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Current Thoughts on the Risks and Benefits of Immunisation

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Summary

Despite a continuous search for safer and more immunogenic vaccines, adverse reactions still occur. Adverse reactions to vaccines are generally mild; severe events resulting in death or permanent damage are rare. In every instance, the benefits of preventing the disease far outweigh the risks of vaccination. In the early days of vaccine development, a number of accidents were associated with faulty production. Most recent problems encountered with the use of vaccines are due to programmatic errors. Because of the large number of doses administered it is probable that there will be some temporal and merely coincidental association between adverse events and vaccine administration. Immunisation has a direct protective effect for the individual and an indirect effect on herd immunity for the community.

The major goal of postmarketing surveillance is the early detection of and appropriate response to adverse events in order to curtail a negative impact on immunisation programmes. Risk-benefit analyses for immunisation are faced with a number of potential difficulties; definition of the risks and benefits themselves, individual versus community risks and benefits, and the continuously evolving nature of risks with changes in disease epidemiology. Based on risk-benefit studies, for an individual just as for the community, it may not always be of interest to use the vaccine with the lowest complication rate. Good immunisation programmes should help to decrease the risk of adverse effects.

Immunisation is one of the most powerful and cost-effective weapons of disease prevention. According to Plotkin and Plotkin (1988), 'With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction and population growth'. In parts of the world, vaccination has played a formidable role in the control of 8 major diseases: diphtheria, tetanus, yellow fever, pertussis, poliomyelitis, measles, mumps and rubella. For smallpox, the dream of global eradication became reality in 1977. For poliomyelitis, the dream might materialise soon in the Americas thanks to a large eradication programme, coordinated by the Pan American Health Organization, and based mainly on immunisation with the oral polio vaccine; at the time of writing, no case had been reported since September 1991.

However, although modern vaccines are well tolerated and effective, no vaccine is totally safe and totally effective, and adverse reactions have been reported with all of them. Wilson (1967) stated that 'The complications and accidents . . . must be looked upon as the price we pay for the protection these agents confer upon us. There is no insurance without a premium. Our business is to provide greater and more comprehensive insurance and to diminish the size of the premium'. In this article we try to present our views on the risks and benefits of immunisation and the issues that we believe are important.

1. Adverse Events with Vaccines

A vaccine may consist of a live attenuated agent, an inactivated pathogen, a fragment, component or product of the wild pathogen. Some vaccines comprise antigen produced either synthetically or biologically after genetic recombination. Clinical trials are carried out to test safety, antigenicity and preliminary efficacy. Mass trials are then conducted to determine if the preliminary results can be generalised. However, these trials are limited by the size and character of the animal and human populations tested and by time, and therefore cannot reveal all that we should know about a vaccine. This emphasises the importance of postmarketing surveillance (PMS) for vaccine-associated adverse events.

Adverse effects or events following immunisation can be classified according to severity into frequent, minor, local or general reactions, and more serious but rare complications. They can also be classified according to probable causation as avoidable and unavoidable or inherent (Dittmann 1988). Avoidable adverse effects are associated with faulty production (e.g. bacterial or viral contamination, presence of foreign toxin) or faulty administration (e.g. use of nonsterile equipment). Since the early days of vaccine development, severe reactions leading to either death or injury have occurred with various vaccines, most of which can be ascribed to lack of scientific knowledge, gross negligence and lack of supervision and control in manufacturing procedures (Wilson 1967). The most famous, the Cutter incident, occurred in 1955 when faulty batches of inactivated Salk-type polio vaccine were released on to the market in the US (Dudgeon 1978). 260 cases of vaccine-related poliomyelitis occurred, the majority of which resulted in paralysis. This accident constituted one of the worst disasters in the history of preventive medicine. Such accidents led to much better control of vaccine production. Most developed countries have established independent laboratories to test vaccines and have obliged manufacturers to conform to very strict tests of efficacy and safety. Very detailed and lengthy control procedures are now essential requirements of good vaccine production.

Nevertheless, and despite a continuous search for more purified and safer vaccines, the question remains whether such events will occur in the future. Hopefully not, possibly yes. The only certainty is that it will be more difficult for them to occur, but the risk is still real as illustrated by 2 recent examples. First, there was the fear that the human plasma-derived hepatitis B vaccines might have been contaminated by the human immunodeficiency virus (HIV) because no specific screening was used when the virus was still unknown. Fortunately, the risk was ruled out on the the basis of the manufacturing process and retrospective testing. Secondly, and more recently, there has been

the fear of possible transmission of the agent for bovine spongiform encephalopathy (BSE). BSE or 'mad cow disease' has become an issue in Britain, causing public panic since animal cases were first diagnosed in 1986. Viral vaccines are prepared in cell culture, which require complex media to support growth, and are, in most cases, supplemented with materials of animal origin such as calf serum. The inactivation and purification stages of vaccine production, being typically designed to eliminate infectivity while retaining antigenicity, are unlikely to be sufficiently rigorous to deal with the scrapie-like agent that causes BSE (Davies 1991). A review of the manufacturing processes indicated a remote and minimal risk, which was still considered as unacceptable. The decision was then made to move to BSE-free sources for bovine material used for the vaccine manufacturing process. These examples indicate that the risk comes from what we are unaware of and, therefore, cannot look for. International collaboration in the use and testing of vaccines and sharing of information will assist in limiting mishaps by creating more awareness of possible risks. It is imperative that we have the capability to react quickly to limit any possible detrimental effects.

Most recent problems encountered with the use of vaccines have been due to programmatic errors. Between 1985 and 1988, for example, there were 17 reported incidents of single cases or clusters of clinical toxic shock following measles immunisation in India, resulting in 43 deaths (Wassilak & Sokhey 1990). In each situation, evidence was found that either unsterile syringes and needles or previously opened vials had been used; *Staphylococcus aureus* was isolated from a few implicated vials.

Inherent adverse effects are those associated with the biological and chemical nature of the vaccine. They include sterile abscesses, cysts, vaccine-associated poliomyelitis and meningitis. Not every complication that follows the administration of a vaccine is linked to the antigenic components. Problems can be attributed to a carrier or excipient rather than to a primary constituent.

Many products are unsuitable for use in the very young or debilitated patient or in persons with specific disease conditions or symptoms such as an immunodeficiency or even the common cold. Such conditions are usually stated as contraindications for these vaccines. The risk of adverse events is not equally distributed in the population and we believe that there is a need for more genetic studies to better identify at-risk populations for vaccine adverse events.

For monitoring purposes, an 'adverse event' can be defined as an untoward event temporally associated with immunisation that might or might not be caused by the vaccine or the immunisation process. Due to the large number of vaccine doses administered at an early age when children are most prone to various illnesses, it is probable that there will be some temporal and merely coincidental association between adverse events and vaccine administration. Moreover, in each individual case, it may be difficult to demonstrate or rule out a definite relationship because there are no clear markers of aetiology.

For some diseases, many vaccines are available that cannot and should not be considered as identical in terms of efficacy and safety, as the manufacturing process and content of the vaccines might be substantially different. Vaccines should not be considered as identical just because they immunise against the same diseases. Furthermore, vaccines that have been available for many years may have evolved substantially with regards to production methods, for example, diphtheria-tetanus-pertussis (DTP) vaccines.

The most obvious and perhaps the most important difference between vaccines and drugs is that the administration of a vaccine is for disease prevention in a healthy person, and therefore is an elective procedure, whereas most drugs are used for the cure or control of an existing disease. This has major implications in terms of accepting adverse effects. Drugs are given mostly (but not exclusively) for the benefit of the individual patient whereas, as stated by Nokes and Anderson (1991), '... immunisation has a dual purpose; a direct protective effect for the individual and an indirect effect of herd immunity for the community'.

Unlike the previous authors, however, we be-

lieve that in an immunisation programme there is no (or there should not be any) conflict between individual interests and community interests. For an individual, just as for the community, it may not always be of interest to use the vaccine with the lowest complication rate. A more reactogenic vaccine may provide better efficacy and, therefore, lead to a much lower risk of serious disease.

2. *Postmarketing Surveillance of Adverse Vaccine Reactions*

Those involved in immunisation programmes have the responsibility for determining the real risk of each vaccine and for constantly weighing the risks and benefits of vaccine usage. The surveillance of vaccines for temporally-associated adverse events should, therefore, receive very high priority. In many countries, however, there are large deficiencies in the PMS of adverse vaccine events compared with the PMS of drugs for which there are fairly sensitive surveillance systems. Very few countries have moderately efficient vaccine PMS systems.

The WHO Expanded Programme on Immunisation (EPI) have published a policy document entitled 'Monitoring of Adverse Events Following Immunisation in the Expanded Programme on Immunisation' (Wassilak & Sokhey 1990). It contains a number of recommendations on adverse event monitoring which were endorsed by the EPI Global Advisory Group at its October 1990 Cairo meeting. These recommendations are summarised in table I.

The EPI's main goal in monitoring is the early detection and appropriate response to adverse events considered to be associated with immunisation, particularly the ones related to programmatic errors, in order to strengthen programme quality and to constructively counter the negative impact of such events so that confidence in the programme is not undermined. In a developing country, where there is no system for monitoring adverse events following immunisation, such a system should be developed within EPI disease surveillance systems, making use of health centre staff as a primary source of reports. The WHO is currently developing a field guide to assist managers of immunisation programmes in the development of surveillance of adverse events following immunisation.

Table I. Expanded Programme on Immunisation (EPI) recommendations on adverse events endorsed by the EPI Global Advisory Group, Cairo, October 1990

1. All EPI programmes should monitor for adverse events following immunisation, with the type and extent of monitoring depending on the stage of the programme
2. WHO should assist with the international standardisation of case definitions, which will be useful in such monitoring
3. Field guides and training materials for surveillance programmes should be developed by EPI
4. Data from national monitoring programmes already in place should be collected and disseminated by EPI to other programmes
5. Guidelines should be developed for monitoring of adverse events in clinical studies sponsored by EPI
6. Position papers on quantifying the risks and benefits of vaccination should be developed and disseminated by EPI

3. *Impact of Adverse Events on Immunisation Programmes*

By far the product that has inspired the most fear is the whole-cell pertussis vaccine, so called because it comprises entire dead bacteria (Royce 1990). Linked with complications ranging from fever to seizures, the vaccine has even been blamed for causing brain damage and death. It was, and still is, the subject of a worldwide controversy. In the mid-1970s, fear of adverse vaccine reactions in the UK drove immunisation rates for pertussis from 70 to 80% down to less than 40% (Stuart-Harris 1979). Several years later, as the herd immunity of vaccination declined, pertussis cases began to increase. As the disease spread, more and more people decided to be immunised. This illustrates the serious detrimental impact that the fear of adverse effects can have, that is a decrease in the acceptance of a vaccine and the subsequent risk of resurgence of some diseases.

Among the major barriers to vaccination, Bergler (1985) lists the fact that a community takes

note of news spread mainly by the mass media, and to some degree by physicians, on damaging sequelae resulting from vaccination. Actually, we believe that genuine concern is raised about vaccines when people hear about adverse effects from the media and not from the physicians. According to Fulginiti (1984), many physicians and parents consider immunisation as a routine and as a result do not discuss it. To ensure that parents will be able to give informed consent and have their children immunised, physicians should provide information on the nature, prevalence and risks of the disease, the type of immunisation product to be used, expected benefits, risk of adverse effects and required follow-up.

Stuart-Harris (1979) emphasises that the attitude of medical and nursing professions is a key factor influencing public confidence in health measures advised by governments and that the possibility of litigation, fear of being blamed, and the possibility of being required to certify post-vaccinal effects for compensation act as deterrents to health care workers in providing immunisation. He also stresses that the stronger the advice of official bodies to health professionals, the better their confidence and consequently the more likely they are to provide assurance to the public.

Vaccines may be said to be victims of their own success. As immunisation programmes successfully reduce their target diseases, adverse events inevitably gain in relative importance and we start to lose the sense that diseases still exist or could resurface. When the devastating effects of diseases such as smallpox, poliomyelitis or even measles are no longer seen, consideration for the benefits of a vaccine decreases. Therefore, the perception of the risks and benefits changes. Moreover, the media are prone to propagate issues of risk, and the public to go along with them, at the expense of benefits. Anything that occurs after vaccine administration is likely to be called an adverse event, particularly in the US. Negative publicity may tend to put the risks of immunisation out of perspective. For example, risks of 1 per million doses of vaccine administered scare people, whereas there seems to be little concern over a risk such as 1 death per million for every 50 miles driven (Nicholson 1986). We believe that the media have a tremendous public health role to play by avoiding the transmission of sensational, and at times biased and unfounded, information about risks without weighing them against benefits.

4. Assessing the Risks and Benefits of Immunisation

How safe? How effective? For many of the vaccines used in children or adults, we have only partial answers to these questions. We should look at the broad picture in terms of both cost-benefit and risk-benefit ratios. There are many reviews of adverse effects but very few risk-benefit and cost-benefit studies. Such studies become more and more important when a choice has to be made between many potential vaccine candidates.

A detailed assessment of risks and benefits is a very challenging and almost impossible task. First, the types of benefits and risks involved must be defined. In assessing benefits, with regard to individual or herd immunity, the reduction in the burden of the disease should be considered, measurable by indices such as the numbers of deaths, sequelae and hospitalisations. In many instances, there are no reliable data to estimate the burden of the disease accurately because disease surveillance is inadequate. Moreover, vaccine efficacy has to be considered over time and for many vaccines which have only been used for a limited number of years we still lack information on the issue of waning immunity. The latter situation applies to the hepatitis B and measles vaccines among others. In addition, when vaccines for a specific disease have been used on a large scale for an extended period it becomes difficult to evaluate vaccine efficacy for new candidate vaccines for 3 main reasons: (a) ethics; (b) new vaccines can only be evaluated in terms of relative efficacy; and (c) if the disease has become rare, efficacy can only be measured by seroconversion rates.

The benefits of one vaccine over another also include such things as ease of administration and

use in programmes, the stability of the vaccine and its availability.

Risks include adverse events of varying nature. Often the rates of adverse events are difficult to estimate precisely since background rates are not available for conditions that also occur spontaneously among nonimmunised people. Postvaccinal adverse events, however, occur far less frequently than the complications caused by the diseases themselves. The fact that reactions may occur is not disputed. What is at issue is the incidence of severe reactions which determines the balance of benefits and risks from the vaccine versus those from the natural disease. Most reactions are not pathognomonic and, therefore, it cannot be said with absolute certainty that a particular case was vaccine attributable and another not. Only in very rare circumstances can a causal relationship be reasonably certain. In poliomyelitis and mumps, for example, there are genetic markers that can be used to differentiate the vaccine versus the wild strains when the viruses are isolated from patients.

Complicating the discussion is the fact that a poorly organised immunisation programme could cause a shift in the age at risk for a disease and temporarily increase the risk of severe conditions. An example of this is the congenital rubella syndrome. When children are immunised on a large scale, older age groups are less likely to encounter the disease and gain natural protection before reaching reproductive age. Therefore, if no consideration is given to immunisation of females before reproductive age, the risk of infections during pregnancy and hence of congenital rubella syndrome might temporarily increase.

Benefits and risks can extend beyond the individual receiving the vaccine. Among the best examples is the oral poliovirus vaccine which allows the Sabin strain to be disseminated to nonimmunised people, providing them with protection. Unfortunately, cases of paralytic poliomyelitis can also occur in contacts of immunised patients. These indirect benefits and risks change according to the proportion of the population that has been previously immunised directly and according to other disease determinants. Another example is the *Haemophilus influenzae* type B vaccine which has been reported to prevent both invasive disease and possibly carriage (Takala et al. 1991). Although there is no definite proof that this is related and there may be some ecological bias, in 3 countries (Finland, US, Canada) that started using the vaccine on a large scale, a coincidental decrease in incidence of reported cases has been observed not only in age groups immunised (15 months and over) but also in younger age groups.

It is important to realise that risks are not constant and that, if properly understood and managed, they become substantially lower. Furthermore, as stated by Ambrosch and Wiedermann (1979) and Wiedermann et al. (1984), the value of a vaccine is not constant and must be evaluated continually with changing morbidity and mortality patterns of an infectious disease. Moreover, any analysis has to be country and vaccine specific.

5. Use of Risk-Benefit Assessment

The balance between risks and benefits is considered in the decision to license a vaccine in some countries, while in others more consideration is given to decreasing the risks associated with immunisation with less regard for the benefits.

According to Koplan (1985), the value of risk-benefit, cost-benefit and cost-effectiveness analyses lies not in providing the final basis for a decision on vaccine use or evaluation but in providing a structured framework to permit decision makers to consider all relevant components in relation to their relative contributions and subsequent effects. It forces key assumptions to be made explicitly and identifies areas in which data are inadequate. The results of such analyses can assist in justifying a vaccination programme, changing health policy, disseminating a programme more widely or planning vaccine utilisation. Cost analyses of vaccination may indicate the value of a vaccination programme, but the programme may not be widely adopted. The reasons for this gap between study conclusions and application may include a disagreement with the estimates and assumptions used in the analysis and scepticism about the conclu-

sions. Risk-benefit assessment should be used to target the proper number of doses and schedule to be used for any vaccine. In many cases, however, such studies are either not done or not done thoroughly.

Risk-benefit analyses are useful in setting up a compensation programme and, when a compensation programme exists, helping to define general and individual criteria for compensation. The idea of compensation comes from the fact that some immunisations are mandatory or strongly encouraged and that immunisation can benefit the community. Mariner and Clark (1986) commented on the positive value of a no-fault compensation programme, the impetus for which is a government's acceptance of responsibility for the financial impact of injury sustained in the common good whether the vaccinations were required by law or merely recommended/provided by government agencies. Physicians may not report reactions because blame may possibly be laid on them; therefore, a no-fault system would alleviate these fears and help to improve reporting and assessment of risks. Compensation schemes for vaccine damage are in operation in several countries, notably Switzerland, Denmark, Germany, Japan and the US.

6. Review of Risks of Adverse Effects for Selected Vaccines

Galazka et al. (1984) compared the risk of adverse reactions associated with the 6 EPI vaccines with complication rates following natural disease, and showed the overwhelming risk difference. They did not, however, take into account the actual disease incidences. Velimirovic (1991) recently reviewed risks versus benefits of various vaccines, particularly pertussis and measles, and showed the overwhelming benefits of the vaccines. Other studies have demonstrated that the benefits outweigh the risks and costs for many vaccines including poliomyelitis, pertussis, measles, mumps and rubella (Koplan 1985; Koplan et al. 1979).

In 1987, in an article about benefits and risks of childhood immunisations in developing countries, Holden (1987) calculated the benefit : harm ratios (number of events prevented for each corresponding event caused by vaccination) for the EPI vaccines as follows: BCG 480 : 1; pertussis 7995 : 1; tetanus >4640 : 1; poliomyelitis 990 : 1; and measles 60 840 : 1. He calculated that a 'typical programme' of immunisation in developing countries could prevent about 45 childhood deaths and 12 serious handicaps per month. In contrast, the programme could cause 1 death every 22 years and 1 serious handicap every 7.5 years.

A comprehensive review of the adverse effects of vaccines was done by Dittmann in 1988. The purpose of the following is not to give an extensive review but to summarise the most important issues raised by Dittmann, and to present recent developments on selected vaccines.

6.1 Bacille Calmette-Guérin (BCG) Vaccine

Suppurative lymphadenitis, the most common local reaction, has been reported in 0.1 to 4.3% of immunised children below the age of 2 years, with the most frequent cause being faulty immunisation techniques (Dittman 1988). Local ulceration and abscess formation have also been documented. Systemic reactions are infrequent, the most serious being disseminated BCG infection (<0.1 per 100 000 vaccinees) and BCG osteitis (<0.1 to 30.0 per 100 000 vaccinees). Hypersensitivity reactions are unusual; however, severe anaphylactic reactions may occur. A fairly extensive review of the risks was done by Lotte et al. in 1988.

6.2 Measles Vaccine

Five to 15% of measles vaccinees will develop a fever (>39.4°C) commencing about 6 days after vaccination and sometimes lasting several days (Report of the Committee on Infectious Diseases 1991). Transient measles-like rashes occur in 5% of vaccinees. Encephalitis occurs rarely and has been reported with an estimated incidence of 1 in every million doses administered, and is not unequivocally linked aetiologically to the vaccine. The

frequency of subacute sclerosing panencephalitis following live attenuated measles vaccine is much lower than after natural measles. Hypersensitivity reactions are rare and mostly consist of wheals and flares at the injection site (Dittman 1988).

6.3 Mumps Vaccine

Allergic reactions temporally associated with the mumps vaccine include rash, pruritus and purpura. Post-vaccination parotitis has been rarely reported. The most recent discussion has revolved around the risk of meningitis following the use of the vaccine containing the more reactogenic Urabe strain. Rates as high as 1 per 62 000 (Canada) to 1 per 100 000 have been reported (Furesz & Contreras 1990). Much higher rates have been reported with the same strain in Japan (1 per 2026) [Sugiura & Yamada 1991], the reason for which is unclear. All the reported cases of mumps meningitis were relatively mild and were without sequelae. Such reactions have not been reported with the Jeryl-Lynn strain.

6.4 Rubella Vaccine

Adverse events include pyrexia, sore throat, swollen glands, reactions at the injection site and a rubella-like rash. The incidence of joint pain and swelling varies with the vaccine strain and is increased in post-pubertal recipients.

A special committee was commissioned by the US Institute of Medicine to examine specific safety issues for pertussis and rubella vaccines (Howson et al. 1991).[1] The committee found insufficient evidence for a causal relationship between the currently used rubella vaccine (RA 27/3) and radiculoneuritis and other neuropathies, or thrombocytopenia purpura. According to the committee, the evidence indicates a causal relationship between the RA 27/3 vaccine and acute arthritis, with incidence rates estimated to average 13 to 15% among adult women and much lower levels noted among other groups. There is evidence, limited to reports from 1 institution, consistent with a relationship between RA 27/3 and chronic arthritis in adult women.

6.5 Pertussis Vaccine

Local reactions and moderate fever following DTP are common (40 to 70% of vaccinees) but are usually self-limiting (Dittman 1988). The special committee of the Institute of Medicine commented on the lack of critical data from which important questions about vaccine safety could be answered (Howson et al. 1991). It concluded that there is no evidence of a causal relationship between DTP vaccine and autism, infantile spasms, hypsarrhythmia, Reye's syndrome or sudden infant death syndrome. Moreover, insufficient evidence exists to indicate a causal relationship between DTP vaccine and aseptic meningitis, chronic neurological damage, erythema multiforme or other rash, Guillain-Barré syndrome, haemolytic anaemia, juvenile diabetes, learning disabilities and attention-deficit disorder, peripheral mononeuropathy or thrombocytopenia. However, there is evidence consistent with a causal relationship between DTP and acute encephalopathy, shock and unusual shock-like state, anaphylaxis and protracted inconsolable crying. On the basis of a review of the available evidence, the range of excess risk of acute encephalopathy following DPT immunisation was estimated to be 0 to 10.5 per million doses. The National Childhood Encephalopathy Study estimated the risk for permanent sequelae of encephalopathy as 1 per 330 000 doses of DPT (Miller et al. 1985). In the US, all immunisation committees have now concluded that pertussis vaccine is not a proven cause of brain damage (Fulginiti 1992).

In the search for a pertussis vaccine with a lower risk of adverse effects, acellular vaccines have been developed and used successfully in Japan, and have been reported in a number of other countries to have a decreased risk of local and systemic adverse

1 The Institute of Medicine will hold a consultation process to review the major issues linked to the safety of tetanus, diphtheria/tetanus, measles, mumps, oral and inactivated poliovirus vaccine, *H. influenzae* type b, and hepatitis B vaccines; completion of this project is expected in 1993.

events (CDC 1992). However, there is currently no proof that they would indeed have a lower rate of more severe events such as encephalopathy.

6.6 Poliomyelitis Vaccine

No serious adverse effects of the inactivated poliovirus vaccine (IPV) have been documented. The risk of paralytic poliomyelitis associated with the oral poliovirus vaccine (OPV) in the US during the period 1980 to 1989 was estimated as 1 case per 2.5 million doses distributed and has remained fairly stable since the 1960s (Strebel et al. 1992). The risk was found to be 1 case per 6.8 million doses in OPV recipients. For children less than 1 year of age with a primary immunodeficiency, the risk was more than 2000 times higher than for the reference group. In Canada for the period 1980 to 1989, the risk of paralytic poliomyelitis associated with OPV was 1 case per 2.8 million doses distributed in contacts and 1 per 16.8 million doses in vaccine recipients (unpublished data).

7. Conclusion

In summary, despite a continuous search for safer and more immunogenic vaccines, adverse reactions still do occur. However, adverse reactions to these vaccines are generally mild. Severe events resulting in death or permanent damage are rare. In every instance, the benefits of preventing the disease far outweigh the risks of vaccination. Awareness of the problems associated with immunisation, the importance of observing the manufacturers' instructions, the general contraindications to immunisation and the specific contraindications for each vaccine will help avoid adverse reactions (Burgess 1987). Also, some simple precautionary measures can contribute to a significant reduction of mild reactions; an example is the administration of antipyretics such as paracetamol (acetaminophen) after DPT vaccination, which has been found to be very effective.

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