

## 20 Vaccination Questions and Concerns

This chapter provides information that can be used when responding to concerns from the public and health professionals about how vaccines work and the safety of vaccines. In particular, it addresses some recent concerns about vaccines and the National Immunisation Schedule.

There is a section discussing how the public's and health professionals' perceptions and concerns are translated and relayed through the media and how this may affect a parent or caregiver's decision to immunise their child. Although there have been enormous benefits from immunisation – such as the eradication of smallpox, near eradication of poliomyelitis, and improved prevention and control of other infectious diseases – there are also new and emerging infectious diseases that challenge our understanding of infectious agents and the body's response to them. These challenges are stimulating research and studies into vaccine safety and any longer term effects of both infectious diseases and vaccines.

The information is grouped under the following headings:

- 20.1 Some commonly asked questions
- 20.2 Responding to concerns about immunisation
- 20.3 Lessons from the past
- 20.4 Conclusion

### 20.1 Some commonly asked questions

#### (a) Which vaccines can be administered together?

There are no known contraindications to administering licensed vaccines together, provided they are administered in separate syringes at different sites. Some liquid vaccines may act as the diluent for a lyophilised vaccine, but this should only be done if specifically recommended by the manufacturer and approved by the licensing authority. If two live vaccines are not given simultaneously, they should be given at intervals of at least four weeks.

#### (b) How should the rest of the National Immunisation Schedule be handled when a complication occurs after administering a vaccine?

Evaluate the probability that the complication is due to the vaccine and, if appropriate, report the reaction to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442 (see section 2.4) or via online reporting at [www.carm.otago.ac.nz](http://www.carm.otago.ac.nz). If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

Consult the relevant section of this Handbook, and if need be seek specialist advice (eg, from the medical officer of health, the Ministry of Health, or the Immunisation Advisory Centre, IMAC).

**(c) What steps are required if the immunisation schedule is interrupted?**

There is no need to repeat prior doses. Simply continue the vaccine schedule as if no interruption had occurred. Remember that children who miss a vaccine dose may do so again, and that close follow up may be required. (See Appendix 2 for immunisation catch-up schedules).

**(d) What if the child had a difficult birth or was premature?**

These are not contraindications to vaccination, which should be carried out at the usual chronological age. However, if the child is still in hospital or recently discharged, please seek the advice of the treating specialist. (See also section 1.8, section 3.5 on hepatitis B, and section 7.5 on *Haemophilus influenzae* type b, or Hib.)

**(e) What special vaccines are offered to newborn babies?**

Babies of mothers who are carriers of hepatitis B virus are given hepatitis B vaccine and hepatitis B immunoglobulin at birth to prevent infection with the virus. They then receive the usual immunisations at six weeks, and at three and five months of age. (See section 3.5 for recommended immunisation schedule for babies of HBsAg positive mothers).

A baby who may be at higher risk of tuberculosis is offered a Bacillus Calmette-Guérin (BCG) immunisation soon after birth. (See section 12.5 for neonatal BCG eligibility criteria.) The lead maternity caregiver will discuss this issue with the mother prior to her baby's birth, and the BCG immunisation may be given while the baby is in hospital or later at a community clinic.

**(f) What if the baby is unwell?**

Minor illness or being in the recovery phase are not reasons to postpone immunisation. If immunisation is postponed it is important to ensure the child is not lost from recall (see section 1.9, and the sections in specific chapters for contraindications of the relevant vaccines). Babies with severe illness should have immunisation postponed until they are better, because complications of the original illness may be misinterpreted as a complication of the immunisation.

**(g) What if the baby is allergic?**

Only anaphylaxis is considered a contraindication or precaution for immunisation. See sections on contraindications, in particular for measles (section 9.7) and influenza (section 13.7). Children with asthma, eczema, hay fever and simple allergies should be immunised in the usual way.

### **(h) What if the child's mother is pregnant?**

This is not a contraindication to giving National Immunisation Schedule vaccines to a child. In particular, measles, mumps and rubella (MMR) vaccine should be given, because it will reduce the risk of the child developing rubella and then infecting the mother.

### **(i) What about recent immigrants?**

Such children should be immunised according to the National Immunisation Schedule with due account taken of prior vaccine administration (see section 1.7). It is important to err on the side of giving rather than withholding vaccines if the vaccination history is uncertain. (See Appendix 2 for immunisation catch-up schedules.)

### **(j) What if the child is due to have an operation?**

Immunisation should be avoided within three days of an anaesthetic (12 days for MMR) in case an adverse event occurs following immunisation and results in the postponement of the anaesthetic.

Individuals scheduled for splenectomy should be immunised at least two weeks before the operation; from 2006 pneumococcal, meningococcal and Hib vaccines are publicly funded for these individuals (see section 1.8 and relevant vaccine chapters).

### **(k) What if the child has a chronic disease?**

Children with chronic diseases should be immunised in the normal way, especially as they may be more likely to suffer the severe effects of vaccine preventable diseases. However, if the illness or its treatment results in impaired immunity, immunisation with live vaccines should be considered carefully (see section 1.8). Consult the child's paediatrician before immunisation.

### **(l) What if the child has had fits or convulsions?**

Stable neurological disease is not a contraindication to any vaccine. However, unstable or undiagnosed neurological disease is a contraindication to pertussis immunisation. After any vaccine a febrile response may occur, and it is possible that such a response could result in a febrile convulsion in a susceptible child. A family history of fits, or epilepsy of any type, is not a contraindication to immunisation.

### **(m) Can children be immunised if they are known to develop a rash with antibiotics?**

Yes. The currently available vaccines do not contain commonly used antibiotics. Some vaccines contain traces of neomycin and/or polymyxin. However, it is extremely unlikely that any child will have been administered either of these antibiotics, and even more unlikely that a child will be allergic to them.

**(n) Is it possible to boost a child’s immune system?**

Children who are healthy have an immune system that functions optimally. Eating a healthy diet, getting adequate sleep and exercise, and minimising stress will help keep the immune system healthy.

**(o) Are live virus vaccines of measles, mumps, rubella and varicella transmissible?**

The live attenuated strains of viruses selected for these vaccines are less likely to cause disease and less likely to be transmitted to a susceptible person. On the very rare occasions when transmission of the vaccine virus has occurred, it has resulted in only minor illness in the person infected (see chapter 9 for MMR and chapter 17 for varicella).

**(p) Can all children receive all the vaccines?**

Rarely a child may have an underlying illness that is a contraindication to a vaccine. The doctor or nurse will assess each child (ie, the family history) to be certain it is safe to give a vaccine.

For example, BCG is contraindicated until after a baby is fully assessed if there is a family history of an immune deficiency disorder. Another vaccine that is not given to some children is varicella vaccine, which is not given to immunosuppressed children. (See chapters 12 and 17, and section 1.8.)

## **20.2 Responding to concerns about immunisation**

### **Introduction**

This section provides information on concerns that have been raised about immunisation, and outlines what is required for a reasoned response. Although much of the section deals with responding to so called ‘anti-immunisation’ views, the approach should be similar for anyone who has concerns. It is important to understand the nature of the parent’s/caregiver’s concern and to respond appropriately with as much information as possible. Individuals have the right to make decisions for themselves and those in their care, and to accept responsibility for their decisions. It is important to respect this right.

In New Zealand, as elsewhere, there are groups of people and individuals who actively campaign against immunisation. Many of those who are active in the anti-immunisation lobby have become so as a result of personal experience, frequently because their child developed a disease or condition they attribute to immunisation. Some individuals who have raised concerns with health professionals have been dissatisfied with inadequate or superficial responses. It is important for all health professionals to be able to provide accurate information about the benefits and risks of immunisation and to respond with as much information as possible to parent/caregiver concerns.

It may be necessary to accept that parents/caregivers have emotional as well as intellectual concerns, and to accept that their opposition may not be changed by rational argument or presentation of evidence. Anti-immunisation arguments are often based on either rejection of the evidence supporting immunisation or on alternative views of health and health care. In any discussion it may help to acknowledge that science does not have all the answers, and that there is more to preventing disease than immunisation. Though at times it may be difficult for those affected to understand, it is also important to point out that an adverse event that follows immunisation is not necessarily caused by the immunisation. It is always helpful to inform parents/caregivers about additional sources of information (see sections 2.2 and 2.3).

### **Understanding anti-immunisation views**

Some of the appeal of the anti-immunisation lobby is based on the increasing popularity of ‘alternative’ views of the world. These views may be summarised in the idea that ‘natural’ is better than ‘man made’. The ecological movement has brought increasing acceptance that technology cannot deal with all of humanity’s problems, and that new problem solving technologies can themselves be the source of new problems.

An Australian analysis identified eight subtexts in press reports of anti-immunisation arguments:<sup>1</sup>

- cover-up – information is suppressed to keep the true facts hidden
- excavation of the ‘facts’ – there is a large amount of scientific evidence against immunisation that can be found if searched for, and many medical experts who oppose immunisation
- unholy alliance for profit – doctors, pharmaceutical companies and the government collude for the sake of the profits made from the sale of vaccines
- towards totalitarianism – government uses the law to force immunisation as the first step towards increased state control
- us and them – caring and concerned friends and parents against doctors, pharmaceutical companies and bureaucrats
- poisonous cocktails – vaccines are toxic and made from undesirable products
- cause of idiopathic illnesses – many illnesses of unknown cause are blamed on vaccines
- back to nature – natural (disease) is better than man made (vaccine).

English researchers have identified five key concerns of parents, and have suggested helpful responses to these concerns.<sup>2</sup> These are summarised in Table 20.1.

**Table 20.1: Concerns about vaccination and suggested responses**

Concern	Response
The disease is not serious.	Healthy children can still die from these diseases.
The disease is uncommon.	The disease is common in <i>unimmunised</i> populations and can easily recur and spread if immunisation rates drop.
The vaccine is ineffective.	Studies showing the effectiveness of a vaccine are needed before a vaccine is introduced.
The vaccine is unsafe.	As with effectiveness, the safety of a vaccine is rigorously tested before, and after, its introduction.
Other methods of disease prevention, such as homoeopathy are preferable to immunisation.	There is no body of scientific evidence that supports homoeopathy or other methods for preventing the diseases.

Source: Bedford H, Elliman D. 2000. Concerns about immunisation. *BMJ* 320: 240–3.

## Questions and concerns on:

### (a) Principles of immunisation and immunity

#### *‘Immunisation is unnatural’*

The claim that immunisation is harmful simply because it is artificial is not based on evidence. Some claim that the immune system was not designed to be exposed ‘directly’ to an antigen, in the manner of an injection. The immune system is designed to deal with invaders, wherever they enter the body. For example, the injectable polio vaccine has been shown to work just as well in protecting against disease as the oral vaccine, which enters the body in the same way as the infection. Immunisation by injection has also been shown to be safe and effective at preventing diseases like measles that normally enter the body through the airways.

#### *‘The germ theory of disease is false’*

The germ theory of disease was a major scientific advance, which has enabled the understanding of many – and the control of some – infectious diseases. However, when germs (bacteria, viruses, etc.) were first discovered, there was no proof that they caused illness. Germs could have been the result, rather than the cause, of disease, and there was debate in the 19th century about their role. However, the roles of bacteria, viruses and other micro-organisms in causing infectious diseases are now scientifically proven. Nevertheless, some people continue to question the role of micro-organisms. For these people, immunity to specific diseases, and hence immunisation, is irrelevant: one simply keeps healthy to prevent infection. It is true that a person’s state of health may sometimes influence how ill they become when infected, but some individuals in excellent health can suffer the severest effects of infections (eg, young adults who suffer meningococcal disease).

## (b) The need for immunisation

*'Immunisation has played a minimal role, if any, in controlling disease'*

It is true that improvements in living standards, in particular clean water, have had a great impact on health, but immunisation has played an important role as well. In the 1950s the incidence of paralytic polio was increasing until the Salk injected vaccine was introduced. The use of the oral vaccine from 1961 led to the elimination of wild polio from New Zealand and elsewhere.

Improvements in living conditions and medical care have reduced the chance of dying from infectious disease, but without immunisation most people will still acquire some infections. For example measles, which spreads through the air, is largely unaffected by improvements in living conditions other than reducing overcrowding. Healthy children living in ideal conditions remain at risk of death and disability from infections that can be prevented by vaccination. Smallpox vaccination led to the elimination of smallpox – this would not have occurred with improvements in living standards alone.

A recent example of the impact of immunisation was seen in New Zealand, and elsewhere, following the introduction of the Hib vaccine in 1994.<sup>3</sup> This led to an approximately 95 percent decline in Hib disease – unrelated to any other change (see chapter 7). Indeed, it is possible that a change in living conditions (ie, an increased number of children attending early childhood services) could have led to an *increase* in the incidence of invasive Hib disease, but this did not happen because of the effective Hib vaccine.

Conversely, when pertussis immunisation coverage dropped in England, Japan and Sweden in the 1970s there were dramatic increases in pertussis disease and deaths. The role of immunisation is discussed in more detail in each chapter, but its overall impact on vaccine preventable diseases and their consequences has been well established. If immunisation coverage is sufficiently high, then polio, measles, mumps, rubella, Hib, and hepatitis B eventually could be eliminated from New Zealand through immunisation.

*'Infectious diseases are not serious, and are needed for normal development'*

The morbidity and mortality of vaccine preventable diseases is detailed in each disease chapter. Some claim that measles is important for normal development and that after the illness children have a leap in physical and mental development. There is no evidence to support this, but given the serious impact of measles on a child's health it is not surprising that a child who has recovered will be noted to have much more energy than during the illness. On the other hand, there is evidence that a child has reduced immunity for weeks to months after measles,<sup>4</sup> and during this time the child is more likely to get other infections.

*‘Natural measles prevents cancer later in life’*

This claim is based (by people other than the original author) on one small Danish study that found a statistical association between certain chronic diseases and cancers, and early exposure to measles infection, possibly modified by the injection of measles antibodies in measles immunoglobulin.<sup>5</sup> The fact that these children failed to develop a rash has been used to claim that it is essential to develop the rash of measles. The study has also been used to suggest that giving vaccine is dangerous if antibodies are present.

These are not the findings of the study, nor does the study author suggest that measles prevents these diseases. The paper concludes: ‘Several types of evidence need to be examined before one can accept the hypothesis that measles virus causes non-measles associated disease.’ No such evidence has been found for these associations.

*‘Vaccines do not work as most cases of disease are in immunised children’*

No vaccine is 100 percent effective and some immunised children will get the disease. As immunisation coverage increases, the proportion of cases that occur in children who have been immunised increases. There is a simple relation between vaccine effectiveness, immunisation coverage and the proportion of cases that are immunised.

To see this clearly, imagine a group of 100 children. If 90 percent of children are given a vaccine that is 90 percent effective, then:

- 81 of the 100 children will be immune
- 10 children will be susceptible because of not having the vaccine and another nine because of vaccine failure.

This means that we expect that nearly half the cases of disease will be in immunised children – even though only 10 percent of immunised children were susceptible.

Of course if all 100 children had been vaccinated only 10 would be susceptible to disease. As vaccine uptake rises, the *proportion* of cases of disease that occur in vaccinated people increases dramatically, but the *number* of cases of disease falls to very low levels.

For pertussis, where the protection following vaccination lasts only a few years, most immunised children will be reinfected but the resultant illness will be milder, with fewer serious consequences and at an older age than if they had not received vaccine. The disease is most severe in infants.

*‘Immunisations are not needed in industrialised countries’*

Many diseases prevented by immunisation are spread directly from human to human. Clean water and good hygiene do not stop airborne infections or those spread by direct personal contact. Despite excellent hospital care, long term

complications and death still occur from diseases that can be prevented by immunisation. Although it is true that the impact of immunisation is greater in non-industrialised countries, it remains very important for children in industrialised countries such as New Zealand.

At present the risk of getting some vaccine preventable diseases is low because most children have been vaccinated. The degree of risk depends on the proportion of children who have been immunised. This is termed 'immunisation coverage'. If enough children have been immunised, the organism will not be able to circulate in the community, and the likelihood that those who have not been immunised, or who have failed to respond to immunisation, will be infected is correspondingly reduced. This is termed 'herd immunity'. Immunisation offers the possibility of eliminating disease, as has happened with smallpox and, in some areas of the world, with polio and measles (see chapters 8 and 9).

#### *'Natural immunity is better than vaccine induced immunity'*

The duration of immunity following vaccination may be less than the duration of immunity after the disease. However, both are protective, and if immunity following immunisation wanes, booster doses may be given. It is important to note that the 'lifelong' immunity following natural measles is in the context of repeated exposure to the organism throughout life. With vaccine induced immunity such boosting is much less likely to occur because of reduced circulation of the organism.

Natural immunity and vaccine induced immunity are virtually identical natural responses of the body's immune system. Those who suffer 'natural' disease run the risks of serious illness, disability and death to acquire immunity. In contrast, the acquisition of vaccine derived immunity is at much lower risk. However, several doses of vaccine, and booster doses, may be necessary to attain and maintain good levels of immunity, and immunisation does fail in a small proportion of vaccinees.

For some organisms (eg, Hib in children under two years, and tetanus at any age) the immunity following vaccination is better than that following infection. With Hib this is because the vaccine can stimulate immune memory in infants in a way that the disease does not. For tetanus this is because the disease can be caused by a small amount of the toxin insufficient to generate an immune response. In 1995 a 40-year-old man developed tetanus for a second time because he failed to complete the recommended course of immunisation after recovering from an earlier episode of tetanus (see chapter 5).<sup>6</sup>

#### *'A healthy lifestyle will protect children from infection'*

A healthy lifestyle does not produce the necessary immune response to protect a child from a specific potentially serious infection. Only immunisation or being infected by the organism can do this. Immunisation poses far less risk than natural infection because it is very unlikely to cause an illness, while those suffering natural infection are very likely to become ill.

The living arrangements of a person (eg, overcrowding, inadequate sanitation and hygiene) will affect the likelihood of exposure to infection. For most diseases, the health of a person makes little difference to the likelihood of being infected if exposed. However, those in good health will be less likely to suffer a severe illness, or complications, as a consequence of infection.

Nevertheless, a healthy lifestyle does not provide secure protection against disease or its complications. For example, over half of all the children who died from measles in the United Kingdom (UK) between 1970 and 1983 were previously healthy.<sup>7</sup>

#### *'Breastfeeding protects against infection'*

There is good evidence that breastfeeding reduces to some degree the frequency and severity of gut, chest and ear infections. The extent to which it protects against other diseases is less clear. The protection from breastfeeding varies from person to person and is of brief duration. Both breastfeeding and immunisation contribute to the health of children.

#### *'Homoeopathic immunisation prevents infection'*

Homoeopathic 'immunisation' offers no proven protection against infectious diseases. Dr Hahnemann, the founder of homoeopathy, considered conventional immunisation to be 'a clear and convincing demonstration of the Law of Similitude'<sup>8</sup> – the fundamental principle of homoeopathy. The UK Faculty of Homoeopathy supports conventional immunisation and is not aware of any evidence supporting the use of homoeopathic immunisation.<sup>9</sup>

Some non-medical homoeopaths do not support conventional immunisation, and state that homoeopathic preparations can prevent disease. There are no published studies to support such beliefs – an extensive review of homoeopathic studies found none on the prevention of the usual childhood immunisation schedule diseases.<sup>10</sup> There were some studies on the prevention of influenza, with all but one showing no effect. The single study that did find a protective effect was rated 'of poor quality'.

Only conventional immunisation has been shown to produce a measurable immune response and protection against disease.

#### *'Other countries have stopped immunisation'*

Every country in the world has some type of immunisation programme, and in some it is compulsory. Individual vaccines have been withdrawn from use in certain countries at different times for differing reasons. In 1979 Sweden stopped using pertussis vaccine because of concerns about the efficacy of the locally produced vaccine and because there were concerns that pertussis vaccine might cause brain damage (see below). Sweden was actively involved in testing acellular pertussis vaccines, and has re-introduced pertussis vaccination. France stopped its school-delivered hepatitis B immunisation programme for adolescents to enable recipients to discuss the issue with their family doctor. Hepatitis B vaccine is still widely used

in France and is part of the routine childhood immunisation schedule. In Japan the use of MMR vaccine was temporarily stopped because of concerns about meningitis following the strains of mumps vaccines used there. In 1992 the Urabe strain of mumps vaccine in MMR vaccine was withdrawn from New Zealand and other countries, and replaced with one that is not associated with an increased risk of meningitis (see chapter 10 Mumps).

### (c) Vaccine content

*'Vaccines contain toxic chemicals, viruses and cells'*

Vaccine production is highly regulated, requiring extensive testing during manufacture and of the final product. The testing standards are rigorous and internationally regulated by independent authorities. The manufacturer must show that each dose is safe, pure and potent enough to be effective. Any toxic substances (eg, formaldehyde) present in vaccines are only permitted in tiny amounts, too small to cause any harm.

There have been unwanted viruses in vaccines in the past: *avian leucosis* virus in yellow fever vaccines, *SV40* in polio vaccines in the 1950s (see section 20.3), and *pestivirus* in some Japanese vaccines in the 1980s. All vaccines are carefully tested now to ensure that no other viruses or bacteria are present. The sophistication of this testing continues to improve.

In 1995 there was concern that a previously unidentified virus could have been the source of an enzyme, reverse transcriptase, found in vaccines grown in chick cells. The finding was made when a new test that was a million times more sensitive than the prior test was used. Further work has identified that the source of this enzyme is the chick cells on which the vaccine is grown, not a virus.<sup>11</sup>

Some vaccines (eg, rubella) are grown in cells of human origin. The source of some of these cells was a fetus aborted for medical reasons in the 1960s. By a process of repeated cultivation it is possible to produce an 'immortal' self replicating group of cells known as a 'cell line'. A cell line is similar but not identical to the original cell, and apart from the origin of the cell there is no connection to any fetus. The cell line can be maintained indefinitely in the laboratory and provides a safe and standardised medium for growing vaccine viruses.

Whether vaccines are grown on cells of human or animal origin, whole cells are not in the final vaccine. Once the virus has been cultivated in cells, it is separated from all cellular material. It is possible that minute traces of cellular material might remain in a vaccine, but not whole cells.

During the early stages of the human immunodeficiency virus (HIV) epidemic it was suggested that an early polio vaccine was cultivated in chimpanzee cells contaminated with the precursor of HIV-1. It was suggested that the use of this polio vaccine resulted in the transfer of the virus to humans, and was the source of

HIV. Investigation of the claim revealed that no chimpanzee tissue was involved in the production of the vaccine. Supplies of the early polio vaccine were discovered in freezers and tested in several laboratories, all of which agreed that no HIV, nor chimpanzee DNA, was present in the vaccine. Thus it has been convincingly demonstrated that polio vaccine was not the source of HIV.<sup>12</sup>

*‘Vaccines contain aluminium – a cause of Alzheimer’s disease’*

The cause of Alzheimer’s disease, a degeneration of the brain leading to dementia, is not known. There have been some studies suggesting a link with aluminium in the water supply, but it remains uncertain if aluminium does indeed play a role in causing Alzheimer’s disease. The amount of aluminium in a vaccine is tiny and within accepted safety limits.

*‘Vaccines contain aluminium – why is it in a vaccine and does it harm my child?’*

Clinical studies have found that the effectiveness of some vaccines is improved by the addition of chemical compounds called adjuvants, which increase the body’s immune response to the vaccine and therefore the level of protection. Aluminium compounds have been used for many years as adjuvants in vaccines, and include aluminium sulphate, aluminium hydroxide and alum (potassium aluminium sulphate). Although there have been some claims of adverse effects from these compounds in vaccines, no major effect has been proven. In a systematic review of the evidence for any adverse events after aluminium containing diphtheria, tetanus and pertussis vaccines, it was found there were no serious or long term adverse effects/illness.<sup>13</sup> This review found that aluminium hydroxide containing vaccines did cause more local reactions in infants, including erythema and induration, but that there was no association between aluminium containing vaccines and severe events such as collapse, and persistent crying or screaming. In older children, 10 to 16 years of age, the only differences were that after an aluminium containing vaccine the children were more likely to have pain at the injection site 14 days after the immunisation.

*‘Vaccines contain mercury – is it safe?’*

The vaccines used on the usual New Zealand National Childhood Immunisation Schedule are all thiomersal free; that is, they do not contain any mercury compound. However, thiomersal is found in both child and adult doses of the combination diphtheria, tetanus vaccines (CDT™ and ADT™; 0.01 percent w/v), and in some influenza vaccines.

Very small quantities of mercury compounds such as thiomersal are used in some vaccines as a preservative. The tiny quantity of mercury in a dose of vaccine is not harmful, but because babies now receive several different vaccines the quantity of mercury that was given in vaccines on the United States (US) immunisation schedule exceeded some exposure guidelines.<sup>14</sup> There have been historical reports of adverse developmental outcomes in infants following ingestion of fish with toxic levels of

methyl mercury by pregnant women. Thiomersal is, however, a different organic compound which is metabolised to ethyl mercury and thiosalicylate.

Because there was a desire to avoid using any extra chemicals, the vaccine manufacturers developed vaccines without the mercury compound as preservative. The Immunization Safety Review Committee of the Institute of Medicine in the US reviewed the data and in 2001 concluded that the existing evidence was inadequate either to accept or reject an epidemiological relationship between thiomersal exposure and neurodevelopmental disorders. Nevertheless, the report stated that a link was biologically plausible and recommended the use of thiomersal free vaccines.<sup>15</sup>

#### *'Vaccines may cause mad cow disease'*

Before extensive controls were put in place, the materials used in some vaccines could, in theory, transmit the infectious agent responsible for bovine spongiform encephalopathy (BSE) or mad cow disease, or its human equivalent variant Creutzfeldt-Jakob disease (vCJD). After billions of doses this has not been documented. In addition, for those vaccines that use material from cows, the manufacturer must ensure that these materials come from BSE free areas and have been purified to reduce any risk.

Authorities in the US have reached the following conclusions about the risk of vCJD from vaccination.<sup>16</sup>

- No evidence exists that cases of vCJD are related to the use of vaccines.
- There is no evidence that any vaccines harbour the BSE agent.
- There have been no reports of BSE contamination of pharmaceutical or biological products.
- No bovine material has ever been used as an active ingredient of any vaccine.
- There is no evidence that vaccines have contributed to cases of vCJD in Europe.
- The distribution of vCJD cases does not support concern regarding vaccines. Vaccines are distributed globally, yet cases of vCJD have almost entirely been restricted to the UK.<sup>17</sup>

There is a theoretical risk that vaccines that contain human blood products (eg, albumin in MMR) might transmit vCJD. There have been two cases of vCJD in the UK that are thought to be the result of whole blood transfusion from donors who were incubating the disease. In vaccine manufacture the blood donor selection and exclusion policies minimise any risk, as would the extraction and preparation of the blood product. There has so far been no evidence of transmission of vCJD from vaccines.

*‘Vaccine viruses persist after immunisation’*

Vaccine viruses are supposed by some opponents of immunisation to persist in the body, leading to chronic disease. Varicella vaccine does persist after immunisation and may rarely cause shingles. There is no evidence that the constituents of other vaccines persist after immunisation.

**(d) Vaccine risks**

*‘Vaccine risks are greater than the disease’*

When immunisation allows us to gain control over a disease, the risk of being infected becomes very low. For example, there is no risk of getting polio in New Zealand unless it is imported. On the other hand, before the change to inactivated polio vaccine (IPV) in 2002 there was a very small risk of paralysis from oral polio vaccine (OPV) at a rate of about 1 in 2.4 million doses. The risk from OPV was then greater than from natural disease, but this is precisely because immunisation has reduced the risk of natural disease in the first place. It is the consequence of any immunisation programme that the risk of vaccination, if the vaccine is successful in eliminating the disease, will become greater than the risk of disease, which will have been reduced to zero. Such a circumstance is evidence of the success of vaccination. This is the reason for the switch to IPV in 2002 (see chapter 8).

In the US there are now more reports of adverse events following immunisation than there are of vaccine preventable diseases. Even if all the adverse events were caused by immunisation – and they are not – this is not a fair comparison. One needs to compare vaccine risks with disease risks in the absence of immunisation. Vaccinating is far less risky than not vaccinating.

*‘Most vaccine reactions are not reported in New Zealand, so vaccine risks are underestimated’*

The usual expected reactions following immunisation are not reported. Practitioners are asked to report serious and unusual adverse events following immunisation rather than mild, expected reactions to CARM (see section 2.4). It is likely a few adverse events are not reported. This can be for many reasons, including failure to recognise that the event may be linked to immunisation. However, vaccine risks are estimated from a variety of sources, including controlled studies prior to licensure and post-marketing surveillance following licensure. Studies prior to licensure are not usually undertaken in New Zealand. The rate of adverse events reported in New Zealand has generally been lower than the rate of adverse events documented in prospective studies.<sup>18</sup> Nevertheless, in New Zealand a greater proportion of serious events than minor reactions are reported.

*‘The follow up in vaccine studies is too short to detect any long term risks’*

In order for a vaccine to be used, a rigorous and extensive process is undertaken to demonstrate that the vaccine is safe and prevents disease. This includes careful follow up to identify any adverse events following immunisation. The nature of these

studies is such that only short term effects can be detected. There are, however, several different sorts of studies that can identify longer term effects. Such studies identified an increased mortality in children who received high dose measles vaccine compared to normal dose measles vaccine. As a result, the use of high dose measles vaccine was stopped. This vaccine was never used in New Zealand. There has also been long term follow up of those people who received polio vaccines contaminated with SV40 virus (see section 20.3).

There have also been allegations of Crohn's disease, autism, asthma and diabetes following immunisation. These have been investigated, showing that studies of long term effects can be, have been and continue to be undertaken. These studies have not shown any evidence of long term adverse effects.

#### *'Children are more susceptible to disease after immunisation'*

There is little evidence to support this statement. Controlled studies monitor adverse events, including any increased risk of infection. By chance, some studies will identify more infections in the vaccinated group. However, most studies have not shown any significant increase in infection. One study followed up more than 60,000 children given DTwP (diphtheria, tetanus and whole cell pertussis) vaccine, and found no difference in serious bacterial infections after immunisation.<sup>19</sup>

A new vaccine (rotavirus) was withdrawn in 1999, shortly after its introduction in the US, when it was found that the vaccine led to an increased risk of a bowel obstruction (intussusception) in about 1 in 10,000 children (see section 20.3 and chapter 19).

A recent study conducted in Guinea-Bissau has raised concerns about the non-specific effects of vaccines in developing countries.<sup>20,21,22</sup> In this study the association between routine childhood vaccinations and survival was examined. Mortality in the group vaccinated with any vaccine was lower compared with those not vaccinated. However, when effects of specific vaccines were examined, the study showed that recipients of BCG alone and measles vaccine at nine months had reduced mortality, while those who received DTwP or polio vaccines had an increase in mortality compared with unvaccinated children that just reached statistical significance.

There are valid concerns about whether the results of this study reflect a real effect of vaccination. If its findings are true it means that the reduction in mortality occurring as a result of DTwP and polio vaccination may be less than expected: 'the large decrease in the number of deaths from diphtheria, tetanus, pertussis and polio would be partly offset by increased mortality from other causes'. The study findings have not been confirmed, and other studies have found that measles immunisation overall decreases mortality.<sup>23</sup>

*‘Vaccines cause the disease they are supposed to prevent’*

Live vaccines can infrequently cause symptoms similar to but much less severe than the disease caused by natural infection. The exception to this is OPV, which can extremely rarely cause vaccine associated paralytic poliomyelitis (VAPP), which is identical to the disease caused by wild poliovirus (see chapter 8).

Inactivated vaccines generally cannot cause the disease against which they protect.

*‘Immunisations “overload” or “overwhelm” the immune system’*

There is no evidence of immune system ‘overload’. The immune system is designed to be able to deal with a very large number of different antigens. All children, and adults, come into contact with many viruses, bacteria and other agents to which the immune system responds every day.

The additional demands placed by vaccines are small compared to the ability of the immune system to respond. In addition, the number of immunogenic proteins and polysaccharides in modern vaccines has decreased compared with early vaccines because of advances in vaccine technology. For example, early whole cell pertussis vaccines contained around 3000 immunogenic proteins compared with two to five in the modern acellular pertussis vaccines. In spite of an increase in the vaccines on the schedule, an infant now receives fewer immunogenic proteins and polysaccharides than with earlier vaccines.<sup>24</sup>

From birth, an infant’s immune system responds to various microbial challenges in the environment. The infant is also able to generate an immune response to vaccines; for example, infants born to mothers infected with hepatitis B virus are protected against infection after receiving the hepatitis B vaccine given after birth (along with HBIG) and at age six weeks, and at three and five months. Eighty-five to 95 percent of infants immunised in the first six months of life against pertussis, diphtheria, tetanus, polio and Hib develop protective vaccine specific antibodies. Conjugation of a vaccine antigen to a carrier protein (eg, Hib or conjugate pneumococcal vaccine) enables the infant to develop a specific immune response using helper T-cells and therefore a specific T-cell memory. The immune response to a polysaccharide vaccine alone is poor in infants under the age of two years.

New technology for producing vaccines has resulted in a more specific and therefore lower antigen load. The table below shows the reduction in antigenic content as the result of using new vaccines.

**Table 20.2: Number of immunogenic proteins and polysaccharides contained in vaccines over the past 100 years<sup>25</sup>**

1900		1960		1980		2005	
Vaccine	Proteins	Vaccine	Proteins	Vaccine	Proteins	Vaccine	Proteins/ poly- saccharides
Smallpox	~200	Smallpox	~200	Diphtheria	1	Diphtheria	1
		Diphtheria	1	Tetanus	1	Tetanus	1
		Tetanus	1	WC- pertussis	~3000	AC- pertussis	2–5
		WC- pertussis	~3000	Polio	15	Polio	15
		Polio	15	Measles	10	Measles	10
						Mumps	9
						Rubella	5
						Hib	2
						Hepatitis B	1
Total	~200	Total	~3217	Total	~3027	Total	~49

Key: AC: acellular pertussis, WC: whole cell pertussis.

The immune system is theoretically able to respond to the simultaneous administration of thousands of vaccine antigens without adverse effects.

### (e) Conspiracy for profit

#### *‘The real facts are hidden’*

Some people claim that governments and the medical establishment are in an alliance with vaccine manufacturers to hide the real facts about immunisation. No evidence has ever been presented for this claim. There is, however, a shared interest between commerce (selling vaccines) and public health (preventing illness).

#### *‘Many studies show vaccines to be dangerous and ineffective’*

Although in direct conflict with the claim of ‘hidden facts’, this claim is often made by the same people. At the extreme is the claim of not being able to find a single paper in the entire medical literature showing that immunisation works.<sup>26</sup> Many papers have reported cases of immunisation failing to protect (this should be expected, given that no vaccine is 100 percent effective), or that some serious events happened after immunisation. Those opposed to immunisation have used such material to create what appears to be a scientific attack on immunisation, by using selective information. Most scientific papers have demonstrated the safety and effectiveness of vaccines and, where appropriate, noted concerns about vaccines either being unsafe or ineffective, which have led to the withdrawal of specific vaccines. Over time, improved vaccines have replaced vaccines that are unsafe or of

poor effectiveness, as well as those that perform less well or cause more reactions; this is standard scientific progress.

*'Immunisation is only for the profit of multinational drug companies'*

The development of new vaccines is an expensive and risky business. The high costs of bringing a vaccine to market can only be justified if the vaccine will be sold at a price that provides a commercial return to the manufacturer. A vaccine can only be profitable if it is shown to be safe and effective. Vaccine manufacturers have a natural interest in producing the best possible vaccine as well as making a profit.

*'Nearly all vaccine research is biased because it is funded by the vaccine manufacturers'*

It is true that the pharmaceutical companies fund most research on vaccines. This funding does not mean that the research is biased, as much of it is undertaken by independent researchers operating under international standards of good clinical practice. Nevertheless, the *potential* for bias is a real one, leading many medical journals to require statements of the funding source and all potential conflicts of interest to be declared and published with any scientific studies.

**(f) Immunisation as a cause of idiopathic illnesses**

In recent years there have been claims that immunisation causes various diseases. These allegations of a link are usually:

- made for a disease of unknown cause
- made by a single researcher or research group
- not confirmed by other researchers.

It is important to identify all the harmful effects of immunisation. Unfortunately, claims are often made without apparent concern for the potential harm resulting from public loss of confidence in all immunisations. The harm from such claims has been documented in relation to pertussis.<sup>27</sup>

It is likely that simply because a link has been suggested, especially if it has been published in a well known medical journal, it will be publicised and many people will feel that there must be something to the claim. When other researchers investigate it and fail to confirm the findings, it is likely that the alleged link was the result of a chance association. Publicity tends to refer to the study suggesting the link and to ignore those studies that found the link was the result of chance association. Publication of refutations of claims seldom achieves the same, at times sensational, prominence as the original claim.

*'Immunisation causes brain damage'*

Two vaccines, measles and pertussis, have been suggested to be possible causes of brain damage, and we will look at each in turn.

### *(i) Measles*

Measles virus causes encephalitis and brain damage. Because the vaccine can cause a mild measles like illness, it is possible that the vaccine could also cause encephalitis. Encephalitis following measles vaccine has indeed been reported at a rate of about 1 per million doses. However, as this is similar to the background rate, it is not certain that the vaccine causes such events. An analysis of claims for encephalitis following measles vaccination in the US found a clustering of events at eight to nine days after immunisation, which supports, but does not prove, the possibility that the vaccine rarely causes encephalitis.<sup>28</sup> The risk was less than 1 per million doses, or about 1000 times less than the risk of encephalitis from measles disease. Thus any risk of encephalitis caused by vaccination is very much less than the risk of encephalitis caused by the disease.

### *(ii) Pertussis*

There have been reports of serious adverse events following whole cell pertussis vaccine since its first use. Despite considerable research, including some large controlled trials, it remains uncertain if the earlier whole cell pertussis vaccine causes brain damage. If the vaccine is ever responsible for brain damage, this is an exceptionally rare event – less than 1 per million doses. The controversy started after some doctors from Great Ormond Street Hospital, London, published a paper in 1974<sup>29</sup> suggesting that serious neurological problems, including epilepsy and learning disorders, might be secondary to pertussis immunisation.

The British National Childhood Encephalopathy Study (NCES) aimed to resolve the controversy. In this study all cases of acute encephalopathy that occurred in England and Wales during the period of the study, 1976–79, were included and their association with whole cell pertussis vaccine assessed. The NCES results suggested, but did not prove, that the pertussis vaccine could cause short term brain symptoms, acute encephalopathy, following 1 per 110,000 doses of DTwP and permanent brain damage following 1 per 310,000.<sup>30</sup>

A 1989 court case led to a review of the NCES findings. The NCES conclusion had been based on seven children who were thought in the original study to have suffered permanent damage. Review showed that three were alive and well, and the other four had died from causes unrelated to immunisation.<sup>31</sup> The court concluded, after careful scrutiny of the NCES data, that there was no evidence that pertussis vaccine could cause permanent brain damage.

The Institute of Medicine (IOM) came to a similar conclusion that there was not enough evidence to resolve the issue.<sup>32,33</sup> The conclusion was based on two years' work by an expert committee that reviewed all the evidence on adverse events from pertussis vaccines. The IOM did conclude, however, that the evidence was consistent with pertussis vaccine causing an acute encephalopathy – largely based on the NCES findings.

However, on further follow up in 1993, children in the NCES who suffered acute encephalopathy were found to have had long term consequences – whether the acute encephalopathy was vaccine associated or not.<sup>34</sup> As a result, the IOM now considers that the evidence is *consistent* with pertussis vaccine causing ‘the forms of chronic nervous system dysfunction described by the NCES in those children who experience a serious acute neurological illness within seven days after receiving DPT vaccine’.<sup>35</sup>

The critical word is ‘consistent’, which does not mean that the link is proven. The case against such a link includes the following facts.

- Brain damage often becomes apparent in the first year or two of life – frequently around the times that immunisations are scheduled.
- There is no specific type of brain damage associated with whole cell pertussis immunisation.
- Four studies (following up a total of over half a million doses of pertussis vaccine) found no association with neurological illness.<sup>36,37,38,39</sup>
- A case control study that identified all neurological illness in a population of 218,000 children aged 1–24 months during one year found no increase in risk with pertussis vaccination.<sup>40</sup>
- There have been several controlled trials for the acellular pertussis vaccine, none of which found any cases of brain damage. One found one case of encephalitis among 82,000 children participating in a pertussis vaccine trial. That case happened several months after immunisation. In contrast, three of 17,000 children not participating in the trial had encephalitis – all of them due to pertussis.<sup>41</sup>

It is not surprising that most medical authorities agree that that pertussis vaccine has not been proven to be a cause of brain damage.<sup>42</sup>

#### *‘Immunisation causes cot death’*

Sudden Infant Death Syndrome (SIDS) occurs under one year of age, and is most common around three months of age, when many immunisations are given. SIDS may occur by chance within a day or so of immunisation. There have been many studies that have conclusively shown that SIDS is not caused by immunisation.<sup>43</sup> In addition, some studies, including the New Zealand Cot Death Study, found a lower rate of SIDS in immunised children.<sup>44</sup> This is consistent with a Scandinavian study, which found that some cases of SIDS were probably caused by undiagnosed pertussis.<sup>45</sup>

Despite the solid evidence against a link, the claims continue to be made, usually on the basis that the studies are faulty. However, consistent findings from several studies using a range of methods make up for any weakness in any individual study.

### *'Immunisation causes asthma'*

There have been three studies suggesting a link between immunisation and asthma.<sup>46,47,48</sup> Other, more definitive, studies found no link.<sup>49,50,51,52,53</sup> The play of chance, as well as bias in study methodology, may allow for the observation of a link when there is none. This is why the consistent findings of several different studies should be given more weight than the findings of a single study. Later studies and a review article, including a large cohort study,<sup>54</sup> have examined whether vaccines are linked with the development of asthma.<sup>55</sup> They concluded there was not the evidence to support the hypothesis that vaccines cause allergic diseases.

### *'Immunisation causes diabetes'*

It has been claimed that immunisation can cause type I diabetes in rats<sup>56</sup> and children.<sup>57</sup> The claim is largely based on the analysis of data from a large Finnish study of Hib vaccine. In response, the Finnish investigators re-analysed their data and concluded that there was no link.<sup>58</sup> Because it is possible to analyse the Finnish data to support such a link,<sup>59</sup> there was debate on the issue, stimulating research by other authors.

It was also suggested that the increase in cases on the Christchurch diabetes register after 1989 arose from the introduction of hepatitis B immunisation.<sup>60</sup> The timing of the increase does not coincide with the time that hepatitis B immunisation was introduced, and the Auckland diabetes register showed no increase at this time (the change in immunisation policy affected the whole country).<sup>61</sup> A review of all the published papers on diabetes found no evidence to support a link with immunisation.<sup>62</sup> In fact, evidence from Finland suggests that the elimination of natural mumps by immunisation may have decreased the risk of insulin dependent diabetes.<sup>63</sup> Studies in Sweden failed to find any change in diabetes incidence as a result of stopping BCG<sup>64</sup> or pertussis immunisation.<sup>65</sup> Other studies in Sweden<sup>66</sup> and Canada<sup>67</sup> have also failed to find any link between immunisation and diabetes.

In 1998 two workshops were held in the US to review all the evidence on the issue of immunisation and diabetes. Both workshops concluded that there was no evidence for any increased risk of diabetes associated with childhood vaccines.<sup>68</sup> Several studies are under way to determine if certain vaccines administered early in life might protect high risk children against diabetes, as has been demonstrated in genetically predisposed animals.

### *'Immunisation causes autism and Crohn's (and other bowel) disease'*

These allegations came from a single group of researchers at the Royal Free Hospital, London. The initial claim was that measles vaccine causes Crohn's disease – an inflammatory bowel disease.<sup>69</sup> The claim was based on evidence of measles virus in diseased bowel, as well as an increased risk in groups who were more likely to have been immunised. However, their studies had several serious flaws, and other studies published since have failed to provide any supporting evidence of a link.<sup>70,71</sup>

The Royal Free Group then published a report implicating measles, mumps, rubella vaccine (MMR) as a cause of autism.<sup>72</sup> Autism is a chronic developmental disorder. The main characteristics of autism are problems in social interaction and communication, and restrictive and repetitive interests and activities. Autism may be initially noted in infancy as impaired attachment, but it is most often first identified in toddlers, mostly boys, from 18 to 30 months of age. Boys are three to four times more likely to be afflicted with autism than girls.

This report was later retracted by all but one of the authors.<sup>73</sup> Subsequent studies looked for a possible link between autism and MMR, and all studies failed to find such a link, as did the UK's Committee on Safety of Medicines, which evaluated hundreds of cases where a claim had been made.<sup>74</sup> The studies have included a Welsh review of 18 autistic children,<sup>75</sup> a review of clinic records over 25 years of 8889 children, a French survey of 6100 school children,<sup>76</sup> a 14 year Finnish follow up of more than three million doses of MMR,<sup>77</sup> and a British case control study.<sup>78</sup>

The British case control study had several lines of evidence that were against a link. First, the diagnosis of autism had been increasing since 1979 but there was no jump after the introduction of MMR in 1988. Second, cases were diagnosed at similar ages whether they were immunised before or after 18 months of age, or not at all. Third, the cases were no more likely to have received MMR than the general population. Finally, the first diagnosis of autism or initial signs of behavioural regression were not more likely to occur within time periods following vaccination than during other time periods. The study did find evidence for some recall bias to link initial parental concern with MMR vaccine. A Swedish study found no difference in the prevalence of autism in children born after the introduction of MMR compared with children born before.<sup>79</sup>

The consistent findings from these studies show that this appears to be another chance association, to be expected given that both MMR immunisation and diagnosis of autism occur in the second year of life. Recently, the NCES was re-examined and found no indication that measles vaccine contributes to the development of long term neurological damage, including educational and behavioural deficits.<sup>80</sup>

The Immunization Safety Review Committee of the IOM in the US has published a review of all current sources of evidence concerning a possible association between MMR and autism.<sup>81</sup> The Committee concluded that 'the evidence favours rejection of a causal relationship at the population level between MMR vaccine and autism'. However, because of the public concern about this association, the Committee recommended, and suggested several avenues for, further research. It did not recommend a policy review of the recommendations concerning MMR vaccine.

### *'Immunisation causes arthritis'*

Arthritis or arthralgia occur after both rubella disease and rubella vaccination, especially in adults. It was previously thought that rubella vaccination might lead to long term arthritis. However, two large controlled studies found no evidence to support a link.<sup>82,83</sup> Another study did find a slight increase in risk from rubella vaccination, but this was of borderline statistical significance (ie, it could have been a chance occurrence).<sup>84</sup> The evidence currently suggests that rubella vaccination does not cause chronic arthritis.<sup>85</sup> (See chapter 11.)

### *'Immunisation causes an increase in autoimmune disease (eg, multiple sclerosis) and cancer'*

After millions of vaccinations over many decades, there is no evidence to suggest that immunisation causes these diseases. In fact hepatitis B immunisation can significantly reduce the risk of liver cancer resulting from chronic hepatitis B. The most common type of childhood cancer is leukaemia. Immunised children may be at lower risk of leukaemia.<sup>86</sup> A New Zealand study found no link between vaccination and leukaemia.<sup>87</sup>

Reports of adults developing multiple sclerosis (MS) after hepatitis B immunisation in France have led to investigation of this claim. The studies have found no link, and it is likely that the reported cases were chance associations.<sup>88</sup> Two large studies have looked at the risk of MS after hepatitis B vaccine<sup>89</sup> and the effect of vaccinations on relapse of MS. Both studies found that vaccination neither caused MS nor caused an exacerbation of MS.<sup>90</sup>

Guillain-Barré syndrome (GBS) is an autoimmune disease of the nerves that causes a temporary paralysis. Although various vaccines have been suspected of causing GBS, some large studies have failed to find a link with measles,<sup>91</sup> polio<sup>92</sup> or tetanus vaccines.<sup>93</sup> There is some evidence that influenza vaccine may cause GBS in one to two people per million doses.<sup>94</sup>

## **20.3 Lessons from the past**

There have been errors in immunisation practice in the past. Lessons learnt from these errors have been used to improve vaccine safety, and to set up better research programmes and clinical trials, as well as systems to monitor vaccine safety.

### **The SV40 contamination of early polio vaccines**

The early polio vaccines of the 1950s and early 1960s were grown on monkey kidney cells, which, in some instances, were shown to be contaminated with the monkey virus, simian virus 40 (SV40). By 1962 around 98 million individuals had been given polio vaccine, of whom 10–30 million may have received vaccine contaminated with SV40. Soon after its discovery, measures to exclude the virus from polio and other vaccines were rapidly introduced and no vaccine manufactured after 1963 contained SV40. SV40 has been shown to cause cancers in animals, and virus traces have

been found in some rare human cancers, mesotheliomas, osteosarcomas and brain tumours. There is no evidence, however, that SV40 causes cancer in humans: several studies have failed to show an association between exposure to SV40 contaminated vaccines and human cancer, the latest after more than 30 years of follow up.<sup>95</sup>

### **The Cutter polio vaccine incident – insufficiently inactivated vaccine**

The first polio vaccine was made from virus that was inactivated. In the early days of manufacture (1955), vaccine from Cutter laboratories was inadequately inactivated. This was because clumping of the virus led to a failure of those viruses in the centre of the clump to come into contact with the inactivating agent, formaldehyde. As a result, children were injected with vaccine contaminated by live virus and 260 children developed polio from the vaccine. There have been no cases of polio from inactivated polio vaccine since the Cutter incident.

### **Killed measles vaccine causing atypical measles**

The first measles vaccine used in the US (from 1963 to 1967) was an inactivated (killed) vaccine. This inactivated vaccine produced immunity that was short lived and placed the recipients at risk of atypical measles. The killed measles vaccine was not used in New Zealand.

### **High dose measles vaccine**

In an attempt to use a vaccine that could be given at an earlier age to infants in developing countries, the World Health Organization (WHO) in 1990 recommended the use of high dose measles vaccine. This vaccine was effective from six months of age. However, the vaccine was found to lead to increased late mortality in girls.<sup>96,97</sup> As a result the WHO advised against its use.<sup>98</sup>

### **Rubini mumps vaccine – failed to protect**

The Rubini strain of mumps vaccine was shown to produce good levels of antibodies against mumps and so was licensed for use. However, studies in Europe and Singapore have shown that it provides virtually no protection against mumps and it is no longer used in most countries (see section 9.4).

### **Mumps vaccine meningitis**

Some strains of mumps vaccine cause aseptic meningitis. Complete recovery after a few days' illness is the norm and sequelae are rare or absent. Taking into account intensity of surveillance, it is likely that rates of meningitis following mumps vaccination with the Urabe strain vary from 1 per 1000 to 1 per 20,000. A rate of 1 per 11,000 vaccinations, as measured in the UK, following immunisation with the Urabe strain (compared to 1 in 800,000 for the Jeryl Lynn strain) led to the withdrawal of vaccines containing the Urabe strain from several countries, including New Zealand. Rates following vaccination with other Japanese strains vary from 1 in 120,000 to 1 in 5000 doses. For the Leningrad-3 strain, rates of 1 in 1000 have been reported.<sup>99</sup>

### **Pertussis vaccines – variable protection**

Until recently, whole cell pertussis vaccines were considered to be generic products (ie, all provided broadly similar levels of protection). However, in the acellular pertussis vaccine trials, conducted during the last decade, it was shown that this was not the case and that one whole cell vaccine provided low levels of protection. This vaccine has not been used in New Zealand.

### **Rotavirus vaccine**

Rotavirus vaccine was introduced onto the US schedule in August 1998. Because it had been observed in pre-licensure trials that intussusception had occurred following administration of the vaccine, the incidence of intussusception was closely monitored using an adverse event reporting system. In 1999, when it was suspected that there was an increased risk of intussusception associated with the vaccine in infants, it was withdrawn.<sup>100</sup> (See chapter 19.)

## **20.4 Conclusion**

Vaccines are not perfect. They cause reactions. Local reactions occur frequently, systemic reactions less commonly, and severe reactions rarely. But vaccines do prevent disease. It is to be expected that agents that are so effective in reducing disease incidence – including the elimination of smallpox, and the potential elimination of polio and measles – produce some adverse events. However, in comparison to natural disease such events are infrequent and almost always less severe. There is no doubt that the benefits of immunisation far outweigh the risks.

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