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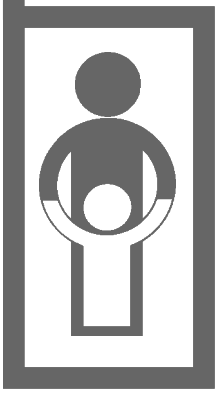
Supplementary information on vaccine safety

Part 1: Field issues



DEPARTMENT OF VACCINES AND BIOLOGICALS

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Abbreviations

AEFI	adverse event/reaction following immunization
EPI	Expanded Programme on Immunization
GBS	Guillain-Barré Syndrome
ITP	Idiopathic Thrombocytopenic Purpura
MMR	measles, mumps, rubella vaccine
NRA	national regulatory authority
PMS	post-marketing surveillance
SIP	safe injection practice
VAPP	vaccine-associated paralytic polio
WPRO	WHO Regional Office for the Western Pacific

Introduction

This document on vaccine safety has been produced in response to specific requests from WHO Regional Office staff, and has been designed to supplement the existing document *Surveillance of adverse events following immunization. Field guide for managers of immunization programmes* (WHO/EPI/TRAM/93.02 Rev.1). Although it is not exclusively written with immunization campaigns in mind, there are a number of features which managers will find helpful in planning and managing campaigns, especially those involving injectable vaccines. Part 1 deals with field issues, while Part 2 deals with expected background rates of adverse events following use of the most commonly-used vaccines, and is supported by extensive references.

Handling vaccine safety issues with the media are touched on, giving a brief selection of what is offered in the workshop on "Partnership Building with the Media", which deals with this subject more fully. The workshop is offered either as a three-day course by itself or as part of the Global Training Network (GTN) course on surveillance and management of adverse events.

1. Glossary

The following is a brief glossary of terms used in public health in relation to the safety of vaccines and injections. The target audience is WHO, the United Nations Children's Fund (UNICEF), and other public health organizations and national programme managers dealing with these issues. The language may need to be simplified if used for general public or media consumption.

Adverse event/reaction following immunization (AEFI). An event that negatively affects the health of an individual who has received a vaccine in the recent past. The category includes coincidental events not caused by vaccines but incorrectly linked to them. An event may be considered adverse because health staff, parents or members of the public are concerned enough to report it. The event may after investigation be found not to be due to vaccine. Most AEFIs occur within one month of receipt of the vaccine, but longer intervals are also reported.

Attributable risk. The rate of adverse reactions in individuals that can be attributed to the administration of the vaccine, usually expressed in terms of number of such cases per number of doses of vaccine administered. It is usually calculated from controlled studies.

Causal association/link. An AEFI which is caused by administration of a particular vaccine. Causally associated events are also temporally associated (i.e. they occur within a limited time after vaccine administration), but events which are temporally associated may not necessariy be causally associated. Causality is usually based on:

- Laboratory findings (e.g. isolation of vaccine virus strain), and/or
- Unique clinical syndrome (e.g. anaphylaxis), and/or
- Epidemiological studies showing an increased incidence in vaccinated groups as compared with unvaccinated groups.

Coincidental adverse event. A medical event that would have occurred whether or not the individual had received an immunization prior to the event.

Cluster. Two or more cases of the same adverse event related in time, the time interval since vaccination, geography or vaccine administered. A more precise definition may be decided upon by national programme managers.

Guillain-Barré Syndrome. An acute demyelinating disease of the peripheral nervous system. This neurological condition comes on suddenly as partial paralysis and disturbed sensation. It can follow a number of conditions including severe infection

such as diphtheria, mumps, influenza, measles, respiratory infections etc. It may also follow administration of some vaccines and occasionally after surgery. After a brief illness during which patients generally need to be admitted to hospital, most recover spontaneously.

Injection safety. The public health practices and policies dealing with various aspects of the correct administration of injections (including waste disposal) aimed at minimizing the risk of transmission of blood-borne pathogens. All injections, irrespective of their purpose, are covered by this term (see definition of safe injection practices).

Immunization safety. The public health practices and policies dealing with the various aspects of the correct administration of vaccines. They focus on minimizing the risk of transmission of disease with the injection and on maximizing the effectiveness of the vaccine. The term encompasses the spectrum of events from proper manufacture to correct administration. The term usually includes both injection safety (programmatic errors compromising injection safety) and vaccine safety (faults in the vaccine itself compromising vaccine safety).

Odds ratio. The ratio of the probability of prior exposure among the cases to the probability of prior exposure among non-cases. It is a measure of the strength of the association between events and a way to estimate the relative risk.

Programme-related adverse event. An AEFI which is shown to be caused by an error or errors in the handling or administration of a vaccine. The error is usually person-based rather than vaccine- or technology-based (e.g. injection site abscess). It can generally be prevented through proper staff training and an adequate supply and proper use of safe injection equipment.

Vaccine reaction. A side-effect (usually mild) such as soreness at the site of injection following administration of a vaccine. It is usually of short duration (two or three days) with no long-term consequence. It may require mild medication such as paracetamol for a short while to alleviate the symptoms.

Relative risk. The comparison of the risk of one intervention with another, or the risk of an intervention compared with no intervention. For instance, it is generally much less risky to be given a vaccine than to contract the disease (with its risk of death and complications) that the vaccine is designed to protect against.

Safe injection practice (SIP). Those public health practices and policies which ensure that the process of injection carries the minimum of risk, regardless of the reason for the injection or the product injected. *This is the preferred generic term for this subject.*

Temporal association/link. An event which occurs close in time to vaccine administration. Temporal association is independent of causal association, and an event which is temporally associated with vaccine administration may or may not be shown to be caused by the vaccine.

Trigger event. A cluster of AEFIs or single AEFI (e.g. a death or hospitalization) that alerts health professionals to the need for action such as a case investigation.

2. Adverse events during immunization campaigns

2.1 Background

During a campaign there may be a real or apparent rise in adverse events. It is an opportunity to strengthen infrastructure, to increase public awareness, to strengthen already-existing surveillance for vaccine-associated adverse events, or to establish such a system. There are, however, special issues related to campaigns that need to be considered in terms of AEFIs. Adverse events and their effects during a campaign can be minimized by proper planning. A campaign is different from routine immunization in that:

An *apparent* rise in adverse events may occur.

- A large number of doses of vaccine is given over a short period of time, and an unexpectedly large number of vaccine-associated adverse events may be detected. This may worry the public, even though the *rate* of adverse events remains unchanged.
- Adverse events tend to be noticed more by both the staff and the public during campaigns, particularly when injectable vaccines are used.
- During campaigns, rumours have an opportunity to spread and have a negative effect on the later part of the campaign. In contrast to adverse events occurring during routine immunization, there may be insufficient time to counter the rumours before they damage the campaign.
- A campaign may generate some antagonism from various quarters. Adverse events occurring during the campaign add fuel to an already negative situation, and can be used by some to justify criticism of the campaign.
- Vaccines may be administered to a wider age group (usually older) than during routine immunization. The programme may have less experience in dealing with the type of reactions or adverse events to be expected in this older group.

A *real* rise in adverse events may occur:

- Staff may be under pressure from a lot of children needing vaccine quickly; they may be tempted to cut corners and not observe normal safe injection practices, thereby increasing the risk of adverse events due to programmatic errors.
- Extra staff may be used who are unfamiliar with a given vaccine or situation – resulting in more programmatic mistakes.

2.2 Action to prevent AEFIs during campaigns

2.2.1 Planning to reduce programmatic errors

- Use only quality vaccine (controlled by UN or national regulatory authority) and only autodisable syringes for injectable vaccines.
- Ensure proper distribution of diluent and injection material together with vaccine.
- Provide training on proper reconstitution of freeze-dried vaccines, and proper administration techniques.
- Plan for safe disposal of injection equipment.
- Decide on which contraindications or precautions should be taken by field staff administering the vaccine.

2.2.2 Implement a rapid, flexible surveillance system for adverse events

Even if a national programme has not yet developed a functioning adverse events surveillance system, some form of adverse-event monitoring is essential in mass campaigns. Without this, the public is likely to hear of an adverse event before the programme manager, and the situation becomes very difficult to control. The surveillance should be simple, flexible and rapid. Planning includes the following actions:

- Decide who will have overall responsibility and who should be the focal point and the spokesperson (e.g. EPI manager, person in charge of surveillance at national level, national regulatory authority – NRA). This is particularly important if surveillance of adverse events is done by a surveillance structure other than EPI, if an NRA exists, or if there is a common monitoring scheme for drugs and vaccines.
- Decide what to report, how to report and what to investigate. Decide who should receive reports and who will be involved in an investigation if needed. Don't make the reporting list complicated – for instance:
  - all injection site abscesses;
  - all deaths due to immunization (or thought by staff or parents to be due to immunization);
  - all hospital admissions due to immunization (or thought by staff or parents to be due to immunization);
  - any severe or unusual events due to immunization (or thought by staff or parents to be due to immunization).
- Train staff about what adverse events to expect and how to manage them.
- Develop rapid reporting channels from the field to the person in charge of monitoring vaccine-associated adverse events (telephone or fax).
- Analyse data quickly (this does not necessarily mean sophisticated analysis), and take appropriate action quickly. A serious report must not sit on someone's desk without attention.
- Provide feed-back on a weekly basis to reassure staff and the community that there are no problems.

- Consider creating a vaccine-associated adverse events review committee to review causality of events reported (this could include, for example, a neurologist, paediatrician and immunologist), to be convened on an *ad hoc* basis. It is advantageous for them to represent officially key professional associations.
- Track the number and lot of all vaccines and where they are distributed.

2.2.3 Communication

- Consider the need for informed consent from the parents or patients themselves, if old enough, and how to obtain it (verbal versus signed consent based on receiving information on risks and benefits from the vaccine) (see chapter 8).
- Prepare in advance "Qs and As" about adverse events. Inform the media and all district programme managers (see chapter 7).
- Be aware of the local perceptions and information about previous adverse events and any allegations about vaccine safety that needs to be responded to with correct information.
- Ensure coordination with WHO and other partners.

2.3 Special considerations for specific antigens

2.3.1 Oral Polio Vaccine (OPV) campaign

Programme errors. These are not likely to cause problems during administration of oral polio vaccine (OPV) during national immunization days.

Vaccine-associated paralytic polio.[1] The incidence of vaccine-associated paralytic polio (VAPP) with OPV has varied between different studies, and depends on whether it was the first or a subsequent dose. No matter what, all studies agree that the risk is less than one case per million children vaccinated. As many as half the affected children are found to have congenital immune deficiency. The majority of children immunized with OPV in national immunization campaigns will have received at least one dose of OPV previously (OPV is recommended to be given at birth, 6, 10 and 14 weeks, while the age range for the NIDs is birth to five years). Thus only those who missed their scheduled birth dose and subsequent doses might be exposed to a higher rate of VAPP during campaigns. It could be expected, then, that the rate of VAPP in any NID should be around one case per 6 million children vaccinated. Analysis has shown this to be the case over a number of years of NIDs and millions of doses of OPV, there having been no increase in the rate of VAPP[2] during campaigns.

[1] Vaccine-associated paralytic polio (VAPP). Acute flaccid paralysis 4–30 days following receipt of oral polio vaccine (OPV), or within 4–75 days after contact with a recipient of OPV, with neurological deficits remaining 60 days after onset, or death.

[2] Andrus JK et al. Risk of VAPP in Latin America, 1989-91. *Bulletin of the World Health Organization*, 1995, 73(1):33-40.

Acute flaccid paralysis (AFP). There are several other causes of flaccid paralysis in addition to polio. The commonest of these (around 50% of AFP) is Guillain-Barré Syndrome (GBS). This syndrome occurs at a fairly constant rate in communities (at around one case per 100 000 population per year) and is the first differential diagnosis of AFP as polio declines. Its cause is unrelated to polio infection or OPV administration.

Coincidental polio. Be alert to the possibility that wild poliovirus may be circulating in the same place the NID is carried out. In this case, paralysis of children receiving the vaccine may be due to prior infection with the wild virus, not the vaccine. The way to prove this is to take stool samples in the normal way and examine which type of poliovirus is isolated.

Provocation polio. Following an outbreak of wild polio, an injection of DTP vaccine or other pharmaceutical product may very rarely "provoke" paralysis in the injected limb. It has been suggested that routine immunization and injections for other reasons should be suspended around the time of NIDs to avoid this possibility. This is not realistic in most situations.

2.3.2 Measles vaccine campaign

Issues relating to adverse events during measles campaigns include the following:

- HIV infection. In countries with high HIV seroprevalence, provide a statement giving the current WHO guidelines on HIV infection and measles vaccine administration. (See chapter 4.)

Safe injection practice. Before the campaign, the following actions need to be taken:

- In collaboration with donors, decide on the type of syringe to use (WHO recommends autodisable A-D syringes).
- Check that bundling together the diluent and vaccine works in a pilot area.
- Train staff to use A-D syringes and plan for their disposal (preferably high temperature incineration rather than burial).
- Observe immunization practices and train up on any deficiencies e.g. reconstitution, disposal of injection equipment.

Press, media and health staff should be given clear information in advance of the campaign on :

- Known complications of disease and vaccine and background rates.
- Relative risk.
- Normal rates of AEFI.
- Temporal vs. causal linkage.

Reporting AEFIs. Because of the increased risk of AEFIs in measles mass campaigns, there must be a surveillance system which is capable of monitoring adverse events, operating during the campaign and immediately afterwards. It is even more important than during routine immunization that these events are reported by the fastest possible method, e.g. telephone or fax. Make sure even hospitals report adverse events during the campaign.

Programme errors. Unlike polio campaigns conducted with oral vaccine, measles campaigns need to use injectable vaccine with all the potential risks that injectable vaccines carry. As well as the risk of AEFIs due to the vaccine (e.g. convulsions, anaphylaxis etc.) there is the risk of unsafe injection practices and other programmatic errors. Guidelines for avoiding programme errors during mass campaigns are provided elsewhere.

Table 1: Number of students suffering adverse events following MMR campaign in Australia, 1998 (n= 651 615 students)*

Adverse event	Number
Faint/syncope	17
Syncopal fit	13
Anaphylaxis	4
Hyperventilation	3
Rash	2
Local allergic reaction	2
Severe immediate local reaction	1
Arthropathy	1
Fever	1
Anxiety	1
Lymphadenopathy	1

* Source: *Communicable Disease Intelligence* (Australia), 29 October 1998.

Health workers and parents should all participate in surveillance for those events selected for reporting. Monitoring should result in prompt case investigation and the following immediate actions:

- Treatment of the patient.
- Communication with parents, the community and/or press to explain honestly the cause of the AEFI (if known) and actions taken; or to explain a lack of association, and thereby dispel rumours and fears.
- Improvement or correction of service delivery if the AEFI was caused by programmatic error. This may require improvements in logistics, training and/or supervision.
- Identification (and removal if necessary) of any implicated vaccine.

Toxic shock. This is such a serious programme error that it deserves separate mention. Incorrect handling of an opened vaccine vial can result in contamination of the reconstituted liquid with staphylococcal or other organisms. The organisms are able to grow in the liquid, all the more so if kept in a warm environment. Left for more than a few hours, the staphylococcus organism produces large quantities of toxin. If the vaccine contaminated with toxin is then used, the recipient can die within hours or become desperately ill. If recognized soon enough, the condition is possible to treat, but often the diagnosis is made too late and the child dies. Tragically, several children are usually affected simultaneously through use of the same contaminated vial.

All staff involved in administration of measles vaccine should be told about this condition and how to avoid it:

- Reconstitute according to guidelines (to ensure sterility of the vaccine is preserved).
- Use a sterile needle and syringe for every injection.
- Do not draw up liquid vaccine with a needle that has been used before (for whatever purpose).
- Keep the vaccine cool and protected from direct sunlight while in use.
- *Always* discard the reconstituted vaccine after six hours – *never* keep it in the refrigerator over night.

Coincident measles. Measles remains a problem in many countries undertaking measles campaigns. It is very likely that at least some wild measles virus will be circulating at the same time as the campaign, and may result in complaints that the vaccine caused the illness or that the vaccine is ineffective.

Mumps meningo-encephalitis. Although many countries are including rubella vaccine (as MR) in measles campaigns, mumps vaccine is mostly avoided for economic reasons, but may also be avoided because of the concern about complications such as meningo-encephalitis following vaccination.

2.3.3 Vitamin A supplementation during mass campaigns

In areas of vitamin A deficiency, vitamin A is frequently administered with polio NIDs and measles campaigns.

Programme error. The vitamin may be given in the incorrect dose. Too high a dose may result in temporarily raised intracranial pressure, as displayed by vomiting, headache and irritability. In infants under the age of six months too, high a dose of vitamin A may also result in a bulging fontanelle. Parents and the child should be reassured that these transient reactions disappear within 24–48 hours and require no treatment.

Nature of the micronutrient. Even when the correct age-specific dose of vitamin A is given, a small number of infants and children (1.5-7%) experience loose stools, headache, irritability, fever, nausea, and vomiting. A transient bulging fontenalle may occur in a small number of children (generally less than 1%) under six months of age. No special treatment is necessary.

Pregnancy. Administration of *high-dose* vitamin A supplements during pregnancy is not recommended because of the potential harmful effects to the fetus. Because of the difficulty of screening for pregnancy, it is not recommended to give vitamin A to women during immunization campaigns.

2.3.4 Tetanus toxoid campaign

Programme error. The risk is as for other injectable vaccines (see measles above).

Nature of the vaccine. Administration of tetanus toxoid (either as TT or Td) in mass campaigns is generally as part of a high risk approach delivering the vaccine to women of childbearing age in a given locality. Most will have had doses of TT in the past, and some may have had many doses – the campaign does not screen for previous doses. A hypersensitivity reaction is possible in those who have had multiple doses in the past, the risk increasing with the number of doses. Full anaphylaxis is uncommon, but milder symptoms are more likely (see chapter 3). Women may complain of severely swollen arms at the site of the injection that take many days to subside.

Pregnancy. Administration of TT or Td during pregnancy has never been shown to cause damage to the mother or fetus.

2.3.5 Yellow fever campaign

Programme error. Because the vaccine is freeze-dried and needs reconstitution, there is the danger of contamination and toxic shock, as with measles vaccine. YF vaccine must not be mixed in the same syringe as measles vaccine, a practice sometimes seen in mass yellow fever campaigns. This is because the diluent for each vaccine is different, and reconstituting the vaccine with other than the correct diluent alters its properties.

HIV infection. Insufficient data are available to confirm the safety of yellow fever vaccine in symptomatic individuals. Non-symptomatic individuals can safely receive the vaccine. Simple questions may have to be designed for vaccinators to administer to those vaccinated before giving the vaccine to ensure they are not HIV-symptomatic.

Post-vaccination encephalitis. Infants less than six months are at increased risk of encephalitis 7-21 days after immunization. The risk to older children and adults is virtually zero. Thus the only precaution in this context is to ensure that no infant less than six months of age is vaccinated with yellow fever vaccine.

Mild systemic reactions. Headache, local reaction and fever are common complaints after the vaccine. They need only supportive measures such as paracetamol.

Pregnancy. Because of the theoretical danger to the fetus, yellow fever vaccine is contraindicated in pregnancy. In a campaign, women should not be vaccinated if they are or might be pregnant (see chapter 8). In situations where there is more time for counselling and weighing up individual risks, the woman may be considered at greater risk from yellow fever infection than the fetus from vaccine damage, and the vaccine given.

3. Recognition and management of anaphylaxis following immunization

3.1 Warnings

Warning 1. Although anaphylaxis is a recognized complication following administration of a number of vaccines, it does not seem to be reported much from developing countries. This may be because children have been less sensitized to components of vaccine than those in industrialized countries, or it may reflect a more limited reporting system. This apparent difference needs to be taken into account when programme managers consider including treatment of anaphylaxis in training.

Warning 2. There is a high risk that peripheral health workers who lack thorough training on the subject will miss-diagnose faints and feeling dizzy following immunization for the onset on anaphylaxis. It cannot be stressed enough that most episodes of feeling ill or faint, or actual fainting that occur immediately after immunization, are *not* due to the onset of anaphylaxis. The administration of adrenaline in faints is not only contraindicated, it is actively dangerous.

Having indicated the problems associated with the treatment of anaphylaxis, it should also be said that on the occasions that it occurs, rapid treatment saves lives. Lack of awareness, training or equipment have, in the past, cost the lives of recently vaccinated children.

Programme managers must take these aspects into consideration before deciding to provide treatment, training and equipment. If these items are to be made available, a decision should be made about whether they should be available in only fixed vaccination posts during measles campaigns, during routine immunization services, or both.

Anaphylaxis occurs only rarely after administration of vaccines.*(1,2,3)* When it does occur, the individual must be diagnosed properly, treated and managed urgently and transferred to a hospital setting.

Staff should be trained in checking for contraindications to vaccination so as to minimize their occurrence; to enable diagnosis and management; to ensure that appropriate drugs are available in the field; and to ensure the reporting of such events immediately. The following is intended for the initial management of anaphylaxis. Hospital treatment of serious cases is not dealt with here.

3.2 Definition

If a decision is made to include it in training, both professional staff and lay persons may need to know about anaphylaxis, and it is worth having definitions suitable for both audiences:

a) Professionals

Anaphylactic shock (anaphylaxis). An immediate (type 1) hypersensitivity reaction. Acute, often explosive, allergic systemic reaction, characterized by circulatory failure (e.g. alteration of level of consciousness, low arterial blood pressure, weakness or absence of peripheral pulses, cold extremities secondary to reduced peripheral circulation, flushed face and increased perspiration) with or without bronchospasm and/or laryngospasm/laryngeal oedema leading to respiratory distress. May also include pruritis, generalized flushes, angioedema (hives), seizures, vomiting, abdominal cramps and incontinence. It occurs in previously sensitized persons who receive the sensitizing antigens again.

b) Lay persons

Anaphylactic shock (anaphylaxis). A rare reaction brought on by a number of causes including administration of foreign proteins such as vaccines, usually occurring within one hour of their administration. The classical presentation is collapse. In severe cases, urgent medical treatment is needed to avert death.

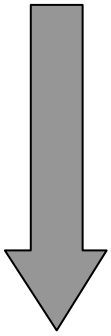
3.3 Contraindications

Before immunization, check for contraindications to immunization by asking about known allergies and previous adverse reactions to vaccines. In the case of a possible serious allergy, check with an appropriate supervisor before giving the vaccine. This procedure will minimize the occurrence of anaphylaxis but will not remove the risk altogether.

3.4 Clinical presentation

Anaphylaxis is *rare* – occurring about once every million doses of vaccine given. Most vaccinators will go their entire career never seeing a case. Fainting and feeling faint, however, are *common* and can easily be confused with anaphylaxis, as can anxiety, breath-holding and convulsion. Fainting has a strong emotional component, and while relatively common after immunization of adults or adolescents, is very rare in young children. Thus, sudden loss of consciousness in very young children after vaccines is much more likely to be an anaphylactic reaction. A strong central pulse (e.g. carotid) is maintained during a faint or convulsion but not in anaphylaxis. Anaphylaxis can present at different time intervals after vaccination (but mostly within 30 minutes) and with differing degrees of severity.

Table 2: Signs and symptoms of anaphylaxis

Clinical progression	Signs and symptoms	Severity of attack
Mild, early warning signs 	Itching of the skin, rash and swelling around injection site. Dizziness, general feeling of warmth.	Mild
	Painless swelling in part of the body e.g. face or mouth. Flushed, itching skin, nasal congestion, sneezing, tears.	Mild to moderate
	Hoarseness, feeling sick, vomiting	Moderate to severe
	Swelling in the throat, difficulty breathing, abdominal pain	Moderate to severe
Life-threatening symptoms	Wheezing, noisy, difficult breathing, collapse, low blood pressure, irregular, weak pulse	Severe

Important points:

- In general, the more severe the reaction, the more rapid the onset of symptoms.
- Most life-threatening reactions begin within 10 minutes of immunization.
- As a general rule, everyone receiving vaccine should remain in the vicinity of the vaccination clinic for at least 15 minutes after the administration of vaccine, and for longer if there is concern.

Symptoms limited to only one body system (e.g. skin itching) can occur, leading to a delay in diagnosis. Occasional reports have described reactions where symptoms recur 8 to 12 hours after onset of the original attack and prolonged attacks lasting up to 48 hours.

3.5 General issues of management

Having made the diagnosis, consider the patient as being in a potentially fatal condition, regardless of the severity of the current symptoms. Begin treatment immediately *and*, at the same time, make plans to transfer the patient swiftly to hospital (if not already in a hospital setting). All patients with anaphylaxis should be hospitalized.

3.6 Injecting adrenaline (epinephrine) as the basis of treatment.

Adrenaline stimulates the heart, reverses the spasm in the blood vessels and the lung passages, and reduces swelling and skin itching. But this very potent agent can cause an irregular heart beat, heart failure, severe hypertension and tissue necrosis if used in inappropriate doses or route.

Each vaccinator who is trained in treatment of anaphylaxis should have rapid access to an emergency kit with adrenaline, and be familiar with its dosage and administration. The expiry date of the adrenaline should be written on the outside of the emergency kit and the whole kit should be checked three or four times a year. Adrenaline liquid that has a brown tinge must be discarded.

3.7 Steps in initial management

- If already unconscious, place the patient in the recovery position and ensure the airway is clear.
- Record heart rate, respiratory rate and blood pressure (if the patient has a strong carotid pulse, he is probably not suffering from anaphylaxis).
- If appropriate, begin cardiopulmonary resuscitation.
- *Give 1 in 1000 adrenaline/epinephrine* (for correct dose for age or weight, see below) *by deep intramuscular* injection into the opposite limb to that in which the vaccine was given. (Subcutaneous administration is acceptable in mild cases).[3]
- And *give an additional half dose around the injection site* (to delay antigen absorption).
- *If the patient is conscious after the adrenaline is given, place the head lower than the feet and keep the patient warm.*
- Give *oxygen* by face-mask, if available.
- Call for professional assistance but never leave the patient alone. Call an ambulance (or arrange other means of transport) and a medical practitioner if necessary, after the first injection of adrenaline, or sooner if there are sufficient people available to help you. If you have made the diagnosis of anaphylaxis, do not wait for the arrival of senior staff before giving the adrenaline.
- If there is no improvement in the patient's condition within 10-20 minutes, of the first injection, *repeat* the dose of adrenaline up to a maximum of three doses in total. Recovery from anaphylactic shock is usually rapid after adrenaline.
- Record, or get someone to record, vital signs (pulse rate, respiratory rate and blood pressure), as well as time and exact dose of any medication given. Make sure the details accompany the patient when he is transferred. Mark the immunization card clearly so the individual never gets a repeat dose of the offending vaccine. At a suitable moment, explain to parents or relatives the importance of avoiding the vaccine in the future.
- Report the occurrence of anaphylaxis to the appropriate officer in the ministry of health by fax or phone when the clinical situation is dealt with.

[3] In a patient with severe anaphylaxis, the situation is life-threatening, and requires the administration of intravenous fluids as well as possible endotracheal intubation. These are best performed in a hospital setting. A skilled physician may also use additional treatment such as hydrocortisone, anti-histamines, nebulised salbutamol (for bronchospasm) and nebulised adrenaline (for laryngeal oedema). However these treatments should not be part of primary care by those unfamiliar with them.

3.8 Adrenaline dosage

The dosage is *not* "one ampoule".

1 in 1000 adrenaline (epinephrine) requires a dose of 0.01ml/kg up to a maximum of 0.5 ml injected intramuscularly (or subcutaneously in very mild cases)

If the weight of the patient is unknown, an approximate guide is as follows:

Less than 2 years	**0.0625 ml (1/16th of a ml)**
2-5 years	**0.125 ml (1/8th of a ml)**
6-11 years	**0.25 ml (1/4 of a ml)**
11+ years	**0.5 ml (1/2 of a ml)**

3.9 Training and equipment

Programme managers should be responsible for ensuring that the appropriate equipment/medicines are available for the treatment of anaphylaxis, and that all vaccination staff are trained in its recognition and management. A summary of the treatment of anaphylaxis and the equipment needed should be available everywhere vaccines are given.

4. Adverse events in HIV-infected individuals

4.1 General

There is a high prevalence of HIV infection in many nations where mass immunization campaigns are carried out or contemplated. In general, EPI vaccines are safe and reasonably effective when given to HIV-infected individuals. Exceptions are BCG and yellow fever (see Table 3). Live vaccines are potentially more of a problem because there is the theoretical risk that the individual may become infected with the vaccine organism such as the BCG bacterium or the live measles attenuated vaccine virus. At a practical level, individuals may not be identified as being HIV-infected before vaccines are administered. There are also major implications for training and the proper supply of injection equipment and its safe disposal.

4.2 Measles vaccine

4.2.1 Background

In many developing countries where measles mass campaigns are planned, there may be a high prevalence of mothers who are HIV-infected (sometimes as high as 35% of pregnant mothers are HIV-positive), resulting in a relatively high proportion of HIV-positive infants.

By 9–12 months of age, the period when most infants receive their measles vaccine, few if any of the HIV-infected infants will be symptomatic for AIDS. If their CD4 count or other parameters for AIDS progression were to be investigated, their immune system would most likely be found only mildly affected, allowing successful immunization and protection in most instances.

Current WHO/EPI policy regarding administration of measles vaccine to known HIV-infected infants is that they should receive an extra dose, if possible, as early as six months of age, in addition to the scheduled dose at nine months. The vaccine has been shown to be safe in this situation and may be effective if the child is not already immuno-compromised. This is not relevant where mass screening for HIV cannot be performed (such as in most developing countries).

4.2.2 Older ages

To date, the Expanded Programme on Immunization has promoted measles mass campaigns as a strategy for controlling measles transmission. These campaigns generally involve national or regional campaigns targeting children of older ages. Some of these children may already be symptomatic for HIV infection. This raises the question whether WHO recommendations regarding immunizing HIV-infected individuals are still valid for the older child.

4.2.3 Risk levels

All severely immuno-compromised children are at high risk of severe complications and death from measles if they become infected. The risk of contracting measles varies with immune status (immunized individuals have a much-decreased risk of contracting the disease, and if they do contract it, the disease will be less serious), and is proportional to the amount of wild measles virus circulating in the community.

There is virtually zero risk of contracting measles in a few countries that have carried out nationwide measles campaigns and have achieved high coverage. There is almost no circulating wild virus. Exceptionally, importations still cause small outbreaks. For some years, certain of these countries were advised not to immunize severely immuno-compromised children with measles vaccine. Individuals with moderate immune deficiency have generally been recommended to have the vaccine if there is even a low risk of contracting wild measles from the community. At least two cases of immune-suppressed individuals who died some time after administration of measles vaccine (*4*,*5*) have recently been reported in the literature. These cases indicate a certain low level of risk for using measles vaccine in individuals who are HIV-infected *and* whose immune system is damaged to the extent they are unable to cope with live vial infection.

4.2.4 What to do in campaigns

Screening for AIDS and immuno-compromised status during mass campaigns is virtually impossible. In addition, it is important to re-emphasize that immuno-compromised children are at high risk from death *or severe complications following wild measles infection*, and the balance of risk to such children clearly favours immunization with the measles vaccine in any situation where wild measles virus may be circulating.

4.2.5 Recommendations

If wild measles virus is circulating in the community, all children, regardless of previous vaccination history or HIV status, should be offered measles vaccine during campaigns (without screening). Where the chance of contracting wild measles infection is virtually zero, countries with the capacity to monitor an individual's immune status with, for instance, CD4 counts, have modified this policy (*6*). A child who is already *severely* affected by the HIV virus may be considered as for any child who is seriously ill – it makes sense to avoid immunization. If the child dies soon after administration of the vaccines, it may incorrectly be assumed that death was caused by the vaccine.

4.2.6 Future policy

WHO continually reviews its policy about immunizing HIV-infected individuals. The current advice is to immunize all children with measles vaccine, regardless of HIV status. There is currently no indication to change this WHO policy. WHO will examine ways of defining more precisely the risk levels in different epidemiological situations.

4.3 Other vaccines

Table 3 shows the current WHO policy regarding immunization of HIV-infected infants and children. As for measles vaccine, the risk from the vaccine (with the exception of BCG and yellow fever vaccine in symptomatic children) is lower than the risk of the disease in such children, and vaccine is recommended. This remains the same whether the vaccine is delivered by routine services or by supplementary activities.

Table 3: World Health Organization/UNICEF recommendations for the immunization of HIV-infected children and women of childbearing age (*7*)

Vaccine	Asymptomatic HIV infection	Symptomatic HIV infection	Optimal timing of immunization as part of routine immunization
BCG	yes	no	Birth
DPT	yes	yes	6,10,14 weeks
OPV	yes	yes*	0, 6, 10, 14 weeks
Measles	yes	yes	6 and 9 months
Hepatitis B	yes	yes	As for uninfected children
Yellow fever	yes	no**	
Tetanus toxoid	yes	yes	5 doses***

* IPV is used in certain countries as an alternative for children with symptomatic HIV infection
** Pending further studies
***5 doses of tetanus toxoid for women of child-bearing age as for non-HIV infected persons

4.4 Vitamin A

Vitamin A deficiency is common during HIV infection. Therefore it is appropriate to provide vitamin A supplementation with immunization campaigns in populations with high prevalence of HIV infection. There are currently several studies investigating the various beneficial effects of giving vitamin A to HIV-infected individuals. These suggest that additional doses of vitamin A may be appropriate (revised WHO guidelines are in preparation).

5. Crisis Management

5.1 What is a crisis?

A “crisis” in the context of adverse events is a situation where there is actual or potential loss of confidence in vaccines or the vaccination service, precipitated by the report of an adverse event (real or supposed). The crisis can often be avoided by anticipation, care and training. If managed properly, the crisis will result in a strengthening of the programme and a bolstering of public confidence.

Adverse events are inevitable, although they can be reduced to a minimum level in good programmes. Accordingly, plans must be in place to react appropriately WHEN (not IF) a crisis occurs. The programme manager must always remember that public support is the foundation for handling adverse events and preventing a crisis.

As an example, an adverse event might be the deaths of three infants following routine measles vaccination by the same vaccinator on the same morning. Or it may be the result of the publication of a piece of medical research that purports to show how damaging a particular vaccine is.

For some years there has been a continuous background of unrest about immunization, especially of infants. There are a number of reasons, including the better level of education of parents in all countries. They are better informed and have access to material for and against immunization. As the vaccine-preventable diseases decline, parents may perceive the risk of vaccination to their children as higher than the risk of getting the disease.

Programme errors are more likely to occur in developing countries, presenting programme managers with problems of public confidence. On the other hand, higher education levels and literacy rates in industrialized countries mean a higher awareness by parents to the issues. Confidence in vaccines is likely to be highest when the public perceives a high level of threat from disease. Even in industrialized countries, for instance, there are unlikely to be complaints about the safety of meningococcal vaccination for teenagers when an outbreak of meningitis is reported at colleges and universities.

5.2 Why does a crisis arise?

A crisis may arise for reasons beyond the manager's control (e.g. publication of an article in the press). Or the report of a programme error may haved been handled badly by a professional or a political spokesperson. This may be the result of a lack of planning, poor media relations, a lack of public support, or poorly communicated immunization policies. Suddenly there is a great media interest in the subject, and the programme manager may find him/herself exposed to the full glare of publicity, having to answer difficult questions and having the whole nation listening or watching!

5.3 Four steps for managing adverse events and preventing a crisis

Faced with a crisis, what can a manager do? Certain actions should be undertaken ahead of time. These include:

1) Be "pro-active". Do not wait for the crisis to happen, prepare for the inevitable.

2) Train yourself and vaccination staff at all levels for appropriate responses.

3) Verify any event before making any public statement.

4) Have a plan ready for reacting to the crisis when it happens.

5.3.1 Be pro-active

- Identify an individual who will be in charge of the response. A senior person should be given this responsibility so that it is clear to outsiders that top staff are concerned and responsible.
- Build up a relationship with the media, especially health correspondents. This should be done by supplying the media with regular health-related information. It is useful to provide facts sheets about expected adverse events and their rates under normal circumstances. Thus when a report announces a given event and its rate, the correspondents have something to compare it with. Forge special relationships with sympathetic correspondents whom you will later be able to call on in a crisis.
- Prepare relevant questions and answers and facts sheets about adverse events.
- In the face of an impending mass campaign, check the facts (see section 2) about what can go wrong. Issue a press statement before it starts. This means that the press knows what levels of adverse events (such as vaccine-associated polio paralysis – VAPP – following oral polio vaccine) to expect.
- Establish reputable information channels such as a regular health spot on the radio or a health magazine.
- Seek top-level advice from a good local public relations (PR) specialist or similar resource on how they would propose you handle anticipated adverse events.
- Ensure there is a budget line for training, planning for and reacting to crises.

5.3.2 Training

Train yourself and other senior staff (include district officers, if that is possible) in handling the media. This includes preparing written material as well as practice in holding interviews for newspapers, radio and television. Sensitize staff to such skills as active listening and the importance of body language (see Section 6 on dealing with the media). This information can be found at http://www.vaccines.who.int ("Vaccines are safe"). In addition, WHO/EPI provides a tool box and training workshop to cover these issues. Details are available from the nearest WHO Regional Office or WHO/EPI, Geneva.

5.3.3 Verify the event

- Verify the facts. The moment an adverse event is reported, steps must be taken to verify what has actually happened. This should be done by going to the source by the quickest means, such as a telephone call. Beware of second-hand reports. Is the source credible?
- Decide if it is a "real" adverse event. Some events are part of a longer-term phenomenon and pin-pointing one event may not be appropriate. For instance, one woman complaining that hepatitis B vaccine has caused her multiple sclerosis is not a crisis – it requires a longer-term response. But the real crisis may be the Minister of Health calling a temporary halt to the use of the vaccine.
- Is there an easy scientific answer to the event, or do more studies need to be carried out? Has a similar event happened in another country?

5.3.4 Planned response

- Create a crisis task force involving the public as partners. Discuss legal, communications and technical issues.
- Issue a preliminary statement within hours. Contact friendly press with whom a relationship already exists.
- Rapidly establish a press office or contact point for the press.
- Initiate a technically competent investigation and keep the press posted on progress.
- Name who is in charge.
- For a major event, call a daily press conference. Accommodate the media in every way you can.
- Refresh media skills if it is some time since training.
- Set up and announce the support for victims, e.g. expenses, hot line etc., without accepting guilt or blame.
- Consider recruiting the support of the "First Lady", a famous footballer or other popular figure who is prepared to "go public" in support of immunization.
- Conduct a rapid survey of public opinion.
- Evaluate what happened and how things could be handled better next time.

5.3.5 In summary

Adverse events following immunization are inevitable. Prevent as many as possible by proper training. If a crisis does develop, ensure that proper handling of the issues results in a “positive spin” and an improvement in public confidence in vaccines.

6. Communicating with the media

6.1 Background

The media play an important role in the public perception of immunization, and can be a positive or a negative influence. Whether the media support immunization, particularly following the announcement of an adverse event, may depend to a considerable extent on the communication skills of the immunization programme manager. Press statements and press conferences are useful tools for managing media interest in an adverse event. The guiding principles in dealing with the media are honesty and the building of trust.

It is important to communicate with professional organizations, health professionals and field workers, if possible, before going to the media. Health staff should be given guidance on how to deal with the public concern on a given issue. If health professionals and workers can reassure the public with accurate and up-to-date information, the potential harm to the programme will be minimized.

The purpose of this chapter is to provide an understanding of the orientation of the media and to give specific information on how to promote messages that will improve the public perception of immunization.

6.2 Understanding the media perspective

Understanding what the media want from a story will help the programme manger to provide information that meets their needs. At the same time, immunization can be cast in an honest and positive light. The media are most interested in stories that will attract the attention of their audience and sell copy or boost audience viewing/ listening. One technique is to dramatize and personalize events. The media can (if you give them inappropriate material) sometimes present the health service or officials responsible for immunization as being uncaring, impersonal, incompetent, or even dangerous.

It is relatively easy for media stories to create a sense of panic and outrage about events which are either unrelated to immunization (coincidental) or are a localized programme error without wider implications. Additionally, the media tend to report on numbers of events, ignoring the context of the very small rate of occurrence. An event of unknown cause, when linked by the media to immunization, is a potent generator of fear. It is important to develop good communication skills to avoid these negative situations.

6.3 Holding a press interview/conference

When there is considerable media interest about an adverse event following immunization, it is a good idea to hold a press conference or to accept to do an interview. When all the reporters have the same access to the information and do not have exclusive coverage, they may give the story less prominence, and may be less likely to sensationalize the events. A press conference is also more efficient when there is wide media interest, as it enables the message to be given to many reporters at one time. It also provides an opportunity to get representatives of other organizations to voice their support for immunization and the approach being taken to investigate the problem. The opinion of certain professional organizations may have greater credibility than the government in some situations.

It is likely that the media interest will be greatest in the initial stage when relatively little is known about what really happened and possible causes. In this environment, rumours can flourish, and the potential for harm is huge. It is wise to call a press conference early, even if there is only very limited information to give. This will build the relationship with the reporters and prevent the circulation of rumours. At the end of the press conference, reporters should be informed that a further conference will be held within a day or so, at which time full details of the event and the investigation will be provided. Regular contact with the media about the progress of the investigation is advisable. Conclude with a summary of the results and any corrective action taken or planned.

6.4 Sixteen tips on "style"

Practical considerations in style and technique in dealing with the media include:

- Be honest. Never lie. If you do not know, say so, but promise to find out. Be frank and open e.g. "Look what has gone wrong – we are handling it". This is important in building long-term relationships with the media and forms the basis of their trust in immunization. A lie or cover-up can become a bigger news story than the news item itself.
- Be caring. Create a strong, compassionate, competent image for yourself and the immunization service.
- Be responsible. Don't be defensive e.g. "We will see if there is any truth in the report". But accept responsibility appropriate to your position and avoid blaming someone else.
- Be responsive. Hold a daily press conference if that is what is needed to meet the needs of the pubic and media. This can become a channel for building a trusting relationship with the media.
- Be comfortable with uncertainty e.g. "We don't know at this time, but we have taken steps to answer that question".
- Be aware of body language. It is powerful – expressions, direction of gaze, gestures and position of your body.

- Be positive. Wherever possible state the situation in positive terms. Avoid negatives or off-hand, disparaging remarks, and use terms such as *vaccine safety* (which has a positive connotation) rather than *adverse event*. Adopt a "positive spin". Just as the media may cast an event as hostile to vaccination, the same event can be reported from a pro-vaccine perspective with some care and thought. However bad the initial contact with a reporter might have been, the situation can be turned around into an advantage for the immunization programme.
- Be prepared to get the key message across. Be prepared well beforehand. Know what you want to say and take the initiative to lead the interview to your chosen area. Tell the story you want to tell. Anticipate what difficult questions might come up and be ready to answer them. Prepare responses to anticipated difficult questions (chapter 7).
- Be serious – jokes can be disastrous. The subject is rarely amusing anyway.
- Be calm! Do not over-react. Do not offer information that has not been asked for and which might lead into areas of embarrassment.
- Be assertive and maintain control of the interview.
- Be polite – even if things get hot! You impress the audience if you do not stoop to rudeness or worse when provoked.
- Understand your most vulnerable points and be ready to respond when asked about them.
- Stick with the questions you are comfortable with and can answer.
- "Bridge" from difficult areas of discussion to safe ground. *(See "Difficult questions" paragraph 7.2 for an explanation of bridging*). Restart the question on your terms if necessary.
- Be clear. Avoid jargon. In the case of complex medical concepts, communicate with simple phrases. Give easy-to-understand examples if they clarify the meaning.

6.5 Skills

The following skills need to be acquired by all those handling relations with the media:

- Ability to communicate the perception of risk.
- Ability to communicate complex issues simply.
- Interpersonal skills such as empathy.
- Specific media skills, e.g. television interview.
- Rapid acquisition and processing of relevant information.

6.6 Preparing a press statement

All the information to be conveyed in a press conference should be prepared in advance and included in a press statement. The statement needs to include:

- A complete account of events (in terms that will be understood by people not familiar with health services or immunization) framed in their appropriate context (i.e. an isolated event, a coincidental event) so that it limits the concern about the event from spreading to the immunization programme in general.
- Whether the event is ongoing – or whether there will be more new cases.
- An outline of actions taken or planned (depending on the stage, this will range from a plan of action to a completed investigation).
- The cause of the event (when identified with reasonable certainty, not just a working hypothesis), and the corrective action that has been, or will be, taken.

6.7 Preparing for a press conference

Before agreeing to an interview find out what subjects are to be discussed and how the materials will be used. Anticipate the questions and prepare the answers. Preparations for a press conference include:

- Identifying the key messages you want to communicate.
- Identifying the spokesperson(s).
- Preparing a media kit for all reporters and other community leaders that consists of:
  - a concise media release with all the essential information;
  - supplementary background information (e.g. on the benefits of immunization);
  - questions and answers that include questions that have been or are likely to be asked by concerned members of the public.

Successful risk communication involves processes such as interactive dialogue, active listening and discussion. Individuals differ in their perceptions of risk depending on their life experience and knowledge and that certain risks may be more acceptable than others. Emphasize that the risk of complications from vaccination is small and the risk from the disease is great – they are not equal, or nearly equal, as many would try to portray them.

The key messages in favour of immunization might include:

- The benefits of immunization in preventing disease are well proven.
- It is more risky not to immunize because of the chance of serious complications from the disease(s). It is much safer to have the vaccine than the disease.
- Vaccines may cause reactions, but these are usually mild, self-limiting and only very rarely cause serious or long term problems.
- Vaccine-preventable diseases caused millions of deaths and/or disability before the introduction of vaccines, and that situation would return without continued use of vaccines.

- Vaccine safety is of paramount importance to immunization service providers, and any suspicion of a problem is investigated (hence the advantage of well-established vaccine-safety surveillance) and corrected.
- The AEFI is currently being investigated, but is expected to be coincidental or due to a local problem (depending on type of event), and the immunization programme must continue to keep the population safe from disease in the mean time.
- Action is being taken.

6.8 Resources

WHO/EPI offers a tool kit and training workshop on how to relate to the media in these situations. Enquire through the nearest WHO regional office or WHO/EPI Geneva.

7. Questions and answers: immunization campaigns and adverse events

7.1 Introduction

Previous sections have alerted the reader to the possibility of the media approaching professionals and asking about some technical aspect of the immunization programme. Sometimes these questions are difficult to answer without prior thought and training. Handling them is a skill that can be learnt.

Often the press are grateful for a prepared list of questions and answers that they can refer to for a given occasion such as prior to a mass campaign. Care in selection of the right questions and appropriate answers can save time and difficulties on both sides.

7.2 Handling difficult questions

Here are some questions the press may ask programme managers, possibly following the occurrence of a serious adverse event after vaccination. The "easy/friendly" questions are not included here! If you find yourself in a confrontational situation with a member of the press, remember not to let the interviewer take or keep control of the interview. You should answer each question in such a way that it naturally leads you on ("bridges") to what you want to say, that is, supportive statements about vaccination. The problem with many of these questions is that there may be an element of truth in them, but it is generally expressed out of context or without the proper balance.

We have not given answers to all these difficult questions, but here is a model question and answer which demonstrates the classical "bridge":

7.2.1 Bridging technique

Question: Does vaccination cause abscesses?

Answer: (*Face the element of truth*) We know that vaccination can rarely cause abscesses. *(Here comes the first bridge.*) That is why we train staff to avoid them by using a sterile needle and syringe for every child. (*Now comes the second bridge.*) When combining this policy with purchasing only the highest quality vaccines approved by WHO and UNICEF, we are able to assure parents that we have one of the safest vaccine programmes in the world (*whew!*).

7.2.2 Examples of other difficult questions

- Why does the government provide inferior vaccines for children that cause bad reactions/death?
- Why does the ministry of health not train vaccinators so these accidents are avoided?
- Why are injections for vaccines and other medical procedures still dangerous in this country?
- Why are vaccines still given that damage our children with serious side-effects?
- Why are parents not given the truth about vaccines. Is there a cover up?
- Does vaccination spread HIV (AIDS) and hepatitis-B infection?
- Does vaccination cause abscesses?
- Have children died after getting reconstituted measles vaccine?
- Does OPV (oral polio vaccine) cause paralysis?
- Why should our children get OPV and risk paralysis when there is no polio in the country any more?
- Why is hepatitis B vaccine still given in our country when one country has said it causes multiple sclerosis and has withdrawn it?
- Does vitamin A cause brain swelling in infants?
- Are vaccines contaminated with other organisms (bugs) from the manufacture process?

7.3 Model questions and answers prepared in advance about general immunization issues and campaigns

Why do more adverse events occur during campaigns?

The reported rate of adverse events may *appear* raised because:

- A large number of doses is given in a short space of time and more events are reported.
- There is increased awareness by staff and/or the public.
- Common symptoms such as fits, which occur for reasons other than the vaccine, may occur coincidentally. But because they occur during the campaign, everyone assumes (incorrectly) they are due to the vaccine.

The reported rate of adverse events may *actually* be raised because there is an increase in programme errors due to lowered standards under the pressure of campaigns.

What adverse events can occur in campaigns?

Certain adverse reactions are unavoidable in a small proportion of children whether vaccines are given in a campaign or not. These include mild side-effects such as a low-grade fever after measles vaccine or a sore arm after the injection of DTP.

The rate at which these occur should not increase in a campaign. Rare, more serious adverse events should not occur at an increased rate either, but because many more children are immunized in a short time during campaigns, it is possible that rare events may occur. For instance, if collapse is know to occur once in every million doses, this is a very rare event. But in a country the size of India which undertakes a campaign to immunize several million children in a few days, there is likely to be at least one child who develops collapse during the campaign, whether or not it is due to the vaccine.

If staff are under a lot of pressure, if supplies such as syringes are not provided to vaccinators, or if training has not been adequate, staff may make mistakes during the campaign. Unsafe injection practices may lead to some children developing abscesses at the site of infection.

What are the background rates for adverse events?

The expected background rates of serious adverse reactions following immunization are:

Vaccine	Reaction	Rate
Oral polio vaccine	Paralysis	1 in 6 million
Measles vaccine	Encephalitis	1 in 1 million

Are vaccines that are injected as safe as vaccines given by mouth?

All vaccines given during campaigns should meet WHO/UNICEF standards of excellence. So there should be no difference in the quality of vaccines administered by mouth or by injection. But those given orally do not need syringes and needles to be administered, and can be given even by relatively untrained workers. Injected vaccines, on the other hand, need to be given using safe injection practices. For instance, each injection must be given with a sterile needle and a sterile syringe. If these practices are not observed, there may be a higher risk level with the injected vaccine.

Why carry out a campaign if some children may suffer damage from the vaccine?

The proportion of children suffering severe adverse events following vaccination is extremely small and reasonably predictable. In well-conducted campaigns, the number of children suffering as a result of poor immunization practice will be approaching zero. On the other hand, in an outbreak of vaccine-preventable disease such as measles, large numbers of children may be involved and many may die or suffer severe complications. The overall rate is many times lower following vaccination than the risk from the wild disease. Hence it is actually much safer for children to be vaccinated than run the risk of the infection.

What is the difference between an adverse event and an adverse reaction?

An adverse reaction following vaccine is one that is expected in a proportion of children – such as mild fever in around half of recipients of DTP vaccine. Treatment is with simple remedies such as paracetamol, and there are no long-term complications. An adverse event is rare and is usually more serious. For instance, around one in every million doses of vaccine results in an anaphylactic reaction of some degree of severity.

Is it safer to have the disease rather than risk having the vaccine?

As many as 1 child in 20 may die in a measles outbreak with many additional complications including deafness, pneumonia and blindness. While some children may have mild side-effects such as a raised temperature, the only serious complication from the vaccine is a rare case of encephalitis (less than one case per million). Although the actual numbers vary from vaccine to vaccine, the principle is the same – it is much safer to have the vaccine than the disease.

7.4 Model questions and answers – campaigns with OPV

Is OPV safe?

Oral polio vaccine is a very safe and effective vaccine for all children. OPV has no contraindications – all children can be immunized with OPV regardless of fever, cough, diarrhoea, malnutrition or any other illness. After three doses of OPV, approximately 85% of children are protected from death, paralysis or lameness caused by infection with poliovirus. Most children immunized with three doses of OPV will not spread the wild poliovirus to other unprotected individuals. It is far more risky not to immunize! In the absence of immunization, between 1 and 5 of every 1000 susceptible children will become lame or paralyzed in countries where poliovirus is still circulating.

Why do children receive polio vaccine during national immunization days even if they are already fully immunized? Is this risky?

Our country is cooperating in a global initiative to eradicate polio from the world forever. In order to accomplish this, all children should receive immunizations through routine immunization services *and* should receive drops of oral polio vaccine during national immunization days. When *all* children receive drops of polio vaccine at the same time, the circulation of the poliovirus is interrupted, driving the poliovirus out of the community. If properly conducted, NIDs will lead to the eradication of polio.

During NIDs, children who are not fully immunized will become protected against polio after they have received at least three doses of oral polio vaccine. Fully immunized children receiving extra doses of polio vaccine during national immunization days will also benefit because their immunity will be boosted, giving extra protection.

Can a child become paralyzed from the oral polio vaccine?

(WHO recommends that this question and answer NOT be included in background information to the press until a country has reached, or nearly reached, zero virus transmission. Until then, the advantages of receiving OPV are so clear that raising the issue will be counter-productive. It becomes an issue when all or most paralytic cases are likely to be caused by the vaccine, i.e. when wild virus transmission has been stopped).

The risk of paralysis from polio infection is very high. The risk from the vaccine is extremely small (around one case per 5–7 million doses administered). An unvaccinated child has a much higher risk of becoming paralysed from wild polio than a vaccinated one. None the less, although OPV is safe and effective, there is a very small risk that immunization with OPV can cause paralysis in a child receiving OPV or in children exposed to a recently immunized child (with OPV). Supplementary doses of OPV administered during NIDs do not increase this possibility. The risk of paralysis caused by the vaccine decreases with every dose administered. It is therefore much safer to have the vaccine than to risk having wild polio infection.

7.5 Model questions and answers – campaigns with measles vaccine

What adverse events can be expected from using measles vaccine, and how many may occur during the campaign?

The reactions reported from a recent measles campaign in Australia included:

fainting, collapse, anaphylaxis, hyperventilation, rash, local allergic reaction, arthropathy, fever, anxiety and lymphadenopathy. There were less than 50 adverse events reported in over 900 000 children vaccinated. There were no deaths and all children fully recovered from the mild reactions.

It is important that reconstitution of the vaccine be carried out properly and a sterile needle and syringe be used for each child. Failure to do this properly can result in contamination of the vaccine, toxic shock and even death. There are several children reported in most years from developing countries with these complications out of over 100 million doses of vaccine given each year.

Is it safe to give measles vaccine to a child who has already had one dose?

If the first dose was given without problems, there is no reason to expect a second or subsequent dose to be a problem either. If a reaction occurred with the first dose, a physician's advice should be sought.

Is it safe to give if a young woman is pregnant?

Measles vaccine is not targeted at the age group normally expected to be pregnant. There is a theoretical risk that the live vaccine could affect the fetus, so live vaccines are generally not recommended in pregnancy.

Can measles vaccine be given to a child infected with HIV virus?

Yes. The vaccine is safe and effective in HIV-infected children. It should be noted that a very small number of HIV-infected children have been reported in the medical literature who had complications following the vaccine. None the less, these children are at even higher risk of complications if they contract measles and it is much safer for them to have the vaccine than not.

Does measles vaccine cause Crohn's Disease or autism?

No. WHO and the medical and scientific community have responded emphatically to a report that there might be a link. There is NO LINK.

7.6 Model questions and answers – campaigns with vitamin A

Why is vitamin A included in the campaign if it is not a vaccine?

In a vitamin A-deficient area, the target groups who need vitamin A are much the same as those requiring vaccines. It makes good sense to use the delivery mechanisms of vaccines to deliver the vitamin A. The vitamin only costs 2 cents a dose and the additional cost of adding it to an immunization campaign is very small (it only requires some training and scissors). There are enormous advantages of giving the vitamin in terms of improving child health and survival. Giving vitamin A prevents blindness and can greatly reduce the number of measles deaths, the length of time a child is ill, and the severity of complications from measles. Vitamin A can also reduce deaths from diarrhoeal disease.

Is vitamin A safe to give to babies?

The most common way for young infants under six months of age to receive vitamin A is from breast milk. In vitamin A-deficient areas WHO recommends providing the mother with a dose of vitamin A 6–8 weeks after delivery (the safe infertile period) to improve the vitamin A status of the mother and increase the vitamin A content of her breast milk. Only young infants below six months of age who are not being breastfed or who require treatment for clinical vitamin A deficiency or measles should receive vitamin A. Consequently, during campaigns it is not necessary to give vitamin A to infants under six months of age. Scientific studies are being proposed to determine when and at what dose infants under six months may benefit from vitamin A supplementation with routine immunization services.

Should pregnant women receive vitamin A?

Administration of *high-dose* vitamin A supplements during pregnancy is not recommended because of the potential harmful effects to the fetus. Because of the difficulty of screening for pregnancy, it is not recommended to give vitamin A to women during immunization campaigns. Daily or weekly *low dose* vitamin A supplementation of pregnant women is safe.

Do vitamin A capsules contain blood or blood products?

No. They are a normal component of certain naturally occurring foods such as dark green leafy vegetables and orange fruits, such as mango and papaya.

When should women and children receive vitamin A with routine immunization services?

In vitamin-A-deficient areas, WHO recommends that postpartum mothers receive a high dose of vitamin A within six or eight weeks of delivery. At the first immunization contact (i.e. BCG or DTP-1) mothers should be screened for previous doses and weeks since delivery, and if eligible they should receive vitamin A. Vitamin A should be given to children when they come for their routine measles vaccination. Ideally, in deficient areas, children need to receive vitamin A every four to six months to maintain their liver stores of vitamin A. Therefore, it is safe and appropriate to give children vitamin A both during campaigns and when they come for routine immunization services.

7.7 Model questions and answers – campaigns with rubella (German measles) vaccine (as MR)

Does rubella vaccine cause arthritis?

Yes. There are reports of a small number of adult women who have experienced temporary pain in the joints after the vaccine. These cases of arthritis have mostly been reported among older females (20 and over) who were still susceptible to rubella and therefore in greatest need of the vaccine.

Is it safe to give if a young woman is pregnant?

Yes. Several studies have shown that there is probably no risk from receiving the vaccine during pregnancy. It is, however, still recommended that live vaccines should not be given to women thought to be pregnant because there is a theoretical risk of damaging the fetus.

Is the vaccine made from human embryos?

No. As with many virus culture media, the vaccine is grown in a culture medium that uses cell lines grown from the tissue of infants who died through natural abortion. Embryos are not damaged or aborted to produce any part of the vaccine.

7.8 Fact sheets

Programme managers may want to prepare facts sheets on some or all of the following subjects. Those marked with * are already prepared on the WHO web site at http://www.vaccines.who.int/safety/ and can be downloaded.

- *Tetanus toxoid and contraception.
- Whooping cough (pertussis) vaccine and brain damage.
- *Hepatitis B vaccine and multiple sclerosis.
- *Vaccines made with cow (bovine) products and mad cow diseases.
- Vaccine Associated Paralytic Polio (VAPP).
- *Measles vaccines (MV) and Crohn's Disease.
- *MV and autism.
- MV and egg allergy.
- MV and gelatine allergy.
- *MV and reverse transcriptase.
- Vitamin A and MV interaction.
- MV, OPV and GBS.
- MV and HIV-infected children.
- MV and ITP (Idiopathic Thrombocytopenic Purpura).
- Rubella vaccine and arthritis.
- *Thiomersal.
- Deaths and cases averted by immunization.
- What has happened when Western countries have stopped immunizing (e.g. in Sweden and Japan).
- Cases hospital admissions, permanent sequelae and deaths due to outbreaks of VP diseases in some countries, e.g. in the last 10 years.

8. Ethical issues related to immunization

8.1 Consent and communication

The mother's action in bringing the infant for immunization is generally assumed to represent parental consent. Nonetheless, parents need to be given information on the risks to their children of vaccination. This information should be presented in a culturally appropriate way and at an educational level suitable for the individual. Explanations of possible adverse events need to be offered in a way that is honest both in fact and in emphasis. It is considered ethically appropriate to explain that the risk of vaccination is very much lower than the risk of acquiring the disease.

While infants and young children naturally fall under the legal protection of their parents, older children and adolescents begin to emerge, in legal terms, as individuals capable of controlling their own lives. Parental consent may no longer be valid for this age group in many countries, and consideration must be given to seeking informed consent from the adolescents themselves prior to immunization.

This carries with it the need to explain possible risks associated with the vaccine. It should be seen as a positive interaction by both parties, as it is a moment when the adolescent assumes a measure of control over what happens to his/her own body. Any suggestion of coercion by schools in school-based interventions must be seen as highly inappropriate in this setting, however desirable it might be to achieve high acceptance from the disease-control perspective.

While adolescents may experience similar or reduced levels of adverse events following immunization when compared with infants, they themselves are aware of the possibility of experiencing negative effects from vaccines. Staff–patient communication therefore becomes important so that the issue of relative risk can be explained. This may be a real challenge for an age group not renowned for their strong communication skills!

8.2 Mass campaigns

The success of mass campaigns depends on the participation of the maximum possible proportion of the target group. And yet it is still important to allow for individual informed consent without pressure from the authorities. These two dynamics are not easy to bring together and need considerable skill in programme managers and others organizing mass immunization. How to strike the right balance will vary depending on the cultural context.

8.3 Pregnancy

Immunization of adolescents as part of routine immunization or during mass campaigns raises the possibility of administering vaccines during pregnancy. Only tetanus toxoid is recommended in pregnancy. Administration should be avoided especially of those vaccines that are contraindicated in pregnancy because of known or theoretical risks to the early stages of fetal development. It is possible that girls attending for vaccination may be unaware they are in the early stage of pregnancy, and others may be reluctant to admit to the pregnancy (which may result in their exclusion from school) and therefore go ahead with vaccination, perhaps despite being warned of the danger.

WHO has not formulated recommendations on this issue, but recognizes the potential difficulties. Bearing in mind the enormous cultural and contextual variations between countries, WHO encourages planners at the national level to decide whether to screen girls during campaigns with questions about the possibility of pregnancy. The practicality of such screening is daunting, and the consequences far-reaching.

9. National regulatory authorities

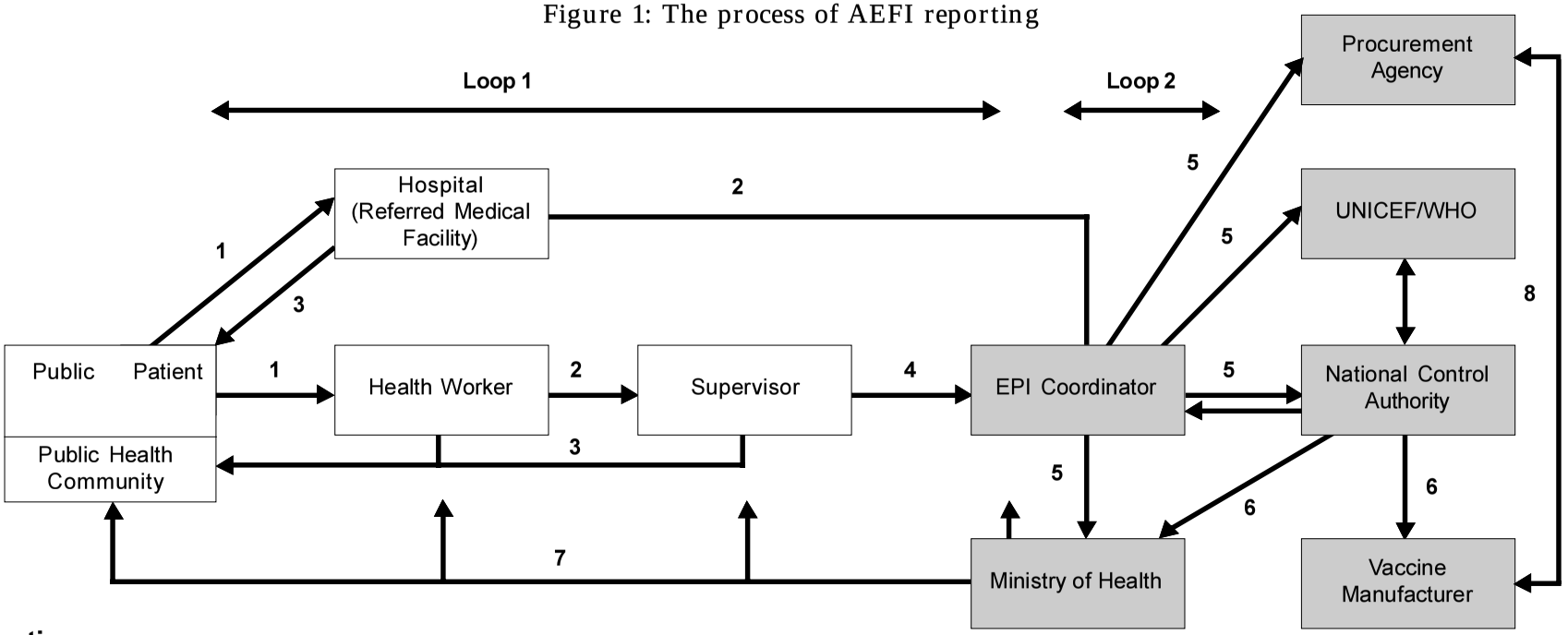
The national regulatory authority (NRA) is responsible for clarifying whether the reported adverse event is in any way related to a vaccine-quality problem. They should be able to decide whether withdrawal of the vaccine lot in question is appropriate. They will follow up with the regulatory authority in the producing country to establish whether it was a vaccine quality-related problem or not. It is their task to contact the vaccine manufacturer and UNICEF (if the vaccine has been purchased through UNICEF). They have the responsibility and right to decide whether supply from that source should be stopped.

Hence, the Immunization Programme Manager is not the only professional with a key role in prevention, detection and response to AEFIs. It is therefore vital that the NRA is included in any and all activities relating to AEFIs.

The Global Training Network is the system that provides training for the NRA staff throughout the world. The training includes how to respond to AEFIs and how to undertake post-marketing surveillance. Programme managers may wish to be involved in training activities undertaken by the NRA.

Surveillance systems set up by the immunization programme for detecting AEFIs should dovetail with any system set up by the NRA for post-marketing surveillance. At all costs, duplication must be avoided. The NRA is responsible for following up the efficiency and safety profile of the vaccine through post-marketing surveillance (PMS) activities and to introduce any required changes into the leaflet information (e.g. contraindications, etc.).

Figure 1: The process of AEFI reporting



Functions:

Health Worker:

- Recognizes and
- Reports AEFIs

Supervisor:

- Stimulates reports
- Investigates
- Filters
- Provides feedback
- Manages data
- Proposes classification

EPI (focal point):

- Receives reports
- Transmits reports
- Triages
- Works with environment
- Manages data
- Ensures response

NRA:

- Receives reports
- Transmits reports
- Shares database
- Evaluates reports
- Takes action
- Notifies

1. **Initial report**
2. **Report to action level**
3. **Investigation**
4. **Send reports meeting criteria onward**
5. **Report for consultation/ action**
6. **Decision communication (regulatory, public health)**
7. **Public statement**
8. **Contract information**

EPI - Expanded Programme on Immunization
NRA - National Regulatory Authority

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