

the MMR vaccine

# Information for Health Professionals



March 2001

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**The final decision on whether or not to vaccinate a child lies with the parents. However, it is essential that all health professionals discussing the issue with parents give them a clear message. Parents should know that the health professional clearly and unambiguously supports the use of MMR and that the benefits to be gained from it by far outweigh any small risks involved.**

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# contents

Page		
1.	The diseases we are preventing .....	1
2.	How common are these diseases? .....	3
3.	If these disease are so rare in the UK now, why should children be immunised? .....	3
4.	What is the MMR vaccine? .....	4
5.	How does the vaccine work? .....	4
6.	How effective is the vaccine? .....	4
7.	How long does a child remain immune after receiving the vaccine? .....	4
8.	Isn't the protection from measles itself better than that from the vaccine? .....	5
9.	Why do people who have been immunised still suffer from measles, mumps and rubella? .....	5
10.	When is MMR vaccine given routinely? .....	6
11.	Why is the vaccine given at these ages? .....	6
12.	Why do we need two doses of MMR? .....	6
13.	If a child didn't respond to the first MMR, will they respond to the second? .....	7
14.	What are the side effects from a second dose of MMR? .....	7
15.	Why not do a blood test to see if each child needs the immunisation? .....	7
16.	What should a parent expect after their child has received the MMR vaccine? .....	7
17.	Can there be serious side effects from the vaccine? .....	8
18.	What should a parent do if their child is unwell after receiving MMR vaccine? .....	9
19.	Are there any children who should not be immunised? .....	9
20.	Is MMR vaccine associated with bowel disease or Autism? .....	10
21.	What evidence is there that MMR is not associated with Autism or bowel disease? .....	11
22.	What about suggestions that MMR was licensed prematurely? .....	12
23.	Why are the numbers of children affected by autism increasing? .....	13
24.	Why do some parents believe their child developed autism as a result of MMR vaccine? .....	14
25.	Aren't experts divided over the issue? .....	14
26.	Why do we not offer measles, mumps and rubella vaccines separately? .....	15
27.	What are the risks of giving three single vaccines? .....	15
28.	But don't other countries give separate vaccines? .....	16
29.	Conclusion .....	17
	References .....	18

## 1. The diseases we are preventing

It is important to start by looking at the diseases we are preventing so that we are fully aware of the benefits of the vaccine.

### Measles

Prior to the introduction of vaccination virtually every child would have caught measles. Outbreaks in the UK involving 800,000 to 1,000,000 children (including 2,000 to 10,000 children in Northern Ireland) occurred every other year. In the last year (1967) before measles vaccine was introduced measles killed one hundred children in the UK in an outbreak that affected half a million children.

There are complications of measles for one in every fifteen cases. These include otitis media, bronchitis, pneumonia, convulsions, encephalitis and death. Meningitis/ encephalitis occurs about once in every thousand cases. (Details are shown in the table)

Despite recent improvements in general health and the quality of treatment, measles still causes serious problems for people who develop complications. A study in 1978 showed that, whilst the number of measles cases had decreased considerably since the introduction of measles vaccine, the rate of serious illness as a result of measles infection remained the same.

There is plenty of evidence that measles still kills, even in developed countries with good nutrition and a modern health service. Fifteen years ago France did not have a good uptake rate for MMR and was experiencing measles outbreaks with up to 35 children dying in a year. Between 1989 and 1991 a measles epidemic in the USA killed 130 children and more than 5,000 children were admitted to hospital. In the year 2000 there were outbreaks in Dublin and in the Netherlands. In Dublin there were 1,500 reported cases, over 100 were admitted to hospital, at least six to ICU and two children have died. The

uptake of MMR in Dublin is about 75%. In the Netherlands there were 2,300 cases, 130 were treated for pneumonia, 53 were admitted to hospital, three with encephalitis and three children have died. The Netherlands generally has a good uptake of MMR, but the outbreak occurred in a religious community who object to vaccinations.

In the past four years Germany and Switzerland have both experienced general community outbreaks. They have uptake rates around 80%.

We can therefore be sure that measles is not far away and will return and will kill children if we don't keep our uptake rates high.

### Mumps

Complications of mumps include pancreatitis, oophoritis, orchitis, meningitis and encephalitis. Prior to MMR being introduced there were 1,200 hospital admissions per year in the UK. It used to be the most common cause of viral meningitis and of permanent unilateral deafness. (An outbreak of mumps occurred in Northern Ireland between 1999 and 2001 - see section 12)

## Rubella

Although generally a mild disease in children, rubella can cause bleeding disorders or encephalitis.

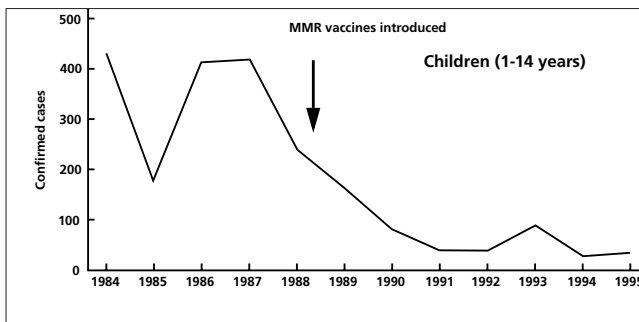
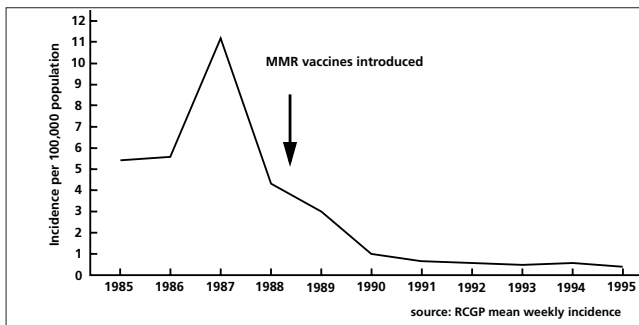
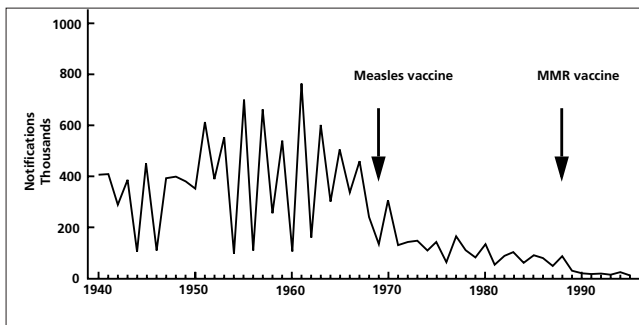
Maternal rubella in the first ten weeks of pregnancy leads to fetal damage in 90% of babies and multiple defects are common.

Symptoms and complications of the diseases and the vaccine

The diseases	Common symptoms or side effects	Serious complications
<b>Measles</b>	Fever, rash, cough, red and painful eyes, swollen glands, loss of appetite, generally unwell	Ear infection (1 in 20) Pneumonia/bronchitis (1 in 25) Febrile fit (1 in 200) Hospital admission (1 in 100) Meningitis/encephalitis (1 in 1,000) Late onset of encephalitis (1 in 8,000 children under 2 years old) Death (1 in 2,500 - 5,000)
<b>Mumps</b>	Painful and swollen glands in the cheeks, neck or under the jaw, fever, headache, abdominal pain, loss of appetite, generally unwell	Swollen, painful testicles in older boys and men (1 in 5) Meningitis/encephalitis (1 in 200 - 5,000) Pancreatitis (1 in 30) Deafness - usually with partial or complete recovery (1 in 25) Mumps during pregnancy can lead to miscarriage
<b>Rubella</b>	Fever, headache, red and painful eyes, rash, sore throat, cough, swollen glands, joint pains (mainly women), loss of appetite, generally unwell	Encephalitis (1 in 6,000) Bleeding disorders (1 in 3,000) Rubella during first 10 weeks of pregnancy can lead to miscarriage or 9 in 10 babies being born with: <ul style="list-style-type: none"> <li>• deafness;</li> <li>• blindness;</li> <li>• heart problems;</li> <li>• brain damage;</li> <li>• other serious problems.</li> </ul>
<b>MMR Vaccine</b>	Redness and swelling at the injection site. A week to 10 days after MMR some children become feverish and develop a measles-like rash. After 3 weeks a few children may get mild mumps.	Febrile fit (1 in 1,000) (due to high temperature) Encephalitis (1 in 1,000,000) Bleeding disorder (1 in 24,000)

## 2. How common are these diseases?

Since the introduction of vaccines against measles, mumps and rubella the incidence of these diseases has decreased considerably. These diseases only became rare after the vaccines were introduced. When a country has high vaccine coverage, as in the UK, the diseases that vaccines prevent become extremely rare. In the absence of immunisation these diseases would become common again and would cause significant amounts of serious illness and potentially some deaths. For example, in the 1970s, when there was a loss of confidence in whooping cough vaccine, and coverage fell, there were three major epidemics of whooping cough, with thousands of children being admitted to hospital. When vaccine coverage rose again, whooping cough declined. The following graphs show how measles, mumps and rubella have declined since MMR vaccine was introduced. All of these diseases are now rare in childhood.



## 3. If these diseases are so rare in the UK now, why should children be immunised?

There are really two key reasons. These diseases are rare in the UK now, but:

- they remain common in many parts of the world;
- if uptake of vaccine falls, the diseases would return in the future.

It is true that the risk of getting these diseases in the UK at present is very low. This is because such a high proportion of the population is immunised. But unimmunised children can still be at risk, either from cases of measles brought into this country, or by travelling to countries where there are many more measles cases than here. The older people are when they catch measles, mumps or rubella, the more serious the disease, and the higher the complication rate. It is estimated that one to two million children worldwide die each year from measles. Even in countries such as the UK, previously healthy children can still die from measles, especially if they catch measles when they are older.

The final decision on immunisation is the parents'. But if a child is not immunised, he/she will remain at risk. The child will then rely on other people immunising their children to avoid becoming infected. There will always be children who are left unprotected because:

- they cannot be immunised for medical reasons;
- they are too young to be immunised;
- they do not access vaccine services; and
- for some, the vaccine didn't work.

If more people choose not to immunise, then there will be pools of susceptible children and before long, outbreaks of disease will occur. The effect of decreased vaccine coverage has been seen in Russia: Russia used to have a well-established vaccine

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programme where a high proportion of children were immunised. Following the dissolution of the USSR, shortages of vaccine and indifference about the need for immunisation, led to a dramatic fall in vaccine coverage. Since then there has been a huge epidemic of diphtheria causing more than 125,000 cases and 4,000 deaths have been reported.

The only time to stop immunising children is when a disease has been eradicated worldwide. When every country had eliminated smallpox, all countries stopped immunisation. Hopefully polio will be eradicated soon, and measles may follow.

#### **4. What is the MMR vaccine?**

MMR vaccine 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.

#### **5. How does the vaccine work?**

A child will be injected with the vaccine and this causes their 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.

#### **6. How effective is the vaccine?**

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.

It is not known why some people don't get a good response. Sometimes the vaccine may have been improperly stored, or the viruses had lost their potency.

#### **7. How long does a child remain immune after receiving the vaccine?**

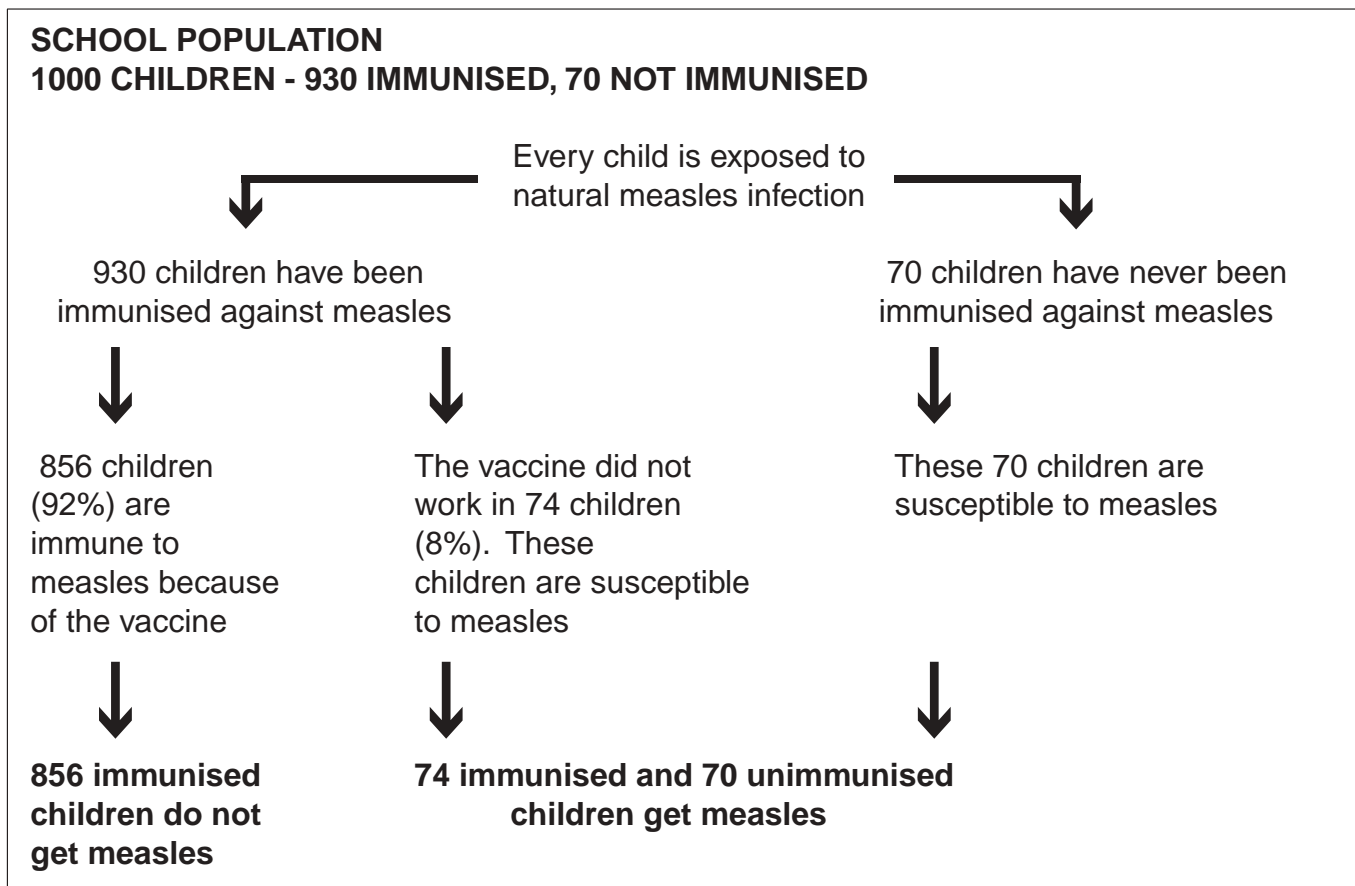
There is very little evidence that immunity to the measles, mumps or rubella vaccines wanes with time. It is known that children will remain immune for at least 30 years against measles, 21 years against rubella and 17 years against mumps - in other words for the amount of time that the vaccines have been available. Even if individuals are not fully protected, the immune system will have some memory and be able to respond more quickly in the immunised than in those who have not been immunised. Immunised children with low levels of antibodies are likely to have a modified, less serious, illness. Long-term studies on the duration of protection are continuing. The immunity against infection has been shown to last such a long time without waning that, in those people with protection, it is likely to be lifelong.

## 8. Isn't the protection from measles itself better than that from the vaccine?

The immunity from immunisation appears to be long lasting and effective. The problem with immunity that follows natural measles is that the child has to have had the disease. That's fine if the child doesn't have any of the complications of the disease, but it's a pretty risky option for the child's health. Recent evidence suggests that natural measles actually damages the immune system, an effect not seen in children who had the measles vaccine.

## 9. Why do people who have been immunised still suffer from measles, mumps and rubella?

As explained earlier, MMR vaccine is not 100% effective. If there are outbreaks, some of the people who are in the 5 to 10% who were not protected by the vaccine will become infected. If almost everyone has been immunised, almost everyone with measles has a history of being immunised. This can be better explained using the following example.



Therefore, in this example, of those who got measles in the school about a half had been immunised. But remember, 856 students were protected against measles and did not get the disease. All of those not immunised got measles

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## 10. When is MMR vaccine given routinely?

First dose by injection at 15 months, usually on its own. Second dose by injection between three and five years of age as part of the pre-school booster programme. Other booster doses of diphtheria/tetanus should be given by separate injection and polio vaccine by mouth at the same time. It is best to have all the vaccines at the same visit.

## 11. Why is the vaccine given at these ages?

Babies are born with some protection against measles, mumps and rubella from maternal antibodies that are passed on to them in the womb. This protection begins to wane shortly after birth as the antibody levels from the mother fall. If MMR vaccine were given before 12 months of age, the antibodies that have been passed from the mother could prevent the viruses in the vaccine from working. It is however important to get immunity to measles, mumps and rubella before children have opportunities to catch and pass these infections to each other. Where rubella is concerned, many cases of congenital rubella syndrome used to occur because mothers got rubella from their own or their friends' children.

The MMR second dose is usually given at the same time as the pre-school boosters to reduce the number of visits needed. The best time to give it is before school entry, before children start to mix with a new group of children.

## 12. Why do we need two doses of MMR?

No vaccine is completely effective. MMR produces immunity in about 90% of children who receive it. Even with a 92% uptake this results in only 83% of the total population being protected. This leaves

enough susceptibility to allow the re-emergence of epidemics.

An example of this was seen with a mumps outbreak in Northern Ireland from 1999 to 2001. The outbreak started around the Carrickmore area in November 1999 and gradually spread. There were over 1,000 notified cases. The vast majority of children affected were at secondary school and several schools experienced large outbreaks. About two-thirds of cases occurred in children who had one dose of MMR. In contrast, whilst a few primary school children were notified there were no outbreaks in primary schools. The reason for this is that when children of secondary school age were young the uptake of MMR was not as good as it is now and more importantly the second dose of MMR had not been introduced. Most primary school children in contrast have received two doses of MMR. The MR campaign carried out in 1994 only included measles and rubella but not a mumps component. It is interesting to note that in spite of the measles outbreak in the Republic in the year 2000 and a couple of cases occurring in Northern Ireland, this did not lead to an outbreak here. This was due to the MR campaign.

This clearly demonstrates the need for a two dose schedule for MMR. It is vital that we achieve high uptakes for both doses.

## 13. If a child didn't respond to the first MMR, will they respond to the second?

A second dose of vaccine has been shown to significantly increase protection. Amongst children who did not respond to a first dose of MMR vaccine, over 90% have a good response to a second dose. Children with low levels of antibodies after the first dose, are boosted.

#### **14. What are the side effects from a second dose of MMR?**

Experience from the USA and Scandinavia has shown that the type of reactions after the second dose are essentially the same as after the first dose, but are even rarer. There are no new side effects after the second dose that do not happen after the first dose. In one study, there were just as many symptoms in students who had not been vaccinated, as in a group who had just had their second dose. This suggests that the 'reactions' reported were probably unrelated to the vaccine. If children have responded to the vaccine the first time, they will not have any problem from being exposed to the viruses again. It's like any of us who are immune meeting someone with the disease - the infection can't get established. If a child did not respond the first time, they remain susceptible to natural infection, and need the second dose.

#### **15. Why not do a blood test to see if each child needs the immunisation?**

First, this would mean that all children would have to have a blood test, which itself is unpleasant. Second, blood tests are not 100% accurate and some children who were not immune would not be identified, would not receive MMR and would therefore remain susceptible to these diseases. Then there would have to be a mechanism for calling back children according to the results, and experience with rubella immunisation in this country, and testing for immunity before immunisation in other countries, has shown that this is not effective. The World Health Organization actually recommends that this is not done. Children who do not have antibodies or who have low levels of antibodies need a second dose. Reactions after a second dose are even rarer than after a first dose, and if they do happen are usually because the first dose did not give them sufficient protection. Over 30 European countries, the USA and Canada, give routine second doses of MMR and nobody tests for immunity beforehand.

#### **16. What should a parent expect after their child has received the MMR vaccine?**

Because MMR vaccine contains viruses that are very similar to those that cause the actual diseases, mild symptoms of the disease can occur. This is a sign that the vaccine is working properly and causing an immune response. Many children will have no symptoms at all. Children cannot infect other children with the viruses contained in the MMR vaccine. Soon after immunisation there may be soreness, redness or swelling at the injection site. After immunisation it is not unusual for children to experience a very mild form of measles with rash (about 1 in 10), fever (about 1 in 15), loss of appetite and a general feeling of being unwell for two or three days. More rarely (1 in 50) a child may develop a mild form of mumps with swelling of the glands in the cheek, neck or under the jaw about three weeks after immunisation. This only lasts a day or two. One to three weeks after the first dose there may be pain, stiffness or swelling in one or more joints because of the rubella component; this usually lasts up to three days. It is rare in young children and seems to occur more often when adult women are given rubella vaccine.

#### **17. Can there be serious side effects from the vaccine?**

Yes, but these are very rare after the first dose of MMR vaccine and are even less likely to occur after the second dose.

All medicines can cause side effects, but vaccines are among the very safest. Because live vaccines contain viruses that are very similar to those that cause natural infection, in theory it is possible for them to cause any illness that has been linked to the natural disease. They are unlikely to cause conditions that are not associated with the natural disease. It is known that if any of these illnesses are caused by the vaccine, they are likely to be milder

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and occur much less often than after the actual disease.

Clinical signs and symptoms that occur shortly after immunisation are often thought to be vaccine reactions, but there is a world of difference between a coincidental illness and a reaction actually caused by the vaccine. Nearly all children in the UK receive MMR vaccine at 12-24 months of age, and so a large number of 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. Additional information is required to prove that the two events are connected: biological plausibility that the illness could be caused by the vaccine; a recognised pattern of illness occurring at a higher rate in those recently immunised than the rest of the population; and laboratory evidence of vaccine involvement.

It is known that the conditions in section 1 can sometimes be caused by MMR vaccine. They occur far less commonly with the vaccine than they do with the diseases themselves. For example, a child is 1,000 times more likely to get encephalitis from the diseases than they are from the vaccine. There are no other serious conditions for which there is evidence from good studies to indicate an increased risk after MMR immunisation.

There is no increased risk from a second dose of MMR vaccine. With the exception of allergic reactions, complications can only occur in the 5-10% of children who did not respond to the first dose. In these children the risk of complications will be the same as that after the first dose.

The overall risk of complications after a second dose of MMR vaccine is therefore about 90-95% less than

that after the first dose.

Vaccines can also cause anaphylactic (allergic) reactions. These occur at a rate of 1 in 100,000. Whilst serious at the time, treatment leads to rapid recovery and there have never been any deaths in the UK from reactions to MMR vaccines.

Vaccines have been linked to certain rare conditions, but the cause of these conditions is not fully understood and may be due to a number of other factors. The possible link between vaccines and such conditions is extremely difficult to study and impossible to prove or disprove, because of the rarity of the conditions. The most compelling argument must be that millions of children are safely immunised in this and other countries each year. There is considerable worldwide experience with MMR vaccine and if the vaccine did cause any of these unusual conditions, this would have come to light over the period of our experience.

## **18. What should a parent do if their child is unwell after receiving MMR vaccine?**

All parents should be advised on the prevention and management of pyrexia following immunisation.

If a parent has any concerns about the health of their child after they have been immunised, particularly if they become seriously unwell, they should be encouraged to consult a doctor. It may be that the child is suffering from an illness that is totally unrelated to the vaccine.

If a doctor suspects a serious adverse reaction to MMR vaccine, he/she should report this to the Committee on Safety of Medicines, using the Yellow Card spontaneous reporting scheme.

## 19. Are there any children who should not be immunised?

Very few children cannot have the vaccine.

Even children with a very severe allergy when they eat food containing egg (involving swollen mouth and throat, breathing difficulties, shock) can be given MMR vaccine. Over 1,000 children with egg allergy have been studied - they were immunised safely with MMR vaccine. If a child has had a serious reaction when eating eggs, or food containing egg, then the parent should talk to their doctor about making special arrangements for the child's immunisation. This can usually be done as a day-case at the Paediatric Department of the local hospital.

Some children who are on medication that affects their immunity should not have live vaccines such as MMR.

The number of children with valid contraindications to MMR is less than one in a thousand. Immunisation may need to be delayed: if a child has a fever; has received another live vaccine recently, such as BCG; or has received immunoglobulin or another blood product in the past three months. Children with suppressed immunity, or those who had a serious reaction after the first dose of MMR, may not be able to receive the vaccine.

Parents should be encouraged to discuss these issues with the doctor or nurse if they are unsure whether their child should be immunised.

## 20. Is MMR vaccine associated with bowel diseases or autism?

With the amount of evidence we have available we can be very confident in saying quite clearly and categorically that there is no causal association at all.

The papers that have suggested there might be a link (and they have done no more than make a

suggestion) have been of poor quality and heavily criticised. On the other hand, there have been some very good papers which have shown no evidence of a link.

The main paper from which the theories around autism and bowel disease being linked to MMR have developed was by A J Wakefield et al and was published in the Lancet in February 1998.<sup>1</sup> This was a report based on 12 children. The parents of eight of these children associated their condition with MMR vaccine. It was therefore a small study and a very biased sample in that the connection with MMR had already been made. The following are quotes from the paper:

- "intestinal and behavioural pathologies may have occurred together by chance, reflecting a selection bias in a self-referred group".
- "we did not prove an association between measles, mumps and rubella vaccines and the syndrome described".
- "further investigations are needed to examine this syndrome".

The paper makes no mention of giving the vaccines separately. The paper itself is therefore not claiming to have proved anything, simply to have found a possible association that needs further investigation. (This further investigation has now been carried out and has found no association - see section 21 for details).

A commentary in the same issue of the Lancet heavily criticises the article and makes the following point:<sup>2</sup>

- "A first dose of MMR vaccine is given to about 600,000 children every year in the UK, most during the second year of life, the time when autism first becomes manifest. Not surprisingly, therefore, some cases will follow MMR vaccination. Biased case-

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ascertainment, as in this study, will exaggerate the association”.

Since publication the paper has been criticised in a number of ways. The epidemiology was very poor in the way the cases were collected and there were no controls. The tests for various factors e.g. immunoglobulins used adult rather than paediatric ranges. Had the correct ranges been used nearly all of the results reported as abnormal would in fact have been normal. Yet the fact that they were supposedly abnormal was used as support for the theory being put forward. Wakefield has also reported the detection of measles virus particles in the intestinal wall of patients with bowel disorders, however, other investigations, using more sensitive and specific assays, have not been able to reproduce these findings.

## **21. What evidence is there that MMR is not associated with autism or bowel disease?**

In contrast there is a lot of evidence that MMR is not associated with these conditions.

The Committee on Safety of Medicine set up a Working Party to examine reports of children whose parents believed that MMR had caused their illness.<sup>3</sup> This examined the records of 92 children with suspected autism and 15 with suspected Crohn’s disease. They concluded the evidence “did not support the suggested causal associations, or give concern about the safety of MMR or MR vaccines”.

The Medical Research Council (MRC) held a scientific seminar in March 1998 to review the work of Wakefield and his colleagues. The meeting included leading experts in virology, epidemiology, immunology, child psychiatry and gastroenterology. Wakefield was given time to fully present his work - both published and unpublished. The meeting reached the clear conclusions that:

- the available virological and epidemiological evidence does not support a casual role for persistent measles virus infection in Crohn’s disease;
- there is no evidence to indicate any link between MMR vaccination and bowel disease or autism;
- there is therefore no reason for a change in the current MMR policy.

Since then the MRC have kept the matter under constant review examining new evidence that has been put forward. In April 2000 they published a report concluding there was no new evidence to suggest a casual link between MMR vaccine and autism or inflammatory bowel disease.

The Joint Committee on Vaccination and Immunisation have kept the issue under constant review, examining all new evidence as it has emerged. They have repeatedly confirmed the safety of MMR and rejected any evidence of a casual link. Their most recent statement (at time of going to press) was issued in January 2001.

A group from the Royal Free Hospital, London carried out an epidemiological study.<sup>4</sup> They investigated all 498 known autistic children in North Thames since 1979 covering the period before and after the introduction of MMR in 1988. This was a well conducted study which included all children with the condition, not just those in whom the parents already suspected a particular cause. The study had the following findings:

- no increase in autism associated with the introduction of MMR in 1988 - but an increase would have been expected if MMR caused autism;
- no difference in age of diagnosis between MMR immunised and unimmunised children - yet if MMR was a cause the onset in immunised children should have been more strongly associated with the age of immunisation;

- no difference in the MMR immunisation rates between those children with autism and the general population - but we would have expected the rate to be higher in children with autism;

- no link between the timing of MMR and the onset of autism - again this would have been expected if there was a link.

The authors therefore conclude that their data do not support a causal association.

In December 2000 Patja et al published a study based on an enormous number of children.<sup>5</sup> The study looked at 1.8 million children who had received a total of 3 million doses of MMR. The study started in 1982 when MMR was introduced in Finland. It involved all children given MMR. Follow-up was for up to fourteen years and involved all hospitals, clinics etc in Finland so that whenever a children presented with a condition would be detected. The paper makes the following statements:

- “No cases of autism were associated with MMR vaccination during this 14 year follow-up”.
- “No cases of ulcerative colitis, Crohn’s disease or other chronic disorders affecting the gastrointestinal tract were reported”.

For a study of this size, with this length of follow-up, to make their statements gives us very strong evidence.

A paper published in the British Medical Journal in February 2001 analysed the incidence of autism for boys from 1988 - 1993.<sup>6</sup> (It was based on boys because they suffer from autism more commonly than girls). The uptake of MMR vaccine stayed virtually constant at 95% during this time, but the evidence of reported autism increased nearly fourfold. Whatever caused the rise in reports it couldn’t have been MMR as it was not increasing during this period.

These are just some of the papers that have not shown an association between MMR and autism or bowel disease. In fact, every paper that has carried out a proper epidemiological study has come to the same conclusion.

## **22. What about suggestions that MMR was licensed prematurely?**

Wakefield and Montgomery published an article entitled “Measles, mumps, rubella vaccine: Through a glass, darkly” at the end of 2000.<sup>7</sup> This article produces no new evidence but reviews a number of published articles. Unfortunately it is highly selective as opposed to the scientific standard of being systematic; and studies that do not support the author’s views are not mentioned. No search for all relevant publications was done.

The authors argue that early trials showed MMR vaccines caused gastrointestinal (GI) symptoms but that this was missed at the time because the data was wrongly analysed. In particular, they quote a paper by Stokes et al.<sup>8</sup> This paper compared children receiving MMR with controls. There were two parts to the study - in the United States and in South America. Wakefield claims the results for both geographical groups were combined for the statistical analysis and that this masked a GI effect in the US children. This is factually incorrect, the original paper does not state that the results were combined for analysis. However, Wakefield and Montgomery then go on to perform an incorrect analysis themselves. The original authors presented the number of children with GI symptoms in days 1-4, 5-12, 12-18, and 19-28. Wakefield and Montgomery have added up all the occurrences of GI symptoms across the entire 28-day period, regardless of whether the same children or episode is being counted more than once. Thus, for example, a child who is sick on days four and five will get counted twice. When analysing data it is essential that each child is only counted once.

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The design of the Stokes paper does nevertheless have its weaknesses. It is therefore surprising that Wakefield and Montgomery fail to mention the classic double-blind cross over randomised “twin” study of Peltola and Heinonen involving 581 twin pairs who received either MMR followed by placebo or placebo followed by MMR.<sup>9</sup> This paper established that, with the exception of fever, irritability and rash in the second week, most of the other symptoms reported after vaccination are co-incidental.

Other problems with the paper can be found on the website [www.immunisation.org.uk](http://www.immunisation.org.uk) Overall the paper is lacking in a coherent scientific rationale, selective in the reporting and interpretation of other work and statistically invalid.

Furthermore, whatever the evidence prior to the introduction of MMR in 1988 (and there was a lot of good quality evidence), we are now in 2001 and need to base our decisions on the evidence available to us now. That evidence, as has already been outlined, is that MMR is safe and effective with benefits by far outweighing any risks and is based on large, well conducted studies.

### **23. Why are the numbers of children affected by autism increasing?**

It is true there has been a steady increase in the number of reported cases of autism since the mid-80s. However, many experts in autism believe that much of this is not a true increase in the condition but is due to a raised awareness among parents and professionals leading to it being picked up more. There has also been greater recognition of the range of different types of autism.

The National Autistic Society have questioned whether there is a real increase (and have expressed their support for MMR).

A recent article in the journal *Pediatrics*, by an expert in this area from the MRC Child Psychiatry Unit, has

examined the data in detail and questioned whether there is any real increase.<sup>10</sup> He was particularly critical of people misusing data to support other theories.

Even if there has been a true increase there is no evidence that this is because of MMR.

### **24. Why do some parents believe their child developed autism as a result of MMR vaccine?**

MMR is given to children during the second year of life. It is around this time that many children with autism start to show signs of it. Over 90% of children have been vaccinated with MMR by their second birthday. Therefore many children who were going to develop autism anyway will do so after having MMR and some, by chance, will be soon after the vaccine.

However, to explain why parents blame MMR it is best to quote from the parent of a child with autism:<sup>11</sup>

“One reaction which we, and other parents in similar circumstances, had was to search for a possible cause. Had there been an infection during the pregnancy, an encephalitic element to Adam’s chickenpox, anoxia during birth, lead in our water supply (this was checked), any family history of learning difficulties, or a metabolic disturbance? An explanation might help us to decide whether or not to have another child but, more importantly, if we found the cause, perhaps, just perhaps, Adam could receive some existing, or yet to be developed, treatment which would reverse his cognitive and social deterioration.

“When, in 1998, Andrew Wakefield and his colleagues hypothesised that there could be an association between MMR and autism, it was entirely understandable to us why many, though not all, parents of autistic children became either partly or totally convinced that this was the answer”.

## 25. Aren't experts divided over the issue?

The way the issue has often been reported in the media would give the impression that doctors and others are split down the middle over this issue. In fact the overwhelming majority strongly support the use of MMR. In January 2001 following a paper by Wakefield and Montgomery a joint statement was issued on behalf of:

Royal College of Paediatrics and Child Health  
Royal College of General Practitioners  
Royal College of Nursing  
Community Practitioners and Health Visitors  
Association  
Faculty of Public Health Medicine

These professional bodies include many of the health professionals who are involved in caring for children with autism. If they had any doubts then they would not be promoting something which might cause autism - they know what a devastating condition it can be, but they fully support MMR vaccination.

Quotes from the statement include:

"Our specialists in immunisation have studied the recent paper by Dr Wakefield and Montgomery with great care... Our professional confidence in the MMR vaccine, its safety and effectiveness remains fully justified. Contrary to what is suggested by the authors there is a large body of evidence showing that the combined vaccine is highly effective and serious side effects are uncommon. The specific suggestions that MMR causes either inflammatory bowel disease or autism have been well researched in recent years by independent scientists. No association has been found and we remain convinced of the safety and effectiveness of MMR vaccine".

"In contrast, the suggested alternative of giving single vaccines instead of MMR is untried and of unproven safety and effectiveness".

"As professionals intimately involved in the long-term care of children, as well as in the immunisation programme, we wholeheartedly endorse the current policy of using the combined MMR vaccine".

## 26. Why do we not offer measles, mumps and rubella vaccines separately?

There are a number of reasons for this but essentially there is not a shred of evidence that it would do any good, but there is plenty of evidence that it would do a lot of harm.

Nothing has been published that even suggests that giving the three components separately would be any safer than giving MMR. The paper published in the *Lancet* in 1998 makes no mention of giving the three separately.<sup>1</sup> What happened was that one of the authors of the paper had speculated to the press that giving them separately might be safer. No trials have been done which support this, it is purely theoretical speculation. Unfortunately, this is an aspect the press have really picked up on and blown out of all proportion. Even some of his fellow researchers don't agree with him. One stated on Radio 4 "what's important is that children are vaccinated ...the risk with splitting vaccinations is that we haven't done specific research on whether individual vaccines, as opposed to the combined, make any difference. Anything that affects uptake rates, perhaps if they're split, some children may not be vaccinated; that increases the risk of disease. So, the message is continue vaccinating, obviously."

## 27. What are the risks of giving three single vaccines?

Dr Wakefield has suggested that not only should the vaccines be given separately but that there should be a year between each one. The main risk from this is that it would leave children unprotected against two of the diseases and we would start to get outbreaks of them again. Some children would undoubtedly suffer serious complications and some would die as a result.

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This approach would also result in six injections instead of two. In addition to the unnecessary stress this could cause a child, it also increases the risk of repeated reactions at the site of injections.

As giving the vaccine separately has never been properly investigated we do not know what other risks there might be. It is somewhat ironic that a doctor who has said there was not enough evidence about MMR (about which at least 30 papers had been published) should propose an alternative approach about which there is no safety information and no papers have been published.

## **28. But don't other countries give separate vaccines?**

No, this is another myth that has been allowed to grow. No country in the world recommends that MMR vaccine is divided into three separate injections. No country in Europe recommends that parents be given the choice of having the three vaccines separately.

France has often been mentioned as a country that gives the three separately - again this is not true. The situation in France is as follows:

They recommend that children aged 9 - 12 months attending nursery school have a single measles vaccine. All of these children then also receive two doses of MMR at the appropriate ages. All other French children receive two doses of MMR - the same as here. There is no appropriate single mumps vaccine available in France and there is no recommendation for it. Single rubella vaccine is available for non-immunised women planning to become pregnant.

Many parents who have obtained mumps vaccine from Europe will have received either the Urabe or Rubini strains. The Urabe strain was withdrawn in this country in 1992 because it was found to be associated with aseptic meningitis. The Rubini strain only has an efficacy of 12%. Obviously neither are therefore licensed in this country. We use the Jeryl

Lynn strain in MMR which has been shown to be highly effective and doesn't cause aseptic meningitis. Japan is another country that is quoted as giving the vaccines separately and as having banned MMR. The MMR vaccine that we use in the UK has never been used, let alone banned, in Japan. A Japanese MMR vaccine containing the Urabe strain of mumps (see above) was withdrawn in Japan in 1993 due to unusually high rates of aseptic meningitis following vaccination. As there is no alternative MMR vaccine licensed in Japan, they were forced to recommend single measles and rubella vaccines. These two vaccines are given simultaneously and not separated by the 'one year' unilaterally recommended by Wakefield. The consequences in Japan have been a dramatic rise in the disease resulting in at least 75 deaths from measles. Rather than supporting the case for single vaccines the situation in Japan powerfully supports the benefits of the combined MMR vaccine.

It would therefore make no sense whatever to offer the vaccine separately, nothing would be gained and a lot of harm would be done.

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## 29. Conclusion

In the mid 1970s there was a scare about whooping cough vaccine. Uptake levels fell from 80% to 30%. Three whooping cough epidemics occurred over the next few years as a result. During these epidemics over 300,000 children were sick, some suffered long-term damage and at least 70 children died. The scare was later shown not to be true - however, in the meantime 70 children had died because of it. It is essential that the same thing doesn't happen with MMR. We can be sure that if uptake levels do drop the diseases will return and children will die as a result. This is a safe vaccine, whose benefits by far outweigh any risks and we need to continue to have very high uptakes for it.

Obviously, the final decision on whether or not to vaccinate a child lies with the parents. However, it is essential that all health professionals discussing the issue with parents give them a clear message. Parents should know that the health professional clearly and unambiguously supports the use of MMR and that the benefits to be gained from it by far outweigh any small risks involved.

**Further information can be found on the following websites:**

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

[www.dhssni.gov.uk](http://www.dhssni.gov.uk)

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**Further references, giving details of these and other papers on MMR, can be found in the publication *Immunisation: Factsheets for professionals* printed by the Health Promotion Agency for Northern Ireland in October 1998.**

### **BE WISE -IMMUNISE**



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