20 year period from 1979, a period which included the introduction of MMR vaccination in October 1988. No significant difference was found in rates of bowel problems or regression in children who received the MMR vaccine before their parents became concerned about their development (where MMR might have triggered the autism with regression or bowel problem), compared with those who had not received the MMR vaccine. The authors concluded that the findings provide no support for an MMR associated 'new variant' form of autism with developmental regression and bowel problems, and further evidence against the involvement of MMR vaccine in the initiation of autism.

## Crohn's disease

- 1 The alleged link between the measles virus and Crohn's was first suggested in 1993, by Dr Andrew Wakefield and other researchers working at the Royal Free Hospital in London.<sup>42</sup> The link was based on the similarities between Koplik spots (an early sign of measles) and ulcers in Crohn's. However, since 1993, the body of scientific evidence has not supported the allegation.
- 2 The measles virus is not found in the gut affected by Crohn's, as was the original claim. This is based on work done using more sensitive tests than were used in the original research.<sup>43</sup> Dr Wakefield has repeated his original work using more sensitive tests which confirmed that measles virus is not present in Crohn's.<sup>44</sup>
- 3 The children of women who catch measles during pregnancy are not more likely to develop Crohn's, as was originally suggested by a study of Crohn's in children born after measles epidemics in Sweden.<sup>45</sup> A similar study in the UK found no such association.<sup>46</sup> A Swedish study found four individuals whose mothers had measles during pregnancy, three of which developed Crohn's.<sup>47</sup> However, two of these cases were known to the research team before the research began, potentially introducing bias into their findings. Two larger and more recent studies looked at a total of 73 individuals whose mothers had measles during pregnancy, and none of them developed Crohn's.<sup>48,49</sup>
- 4 Dr Andrew Wakefield, and others at the Royal Free Hospital, also suggested that the weakened (attenuated) live virus used in single antigen measles and MMR vaccine could cause Crohn's.<sup>50</sup> Again, the evidence used to support this view has not been confirmed by more recent research.<sup>51-55</sup>

- 5 The original study by Thompson and colleagues found the incidence of Crohn's in children who were given measles vaccine in 1964 was higher than in another group recruited in 1958.<sup>50</sup> However, the study had serious flaws. The groups were recruited in different ways, at different times, came from different areas, the questions used to identify those with a history of Crohn's were different, and Crohn's was defined differently for each group. It was only possible to trace 26% of the measles vaccine group, compared to 66% of the comparison group and it is quite likely that those with Crohn's are more likely to stay in touch with medical services and this on its own might explain the apparent increased incidence. This led independent researchers to conclude that because of these many important differences between the groups studied, Crohn's could not be linked to measles vaccine. The *British Medical Journal* concluded in 1998 that the hypothesis could not be upheld.<sup>56</sup> The World Health Organization also concluded that the evidence did not support a link.<sup>51</sup>
- 6 Several large case control studies have not shown an increased risk of Crohn's after measles vaccination or MMR vaccination, i.e. individuals with Crohn's were no more likely to have had measles or MMR vaccine than individuals without Crohn's.<sup>52,54,55</sup>
- 7 In the UK, the incidence of Crohn's started to rise before measles vaccine was introduced in 1968.<sup>57</sup> In fact, if Crohn's was linked to the measles virus we might have expected to have seen a fall in the number of cases by now, because vaccine protects against complications of wild virus infection. By analogy, the brain disease SSPE is caused by wild measles virus but is now rare because vaccination has resulted in fewer cases of infection with wild virus.<sup>3</sup>
- 8 A study to be published in *Molecular Pathology* in April 2002 investigated the presence of persistent measles virus in the gut of children with developmental disorders and inflammatory bowel disease<sup>58</sup>. They found persistence of measles virus in 75 of 91 patients with bowel disease compared to five of 70 controls. However, Dr O'Leary, lead author, commented "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".<sup>59</sup> An editorial accompanying the article 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.<sup>60</sup>

What do we really know  
about the safety and side-effects?





# What do we really know about the safety and side-effects of MMR?

## Question 5

- The MMR vaccine has been used for 30 years with an excellent safety record.
- 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.
  - The UK has given around 13 million doses since its introduction in 1988.
- Side-effects of the MMR vaccine are carefully researched and findings are published in professional journals.

The table below compares the serious effects of the disease and reactions to MMR.

condition	children affected after the natural disease	children affected after the first dose of MMR
Febrile convulsions (temperature fits)	1 in 200 (measles)	1 in 1000
Meningitis/encephalitis	1 in 1000 (measles, mumps encephalitis) 1 in 20 (mumps meningitis) 1 in 6000 (rubella encephalitis)	less than 1 in 1 000 000
Conditions affecting blood clotting (ITP)	1 in 3000 (rubella) 1 in 6000 (measles)	1 in 22 000
Severe allergic response (anaphylaxis)	-	1 in 100 000
SSPE (a delayed complication of measles that causes brain damage and death)	1 in 8000 (children who get measles under 2)	0
Death	1 in 2500 to 1 in 5000 (measles - higher in children under 1) 1–2 in 1000 for notified cases of measles in recent years	0

Table 1: Rates of conditions after the natural disease and after the MMR vaccine

- Continued surveillance of potential adverse effects by the Irish Medicines Board – ‘Yellow Card Scheme’.
- Specialist information on all established side-effects is distributed to all health professionals.
- Independent expert groups regularly review evidence.
- MMR vaccines have been through a licensing process which requires safety, quality and effectiveness to be carefully reviewed before a licence is granted.
- All medicines can cause side-effects, but vaccines are among the safest.

## What do we really know about the safety and side-effects of MMR?

### Key Notes

- 1 The MMR vaccine has been used worldwide for 30 years with an excellent safety record.
- 2 Extensive research continues to be published in peer-reviewed (i.e. independently checked before publication) professional journals.
- 3 Manufacturers provide guidance including contraindications and side-effects in their data sheets for health professionals. All healthcare professionals including doctors, nurses and pharmacists are routinely reminded to report suspected adverse reactions including side-effects of vaccines to the Irish Medicines Board (Yellow Card Scheme).
- 4 Established adverse effects are fully described in *Immunisation Guidelines for Ireland*, produced by the National Immunisation Committee of the Royal College of Physicians of Ireland, and distributed to all relevant healthcare professionals.
- 5 The safety of vaccines is regularly reviewed by independent expert groups who assess any new evidence. These include the National Immunisation Committee and the Irish Medicines Board.
- 6 Before any vaccine is licensed for use it has been through a licensing process which requires quality, safety and effectiveness to be carefully reviewed.
- 7 No one claims medicines and vaccines never have any side-effects, but vaccines are among the safest treatments.
- 8 Anyone becoming ill after a vaccination may naturally think the vaccine caused it. Studies show many illnesses that occur shortly after immunisation are coincidental.
- 9 Very rarely, MMR can cause serious adverse effects, but adverse effects are significantly more common following the natural disease.
- 10 The risk of side-effects is 10 times lower with a second dose of MMR vaccine.



- 1 MMR has been used around the world for 30 years, with an excellent safety record. Worldwide, over 500 million doses of MMR have been given since the mid-1970s. The US alone has used over 200 million doses of MMR routinely since the mid-1970s. The UK has given around 13 million doses since its introduction in 1988.

A two-dose MMR programme (very similar to the current Irish programme) was started in Finland in 1982. A study was published in December 2000, which identified serious adverse events causally related to MMR vaccination in Finland.<sup>35</sup> A total of 1.8 million individuals were immunised and almost 3 million doses of vaccine administered. There was an incidence of adverse events with possible causal relation with MMR of 5.3 per 100,000 vaccinees, or 3.2 per 100,000 vaccine doses. The reactions were neurologic, allergic and miscellaneous reactions. The study concluded that serious events causally related to MMR vaccine are rare and greatly outweighed by the risk of the natural measles, mumps and rubella diseases.

- 2 There is an independent, worldwide, research community who publish their findings in peer-reviewed journals.
- 3 There are systems for the continued surveillance of adverse effects. Serious reactions are reported to the Irish Medicines Board. Doctors and pharmacists are urged to be meticulous in reporting reactions and in obtaining the details and appropriate specimens that will help in their thorough investigation.

The success of the spontaneous reporting system for vaccines depends on early, complete and accurate reporting of suspected adverse drug reactions (ADRs) to the Irish Medicines Board using the Yellow Card Scheme. The Irish Medicines Board encourages healthcare professionals to report any suspected adverse reactions associated with the use of vaccines and regular reminders regarding reporting are included in the IMB's *Drug Safety Newsletter*, which is circulated to all doctors, dentists and pharmacists.

Particular care was taken to monitor and investigate the apparent adverse reactions that occurred during the measles/rubella (MR) schools immunisation campaign in the UK in 1995. Over 8 million children aged between 5 and 16 years were immunised with MR vaccine. Reports of serious adverse reactions to the vaccine were very rare (0.007%).<sup>61</sup>

- 4 There are independent, expert groups who assess the evidence from primary sources of information and provide advice on immunisation policy and the quality, safety and efficacy of vaccines. These include the National Immunisation Committee and the Irish Medicines Board. In the USA, the National Childhood Vaccine Injury Act 1986 mandated that the Institute of Medicine conduct scientific reviews of the evidence bearing on causality and possible adverse consequences of vaccines. A number of studies have been completed on childhood immunisations including an immunisation safety review on MMR vaccine and autism in April 2001. The Committee concluded that 'the evidence favours rejection of

a causal relationship at the population level between MMR vaccine and autistic spectrum disorders (ASD)'. However, the Committee noted that 'its conclusion does not exclude the possibility that MMR vaccine could contribute to ASD in a small number of children, because the epidemiological evidence lacks the precision to assess rare occurrence of a response leading to ASD and the proposed biological models linking MMR vaccine to ASD, although far from established, are nevertheless not disproved'.<sup>62</sup>

- 5 All vaccines are extensively tested for quality, safety and efficacy by their manufacturers, prior to licensing.<sup>63</sup> MMR vaccines have been through a licensing process which requires safety, quality and effectiveness to be carefully reviewed before a licence is granted. In addition, manufacturers must submit samples of each batch and results of their potency, safety and purity tests for independent assessment from the National Institute for Biological Standards and Control (NIBSC) before that batch can be released into general use.

Following authorisation (i.e. licensing) and in keeping with requirements laid down nationally and internationally, pharmaceutical companies are required, as a condition of authorisation, to submit information on suspected adverse reactions associated with the use of their product to regulatory authorities, such as the Irish Medicines Board. Such information is provided in the form of individual case reports for all serious suspected cases, which are submitted on an expedited basis (i.e. within 15 days) and Periodic Safety Update Reports (PSURs). PSURs provide an overview of the world wide safety experience of a product and are submitted six monthly for two years, yearly for three years and five yearly, at the time of renewal thereafter. Information and analysis of suspected adverse reaction reports together with data from the medical and scientific literature, an update on the worldwide status of the product, details of study findings, information on patient exposure and regulatory changes undertaken elsewhere are all included in the PSUR.

- 6 Clinical signs and symptoms that occur shortly after immunisation are often thought to be vaccine reactions, but there is a significant difference between a coincidental illness and a reaction actually caused by the vaccine. Nearly all children in Ireland who receive MMR vaccine receive it at 12-24 months of age, and so a large number of the children in that age group have been recently immunised at any one time. And this is an age when children often develop illness, regardless of whether or not a vaccine has been given. Sometimes illness will occur, by chance, shortly after MMR immunisation. This does not mean that the two events are linked by anything other than coincidence.
- 7 It is known that the conditions in Table 1 can sometimes be caused by MMR vaccine. There are no other serious conditions for which there is evidence from good studies to indicate an increased risk after MMR immunisation.

**Table 1: Rates of conditions after the natural disease and after the MMR vaccine**

condition	children affected after the natural disease	children affected after the first dose of MMR
Febrile convulsions (temperature fits)	1 in 200 (measles)	1 in 1000
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Death	1 in 2500 to 1 in 5000 (measles - higher in children under 1) 1–2 in 1000 for notified cases of measles in recent years	0

- 8 Idiopathic thrombocytopenic purpura (ITP) is a condition that affects blood clotting due to a shortage of platelets in the blood. This causes the blood to be less 'sticky' and can result in a purple rash on the patient's body as mild bleeding beneath the skin can occur. ITP often follows viral infection and most cases do not follow vaccination. ITP occurs much less frequently after MMR vaccination, than it does after natural infection.<sup>64</sup>
- 9 There is no increased risk from a second dose of MMR vaccine, with the exception of allergic reactions. If complications were to occur they would most likely be in the 5-10% of children who did not respond to the first dose: the weakened virus is killed as soon as it enters the body of a child who is already immune. The overall risk of complications after a second dose of MMR vaccine is therefore 90-95% less than that after the first dose.<sup>65</sup>
- 10 As with any medical procedure, health care professionals are obliged to explain the advantages and disadvantages of vaccination. The literature provided for parents and professionals describes all the known adverse effects of MMR.





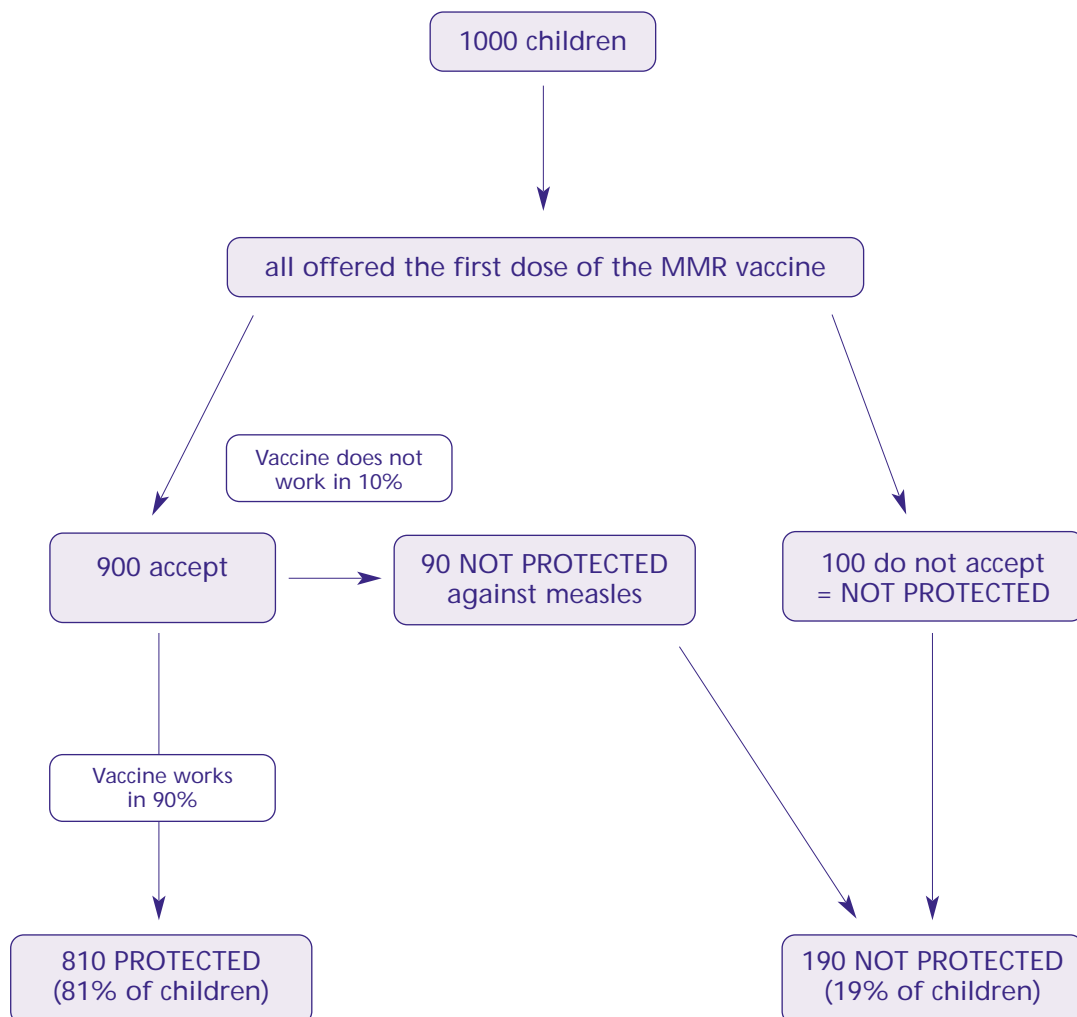
Why does my child  
need a second dose?



# Why does my child need a second dose?

## Question 6

The first dose of the MMR vaccine protects approximately 90% of children against measles, approximately 90% against mumps, and approximately 95% against rubella.





## Why does my child need a second dose?

### Key Notes

- 1 In approximately 10% of children who receive one dose of MMR, it does not work against the measles virus. The figure is 10% for mumps, and 5% for rubella. In addition, in Ireland about 20-30% of children do not receive the first MMR vaccine, for various reasons (e.g. missed appointment or parental concern).
- 2 Thus, with more than 30% of children still vulnerable to measles, outbreaks would occur. These would involve older children and infants under one year (when measles results in more complications) and those with reduced immunity (those who cannot have MMR vaccine and have to rely on everyone else's immunity for their protection).
- 3 The chance of your child not being protected against measles after one dose of MMR is around 1 in 10. After two doses the chance of your child not being protected against measles falls to around 1 in 100, i.e. 99% protection. The second dose also gives children who missed the first dose another chance to be vaccinated.
- 4 Blood tests to check immunity before giving a second dose or targeting only non-recipients are not recommended because there are drawbacks. The risk of side-effects is 10 times lower with a second dose of MMR vaccine.



## Why does my child need a second dose?

### Additional Notes

- 1 On an individual level, for approximately 10% of children who receive one dose of MMR, it does not provide protection against measles. The figure is approximately 10% for mumps, and 5% for rubella.<sup>5,17,66</sup> In addition, in Ireland about 20-30% of children do not receive the first MMR vaccine, for various reasons (e.g. missed appointment or parental concern). These groups therefore remain susceptible after only one dose of the MMR vaccine has been offered.
- 2 On a community level, it is impossible to achieve 'population protection' (herd immunity), and therefore effective disease control, using a one-dose schedule. For example, if 90% of children receive a dose of MMR, and in 10% of these the vaccine fails to work, only 81% will be immune after one dose. However, more than 90% of the population needs to be immune for measles to be eliminated.<sup>67</sup>

If 'population protection' is not achieved, breakthrough outbreaks will occur. Cases will occur among non-recipients, non-responders and infants aged less than one year (who are too young to have the vaccine). Children who are immunocompromised, in whom MMR vaccine is contraindicated, and in whom measles has a high fatality, will also be at risk. This has been the experience in the USA, which saw large breakthrough outbreaks in the early 1990s, resulting in 55 000 cases and over 100 deaths.<sup>68</sup>

In a setting where the level of population immunity is high, but not high enough to achieve 'population protection', outbreaks will tend to affect older children. If, for example, 81% of children are immune after one dose, the circulation of wild measles virus is interrupted to the extent that the children who remain susceptible have a reduced chance of being exposed to it during early childhood. With time, a growing number of non-immune, older children will accumulate. Eventually, there will be enough of them to allow epidemics to occur.

Even when indigenous measles is eliminated, imported cases may still occur and Irish children may be exposed abroad and by returning travellers. Maintaining the highest possible level of population immunity is therefore vital.

- 3 A second MMR vaccination protects most children who do not respond to the first dose: around 90% will have a good response to the second dose. The chance of an individual remaining susceptible is reduced from 1 in 10 to around 1 in 100 after a second dose.<sup>16</sup> By offering a second dose of MMR vaccine, those children who did not even receive the first dose get a second chance. A further benefit is that it boosts the antibodies of children who did respond to the first dose.<sup>16</sup> A two-dose schedule is the only strategy that will eliminate measles.<sup>67</sup> If only non-recipients were targeted the 10% of children that have received the first dose, but have not responded to it, would remain susceptible.
- 4 Mass antibody testing and recall of non-immune children would be difficult to implement, and would add greatly to the cost of the measles vaccination programme. Serum antibody testing would mean taking a blood sample from four year-olds - an invasive procedure that is traumatic for a young child. The test is not 100% accurate and it would fail to identify some susceptible children, who would consequently not receive a further dose of MMR, and who would therefore remain at risk.

Why aren't the  
vaccines given separately?





# Why aren't the vaccines given separately?

## Question 7

### MMR

2 injections of combined MMR

MMR	MMR
1st	2nd

- Very low risk of reactions
- Effective protection against disease

### Separate vaccines

6 injections of separate measles, mumps and rubella

Measles	Mumps	Rubella	Measles	Mumps	Rubella
1st	1st	1st	2nd	2nd	2nd

- Increased risk of disease
- Increased risk of missing a dose completely
- Increased risk of local reactions at injection site
- Increased trauma to child



## Why aren't the vaccines given separately?

### Key Notes

- 1 The issue of giving vaccines separately was raised in the UK by Dr Andrew Wakefield in a 1998 press interview. The suggestion came from a belief that if children catch measles and mumps within one year of each other they are more likely to develop Crohn's disease later. It was also claimed that MMR causes excess diarrhoea compared to single vaccines. There is no evidence to support these claims - in fact the evidence strongly rejects any link between MMR and autism or inflammatory bowel disease.
- 2 MMR vaccine is as effective in protecting against measles, mumps, and rubella as when each component is given on its own. The component viruses do not interfere with each other and there is no advantage in receiving the vaccines separately.
- 3 Giving the vaccines separately would mean a child needing a total of six injections to complete the course, instead of two. These children would remain unprotected and at risk of disease for longer. Six injections could also mean an increased risk of local reactions at the injection site. Control programmes would be less effective and this would lead to more cases of measles, mumps and rubella.
- 4 The use of three separate vaccines for measles, mumps and rubella has never been used 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? What order should the vaccines be given? How much time should be taken between vaccine doses?
- 5 In contrast the MMR vaccine has been in use for over 30 years and underwent rigorous studies to ensure that it was safe and effective before it was released for general use. The combined research evidence and decades of experience with MMR has confirmed that it is safe and effective. Indeed, the World Health Organisation recently concluded that MMR is one of the safest vaccines ever produced.
- 6 Although licences for single measles and mumps vaccines do exist in Ireland, no licensed single measles or mumps vaccine are manufactured for, or available for the Irish market.
- 7 Some of the unlicensed single antigen vaccines imported into Ireland may be less effective and some may have a higher risk of side-effects than the MMR vaccine.
- 8 Three separate injections to protect against measles, mumps and rubella has never been recommended in Ireland and no country in the world has recommended single measles, mumps and rubella vaccines, where combined MMR is available.



- 1 The idea of giving single antigen vaccines, with an interval of at least 12 months between vaccines, instead of the combined MMR vaccine was first publicised in the UK by Dr Andrew Wakefield in press interviews given after the publication of a paper in the *Lancet* in 1998, describing children with developmental and bowel problems.<sup>26</sup>

The idea is based on a belief that children who catch measles and mumps within one year of each other are more likely to develop Crohn's disease later.<sup>69</sup> Wakefield and Montgomery have also claimed that the incidence of gastrointestinal adverse events is significantly higher after MMR vaccination in the few weeks following its administration in comparison to single antigen vaccines.<sup>70</sup> They claim that this leads to gut damage and subsequent autism. However, there is no evidence of significantly excess gastrointestinal events following MMR vaccination in the original trial data.<sup>71</sup> Indeed there is excellent evidence for a lack of significant diarrhoea following MMR. In a study from Finland, 581 twin pairs were randomised for one twin to receive MMR and the other twin a placebo injection, then vice versa three weeks later. Diarrhoea was as common in those receiving MMR as in those receiving a placebo.<sup>72</sup> A trial in the UK compared MMR to a single antigen measles vaccine. In a six-week period of follow-up there was no statistically significant difference in diarrhoea between the two groups.<sup>73</sup>

- 2 The evidence strongly rejects any link between measles or MMR and Crohn's or autism (see Question 4). The original rationale for suggesting single antigen vaccines is therefore without substance. However, some anti-vaccination groups have supported these views, which have since gained a high profile through national media and dedicated websites, resulting in increased perceived credibility.
- 3 The MMR vaccine is as effective in protecting against measles, mumps, and rubella as when each component is given on its own.<sup>16</sup> There is no evidence that the component vaccine viruses interfere with each other. Immunity to the measles component and other antigens in MMR occurs at different times; measles after 6-11 days, rubella after 10-15 days and mumps after 15-21 days. It is normal for children to be bombarded with microorganisms via the gut and air, yet their immune systems cope very well.

If single antigen vaccines were to be given one year apart, a child would need a total of six injections at ages 1, 2, 3, 4, 5 and 6 years, to complete the course, instead of just two MMR vaccinations. These children would be susceptible to those diseases for longer, and there is good evidence that some children would miss doses altogether, resulting in more unvaccinated children. The result would be to undermine measles, mumps and rubella immunisation, reduce population immunity and increase the risk of children catching these diseases. The policy is not based on financial considerations, but on the best way to protect children. There is no scientific evidence to support the safety or efficacy of giving MMR as three separate vaccines at defined intervals. In contrast, MMR vaccine has been used for 30 years with an excellent safety record.

- 4 Although licences for single measles and mumps vaccines do exist in Ireland, no licensed single measles or mumps vaccine are manufactured for, or available for the Irish market.
- 5 The safety and efficacy of unlicensed measles and mumps vaccines administered in Ireland cannot be assumed. Batch testing and cold chain information is most often lacking and some strains are known to have unacceptable safety or efficacy profiles, in particular, the Urabe and Rubini mumps strains. The manufacturers withdrew Urabe from Ireland in 1993 and it has been shown to be associated with mumps meningitis post-vaccination.<sup>74</sup> Rubini has been shown to be of extremely low efficacy and has been associated with subsequent outbreaks of mumps in Spain, Portugal, Italy and Switzerland because of the extremely low level of protection it provides.<sup>75-77</sup> The MMR vaccine contains the safe and efficacious Jeryl Lynn mumps strain.<sup>78</sup>
- 6 Single antigen measles, mumps and rubella vaccines as an alternative to MMR has never been recommended in Ireland. Single antigen measles vaccine was introduced for all children in Ireland in 1985, but was superseded by MMR in 1988. Single antigen rubella vaccine was introduced in 1971 as part of a schoolgirl immunisation programme to protect women of childbearing age against rubella. Single antigen mumps vaccine has never been part of the Irish childhood immunisation programme. Licensed single antigen rubella vaccine continues to be available in Ireland, but this is primarily for non-immune women of childbearing age.

The MMR vaccine is used in 93 countries around the world and no country in the world recommends single antigen measles, mumps or rubella vaccines, where the combined MMR vaccine is available. The use of MMR vaccine, when available, is strongly supported by the World Health Organization.

France is often mentioned as a country where single antigen vaccines are given. However, the position in France is that children are given a single antigen measles vaccine from nine months of age only if they are in a nursery, and there is a risk of a measles outbreak. These children then receive two further MMR vaccinations, as in Ireland. France does not recommend single antigen mumps vaccine.<sup>79</sup>

In Japan, single antigen measles and single antigen rubella vaccines are recommended, as no MMR vaccine is available. However, Japan has suffered from endemic and epidemic measles. Over the period 1992-1997, there were 79 measles deaths in Japan. In the UK where the uptake rate of MMR has been over 90%, there have been no acute measles deaths since 1992.<sup>79</sup> However In Ireland where the uptake of vaccine has never reached the target of 95% there were 8 deaths reported in the years 1990-1999 and 3 deaths in the year 2000.





Are there some children who  
cannot have the MMR vaccine?



## Are there some children who cannot have the MMR vaccine?

### Question 8

#### Absolute reasons not to have MMR:

- children with untreated cancer or diseases of the immune system; those receiving immunosuppressive therapy or highdose steroids
- children with allergies to neomycin or gelatin (very rare)
- severe reaction to previous MMR.

#### Reasons to postpone MMR:

- the child is generally unwell with a fever
- the child has had another live vaccine (including BCG) in the last three weeks
- the child has been given an injection of immunoglobulin in the last three months.



## Contraindications

- ① There are a few reasons why a child may not have the MMR vaccine:
  - *absolute*: untreated malignant disease, immunosuppression, allergy to neomycin or gelatin, severe reaction to previous MMR
  - *postpone*: acute febrile illness, another live vaccine (three weeks), immunoglobulin (three months).

## Not contraindications

- ② Concerns about giving MMR to a child who has a severe egg allergy, who may already have had measles, or who has a cold, are quite common. None of these is a reason not to have the vaccine, i.e. they are not contraindications.
- ③ *Egg allergy*:
  - although tissue derived from eggs is used to grow the vaccine virus, as much as possible is removed
  - a number of scientific papers have been published which demonstrate the safety of MMR vaccine, even in children with a known severe egg allergy
  - MMR vaccine can be administered in hospital to children with a history of anaphylaxis to eggs, if there is particular parental concern.
- ④ *Had measles*:
  - MMR vaccine should be given despite a history of measles, mumps or rubella infection since the clinical diagnosis is unreliable.
- ⑤ *Has an infection*:
  - minor infections without fever or systemic upset are not reasons to postpone immunisation
  - asthma, eczema, hay fever or 'snuffles' are not reasons to postpone the MMR vaccine
  - treatment with antibiotics or locally-acting steroids are not contraindications.



## Are there some children who cannot have the MMR vaccine?

### Additional Notes

- 1 **Egg allergy.** There are theoretical concerns about egg allergy and potential anaphylaxis, since the live attenuated measles and mumps viruses used in the vaccine are cultured in chick-embryo fibroblasts. However, during the process of vaccine production the egg is removed and very little (if any at all) reaches the vaccine, therefore the risk of a severe reaction is very low.
- 2 Severe egg allergy means essentially the occurrence of anaphylaxis after eating eggs, not food intolerance or dislike of eggs. There is increasing evidence that MMR vaccine can be given safely to children even when they have previously had an anaphylactic reaction following food containing egg (generalised urticaria, swelling of the mouth and throat, difficulty breathing, hypotension or shock). Scientific papers have been written advocating the safety of administering the MMR vaccine to children with egg allergy.<sup>15,80,81</sup> In one such study, 54 children with known severe egg allergy, confirmed with skin tests and double blind placebo controlled food challenge tests, received the MMR vaccine with no immediate or delayed adverse reaction. At least 1265 patients from 16 separate studies have been reported. None of 284 patients with histories of egg allergy had any adverse reactions. There were only two reports of symptoms suggestive of anaphylaxis. The combined data indicated that over 99% of children who are allergic to eggs can safely receive the MMR vaccine.<sup>15</sup>
- 3 On a precautionary basis, however, children with a known severe reaction to eggs can receive their MMR vaccine under controlled conditions, for example on a Paediatric Ward in hospital, if there is particular parental concern.
- 4 **Had measles.** Measles is now rare therefore clinical diagnosis is nearly always incorrect.
- 5 MMR vaccine should be given irrespective of a history of measles, mumps or rubella infection. If there is any doubt about a child's immunity, MMR vaccine should be given since there are no ill effects from vaccinating individuals who are already immune.

- 6 **Has an infection.** If a child is suffering from an acute illness with associated pyrexia, immunisation should be postponed.<sup>82</sup>
- 7 Minor infections without fever or systemic upset are not reasons to postpone immunisation. A study in 1996 examined seroconversion responses to MMR vaccine among children with and without minor illness.<sup>83</sup> A total of 386 children were examined. Some 33% had acute upper respiratory tract infection, 11% had otitis media and 3% had diarrhoea. A total of 157 children had one of these minor illnesses, 229 were well. The overall seroconversion rates were the same in the children with or without minor illness. Giving MMR vaccine to children with minor illness results in effective seroconversion.
- 8 Asthma, eczema, hay fever or 'snuffles' are not reasons to postpone the MMR vaccine.
- 9 Treatment with antibiotics or locally acting steroids (e.g. topical or inhaled steroids) are not reasons to postpone or withhold the MMR vaccine.
- 10 Health professionals have a responsibility to provide parents with consistent evidenced-based information relating to the MMR vaccine, to enable them to make an informed decision. Very few children have a 'true' contraindication to MMR vaccine.

What would happen if we  
stopped vaccinating?

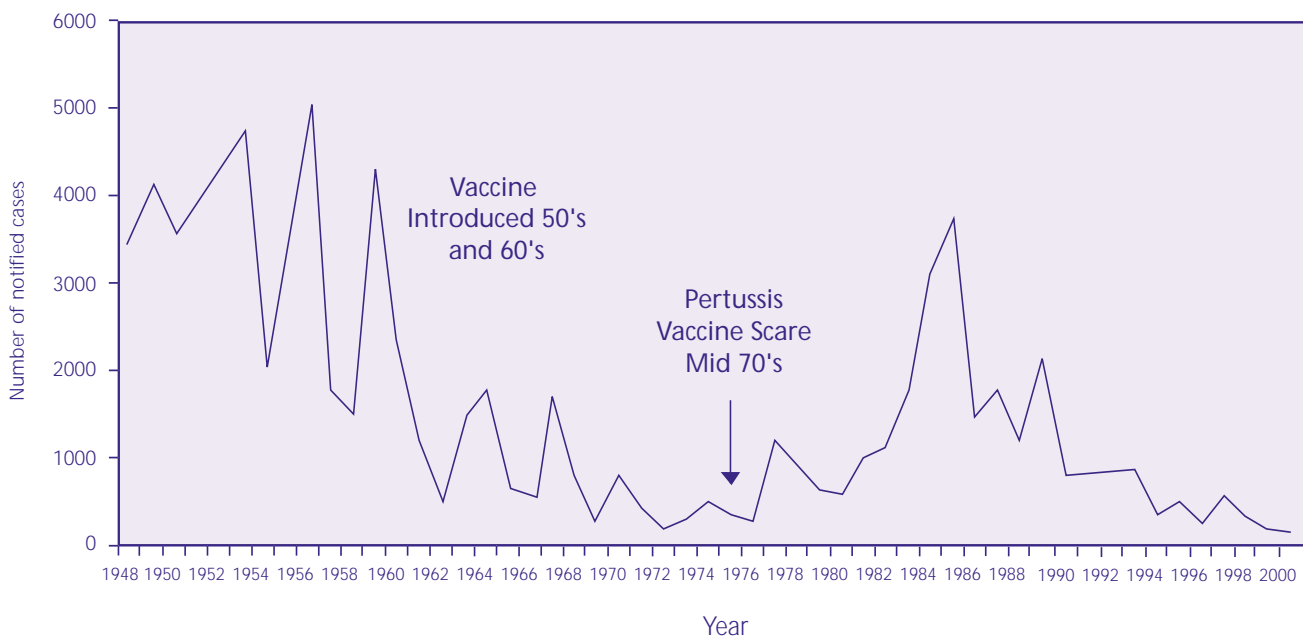




## What would happen if we stopped vaccinating?

### Question 9

Graph 4: Pertussis (Whooping cough) Notifications Ireland, 1948 - 2000



- Before the introduction of immunisation against whooping cough (pertussis) in the 1950s, large epidemics occurred every three to four years. Immunisation led to the size of these epidemics gradually decreasing, with fewer children becoming ill and fewer children dying.
- In the mid-1970s, rates for vaccination against whooping cough dropped dramatically as the result of unfounded anxiety about the safety of pertussis vaccine. This led to whooping cough epidemics. It is only in the last decade that the number of whooping cough cases has returned to levels occurring before the adverse publicity.
- This experience demonstrates that if vaccine uptake levels fall, diseases do return, with many cases and deaths occurring that could have been prevented by vaccination.



## What would happen if we stopped vaccinating?

### Key Notes

- 1 When the use of vaccine falls, outbreaks occur and cases of disease rise. A scare about the whooping cough vaccine in the 1970s caused a fall in uptake.
- 2 Vaccination has had a clear impact on the control of many diseases, including polio and measles.
- 3 If we did not vaccinate against measles in Ireland, about 5-10 children a year would die from it.
- 4 Providing clean water and better living conditions together with improved general health has helped to lessen the impact of infectious diseases, particularly water-borne diseases such as typhoid, but these are not enough on their own.
- 5 Diseases such as measles and polio cannot be cured with antibiotics, but they can be prevented by vaccination.
- 6 Low MMR vaccine uptake has led to measles outbreaks in Ireland and The Netherlands.



## What would happen if we stopped vaccinating?

### Additional Notes

- 1 Some people claim that infectious diseases would have disappeared without mass vaccination. However, the evidence does not support this view, and the experiences of many countries when vaccination rates have fallen have proved this view is wrong. In Ireland and the UK in the 1970s, public concern about the safety of whooping cough vaccine (pertussis) led to a fall in its uptake. As a consequence the numbers of pertussis notifications rose dramatically. Uptake rates gradually rose again during the late 1980s and 1990s, and the annual number of cases fell. Graph 4 shows pertussis notifications to the Department of Health and Children. Many other countries have seen similar epidemics following a fall in the uptake of pertussis vaccine.<sup>84</sup>
- 2 Following the introduction of vaccination against specific diseases, the incidence of those diseases fell dramatically as uptake of the vaccine increased. For example, there were 499 cases of paralytic polio in Ireland in 1956, the year before mass vaccination was introduced. In 1957, injectable vaccine (Salk) was introduced, and in the early 1960s, this was replaced by oral vaccine (Sabin). By 1965, there were less than 10 cases each year, and by the mid-1970s on average less than 1 a year, most of these occurring in individuals who had not been immunised. There have been no cases of indigenous wild type polio in Ireland for over 15 years now.
- 3 Even with 'high tech' modern medicine, measles can cause severe disease. One in 15 cases of measles will suffer some complication, such as ear infection, bronchitis, pneumonia, convulsions or encephalitis (infection of the brain), 1 in 100 will need hospital admission and up to 1-2 in 1000 will die.<sup>2,5-7</sup> If we did not vaccinate at all against measles, we would see around 5-10 measles' deaths each year in Ireland
- 4 Many infectious diseases which were once common in Ireland declined gradually as living conditions improved early in the twentieth century, but the fall had levelled off by the 1940s and 1950s, before many of the vaccines now in use were first introduced.
- 5 Antibiotics do not work against viral diseases such as measles or polio. The only way to prevent children getting these diseases is to immunise them.
- 6 There have been measles outbreaks in Ireland and The Netherlands in 1999-2000.<sup>6,7</sup> In Ireland there were over 1600 cases of measles, with over 110 hospital admissions and three deaths. In The Netherlands, there were 2961 cases, sixty-eight hospitalisations and three deaths from measles. These outbreaks were due to low vaccine uptake.



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## Helpful websites and organisations

[www.hebe.ie](http://www.hebe.ie)

The Health Boards Executive, (HeBE) is a modern, responsive and dynamic statutory health agency, established by the Minister for Health and Children. Its board comprises the Chief Executive Officers of the seven health boards, three area health boards and the Eastern Regional Health Authority. The Executive was established to facilitate joint working between health boards.

[www.ndsc.ie](http://www.ndsc.ie)

The National Disease Surveillance Centre (NDSC) is Ireland's leading specialist center for surveillance of communicable diseases. The center was set up in 1998 conjointly by Ireland's eight Health Boards and with the approval of the Minister for Health and Children.

The aim of NDSC is to improve the health of the Irish population by the collation, interpretation and provision of the best possible information on infectious diseases. This is achieved through surveillance and independent advice, epidemiological investigation, research and training.

The NDSC works in partnership with health service providers and sister organizations in other countries to ensure that up to date information is available to contribute to the effective control of infectious diseases.

[www.shb.ie](http://www.shb.ie)

The Southern Health Board provides health and social services to the people of Cork and Kerry.

See also [www.shb.ie/class-304147592.cfm](http://www.shb.ie/class-304147592.cfm)

[www.erha.ie](http://www.erha.ie)

The Eastern Regional Health Authority is responsible for planning, arranging, overseeing and co-ordinating health and personal social services for the 1.5 million people who live in the eastern region of the country in Dublin, Kildare and Wicklow.

[www.mhb.ie](http://www.mhb.ie)

Ireland's Midland Health Board exists to improve the health (Health gain) and quality of life (Social gain) of the population of Laois, Offaly, Longford and Westmeath.

[www.mwhb.ie](http://www.mwhb.ie)

The MWHB region covers the counties of Clare, Limerick and Tipperary North Riding.

[www.nehb.ie](http://www.nehb.ie)

The NEHB region covers the areas of Louth, Meath, Cavan and Monaghan.

[www.nwhb.ie](http://www.nwhb.ie)

The North Western Health Board, which was established under the 1970 Health Act, has responsibility for the administration and provision of health and personal social services in the counties of Donegal, Sligo and Leitrim.

[www.sehb.ie](http://www.sehb.ie)

The South Eastern Health Board provides health, welfare, personal and social services to people living in the South East i.e. Carlow, Kilkenny, Wexford, Waterford and South Tipperary.

[www.whb.ie](http://www.whb.ie)

The Western Health Board serving the people of Galway, Mayo and Roscommon.

[www.doh.ie](http://www.doh.ie)

The mission of the Department of Health and Children is:  
"In partnership with the providers of health care, and in co-operation with other government departments, statutory and non-statutory bodies, to protect promote and restore the health and well-being of people by ensuring that health and personal social services are planned, managed and delivered to achieve measurable health and social gain and provide the optimum return on resources invested."

[www.irlgov.ie/Committees-01/c-health/rep-childhood/default.htm](http://www.irlgov.ie/Committees-01/c-health/rep-childhood/default.htm)

Joint Committee on Health and Children – Report on Childhood Immunisation

[www.imb.ie/update271101/issue12.pdf](http://www.imb.ie/update271101/issue12.pdf)

Irish Medicines Board – Drug Safety Newsletter – MMR Vaccine 12th Edition,



April 2001 Issue 12.

[www.cdc.gov/nip](http://www.cdc.gov/nip)

The National Immunization Program (NIP) is part of the Centres for Disease Control and Prevention, located in Atlanta, Georgia. As a disease-prevention program, NIP provides leadership for the planning, coordination, and conduct of immunization activities nationwide.

[www.immunisation.org.uk](http://www.immunisation.org.uk)

This site is published by Health Promotion England for the NHS and Department of Health. The site provides comprehensive information on general immunisation issues including safety and comparative risks.

The latest information on MMR can be downloaded. This includes extensively researched and fully referenced factsheets on MMR for health professionals.

[www.who.int/vaccines-diseases/safety](http://www.who.int/vaccines-diseases/safety)

This is the official website of the World Health Organization (WHO). Position statements are displayed about MMR safety as well as information about the diseases themselves.

The library catalogue lists bibliographic references of all WHO documentation.

[www.aap.org](http://www.aap.org)

The American Academy of Pediatrics is dedicated to the health of all children. It is also committed to continuing professional education. The full texts of policy statements are available and can be downloaded. MMR specific reviews and advice are at:

[intl.aapnews.org/cgi/content/short/18/5/197-c](http://intl.aapnews.org/cgi/content/short/18/5/197-c)

[www.aiom.org](http://www.aiom.org)

The American Institute of Medicine is undertaking a series of reviews of vaccine safety at the request of the US Centers for Disease Control. The first review, into MMR and autism, was published in April and is available in pdf or online at:

[books.nap.edu/html/mmr/](http://books.nap.edu/html/mmr/)