SPECIAL ARTICLE

ADVERSE EVENTS FOLLOWING IMMUNIZATION: 1990

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ABSTRACT

The vaccines used under the Immunization Programme are safe and effective. However, as no vaccine is 100% effective, none is entirely without risk. The benefits of immunization greatly exceed the risks because of the large number of complications and deaths prevented.

Although, the risks of vaccine-associated adverse events are extremely low, the occurrence of such events in areas with high immunization coverage levels and low incidence of vaccine preventable diseases can influence public acceptance of immunization services. Moreover, since infections and neurological syndromes are common in the age-groups in which immunizations are given and there are a number of contacts with an infant under the programme, there is a risk of temporally-related severe adverse medical events being attributed to immunization. Monitoring of adverse events is essential to document low risks and to identify programmatic errors, if any, for corrective action.

An important, aim of the monitoring system is to disseminate such information to the medical professionals and others associated with the immunization programme. The paper summarizes reports received in 1990, including reports of temporal events where the cause of death was other than immunization.

Key words: *Immunization, Adverse events, Monitoring.*

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Introduction

The immunization programme in India has made tremendous progress in the control of vaccine preventable diseases during the last decade. Immunization coverage levels in the susceptible age-groups has recorded dramatic increase. Despite improved reporting of vaccine preventable diseases due to greater emphasis on surveillance, increased awareness of these diseases in the community and greater accessibility to health care facilities, there is a significant declining trend of vaccine preventable diseases in many states and districts in the country.

During the last decade, millions of doses of various vaccines have been utilized. The experience in India, as also in other countries, has documented the efficacy and safety of the vaccines used in the programme. However, as no vaccine is 100% effective, none is entirely without risk. The occurrence of some severe adverse events, although rare, can be expected. The risks of immunization are greatly exceeded by benefits because of the large number of complications and deaths prevented. However, in areas where the incidence of vaccine preventable diseases and their complications have declined to negligible levels, the preserved relative importance of adverse events can increase and influence public acceptance of immunization services.

Types of Adverse Events

Inherent Vaccine-Induced: The risks of severe inherent vaccine-induced reactions leading to death or permanent disabilities,

are low(1-3). The comparative rates in India are not known but are no higher than those reported from other countries. Among the commonly reported severe adverse events in the literature are hypersensitive reactions and neurological syndromes, including vaccine encephalopathy.

Programmatic: Severe adverse events have been reported due to mishandling of vaccines and poor administration techniques. The most common event in this category are injection-site abscess. Such events are avoidable and risks can be minimized through early recognition, retraining, improved field supervision and logistic support.

Temporal or coincidental: The vaccines are given to children at an early age when acute viral and bacterial infections are common. Some neurological syndromes known to occur as a complication of immunization, can also occur spontaneously or be due to causes unrelated to immunization, at the age at which children are immunized. If there is a history of immunization in the recent past, these temporally-related events are often assumed, incorrectly, to be due to vaccine, especially if a similar non-specific syndrome is also known to occur after immunization.

Some temporal events, although, clear to a medical professional as being unrelated to immunization, must still be examined by senior professionals, who carry credibility in the community, to convince public opinion.

Monitoring of Severe Adverse Events in India

The monitoring of severe adverse events following immunization was started in India in 1985. The main objectives of the monitoring are:

(*a*) to identify programmatic errors, if any, so that preventive measures are taken to avoid recurrence in future;

(*b*) to allay public fear and to assure the community of the low risk of inherent vaccine-associated severe adverse events; to document the concern of the health authorities to the sudden death of a child, especially when it is temporally related to immunization;

(*c*) to provide moral support to the peripheral health staff, as with the improvement in the quality of services, strengthening of the surveillance system and better recognition and recording of adverse events, majority of the adverse events can be expected to be due to reasons other than programmatic errors; and

(*d*) to pool data on rare adverse events and to disseminate relevant information to those associated with the immunization programme.

To be effective, the investigations of severe adverse events must be prompt, thorough and well documented. State and regional expert teams, with an epidemiologist, a pediatrician and a microbiologist have been constituted by the state health authorities for the investigation of severe adverse events. Medical college professors have been associated with most of the teams. All deaths, especially in clusters, following immunization are expected to be investigated within 48 hours. Formats for the investigation of the adverse events have been circulated through Government circulars and printed documents(2,4).

Adverse Events Reported in 1990

Number of incidents investigated: Twenty nine incidents of severe adverse events following immunization were reported in 1990, including events where the

cause of death was temporally related to immunization or could not be determined but was most likely to be coincidental to immunization. In four of the reported incidents, the children recovered completely and there were no deaths. In the remaining incidents, except for one in which a clustering of 6 deaths was seen, only one death was reported in each incident. Of the 57 children with severe reactions (including abscess), 30 children died. A total of 566 children were immunized with the concerned vaccine in the 28 immunization sessions [encephalopathy and probable toxic shock syndrome (TSS; child recovered) was reported in two children immunized at the same session with DPT and measles vaccines, respectively]. The number does not include children immunized with other than the implicated vaccine. Overall in the country, more than 18.2 million children received 3 doses each of DPT and OPV; 20 million BCG and 15 million measles vaccine in 1989-90 through Government sources. Coverage in 1990-91, for which final figures are not yet available, is higher.

The incidents were reported from different parts of the country in all seasons. Majority of the deceased children were under one year of age; one death was reported in a 9-year-old girl following TT immunization. Including deaths not directly related to immunization, 18 children were males and 12 female. Major symptoms and interval between immunization and death have been summarized in *Table I*.

Vaccines

Majority of the incidents were following DPT immunization; five incidents were reported following measles immunization, two following BCG and one following TT immunization.

DPT vaccine: Severe reactions and deaths were reported following DPT immunization in 21 incidents, including incidents where the cause of death was other than immunization. All children who received DPT were also given OPV at the same time; some children also received BCG. In 7 incidents the children had allergic manifestation within 20 minutes to a few hours. One child had erythematous rash and recovered after 2 days of anti-allergic treatment. In 6 other children the reactions were manifested as crying spells, respiratory distress, refusal of feeds or restlessness. In all, but two children, the reactions were reported after the first dose; the condition of the two children with history of previous DPT immunization to the earlier doses was not mentioned in the reports. Four children died within 2 to 24 hours of immunization and two children between 56 and 60 hours.

Encephalopathy following the first dose in one child and the third dose of DPT in two children (first two doses were without any untoward reactions) was reported from Madhya Pradesh and West Bengal. The children had fever and convulsions within 24 hours of immunization. Disturbances in sensorium or changes in behavioral pattern were not mentioned in the reports; one child became unconscious prior to death. Another death due to vaccine encephalopathy was reported from Haryana. A two-and-a-half month old child, developed mild fever 5 hours after the first dose of DPT, OPV and BCG vaccines. An hour later crying, frothing and unilateral convulsions were reported. The child lost consciousness during the episode. The episode was repeated early next morning and again within three hours. The child died in a doctor's clinic after the third episode. The child had high fever and was

TABLE I–*Major Symptoms and Interval between Immunization and Death*

Vac	Mth	No. imm	No. died	Death in hours	Age in mo	Sex	Major symptoms	Diagnosis
DPT1	Jan	25	0	0	3	F	Erythematous rash all over body within 30-45 minutes. Anti-allergic treatment for 2 days. Recovered fully.	Hypersensitivity
DPT1	Mar	2	1	60	3	F	Crying spells; loss of voice & respiratory distress 6 hours after immunization. Hospitalized. Died of respiratory failure	Hypersensitivity
DPT1	Jul	10	1	3	2	F	Incessant crying & respiratory distress within 20 minutes. History of refusal to breast-feed & respiratory distress of 1 day prior to immunization. Another child in family died 4 years earlier of similar symptoms unrelated to immunization.	Hypersensitivity
DPT1	Jul	11	1	<6	8	M	Restlessness, seizures, frothing & respiratory distress an hour and hospitalization within 4 hours of immunization. Child was gasping, pulse thready & body cold at admission. No rash. History of temporary impairment of consciousness & cold & clammy extremities about 3 months prior to immunization. No history of asthma, allergy, convulsions or hyperpyrexia.	Hypersensitivity
DPT3	Jul	12	1	6	4½	M	Fever, crying spells, severe spasms & restlessness within 1 hour. Became unconscious within 5 hours about an hour and 15 minutes before death. The child had real red rash all over the body.	Hypersensitivity
DPT2	Oct	56	1	<24	5	F	Mild fever a few hours after immunization. Child found crying	Hypersensitivity

Vac	Mth	No. imm	No. died	Death in hours	Age in mo	Sex	Major symptoms	Diagnosis
							around 3 am next day. When the child refused the bottle, mother found the nipple blocked and made the hole bigger. Gave bottle to the child and went back to sleep. Found the child dead in the morning. Twin sister immunized at the same session was well. Post-mortem showed pulmonary edema of allergic nature and semi-digested milk in the stomach.	
DPT1	Nov	9	1	56	6W	F	Mild fever. Deterioration on third day. Refusal of breast-feed and dribbling of milk. Died on morning of 4th day. Not taken for treatment	Hypersensitivity Septicemia
DPT3	Feb	14	1	24	36	F	Respiratory distress and convulsions about 24 hours after immunization. Died in hospital within a few hours of admission. Treated for bronchopneumonia. No previous history of convulsions. No reactions after first 2 doses. No illnesses except otitis media.	Encephalopathy? Broncho-pneumonia
DPT3	Mar	3	1	<24	6	M	Fever within 2 hours & convulsions within 5 hours. Cyanosed & gasping during convulsions.	Encephalopathy
DPT1	Sep	14	1	8	3	M	Convulsions, restlessness & frothing within half hour. Convulsions were intermittent. Urticaria within 2 hours. Loss of consciousness & cyanosis prior to death. Taken to two private practitioners and Government dispensary. Treatment inadequate.	Encephalopathy
DPT1	Oct	36	1	22½	2	M	Mild fever 5 hours after immunization; episode of crying,	Encephalopathy

Vac	Mth	No. imm	No. died	Death in hours	Age in mo	Sex	Major symptoms	Diagnosis
							frothing, unilateral convulsions & loss of consciousness an hour later. Repeated next morning about 17-18 hours after immunization. Child died three hours later after a similar third episode. No history of convulsions prior to immunization.	
DPT	Apr	11	0	0	–	–	Injection-site abscess. Full recovery following treatment.	Abscess
DPT	Dec	38	0	0	–	–	Injection site abscess in 5 children. Full recovery following treatment.	Abscess
DPT2	Mar	6	1	13	7	M	Crying spells, watery diarrhea followed by bloody & mucoid diarrhea within 9 to 10 hours of immunization. Few spots of petechial hemorrhage with mediate intravascular coagulopathy. History of diarrhea for 3 weeks, under treatment up to 5 days prior to immunization.	Entero-colitis; unrelated to immunization
DPT2	Sep	23	1	24	4	M	Swelling of both feet & anuria after 5 hours. In the early hours febrile, cardiomegaly (*X*-ray confirmed) & tachycardia. Abdomen distended & tense. Breathing normal. Pupils normal and no neck-stiffness. Hospital delivery by cesarean section. No congenital disease & growth normal. Clinical management in hospital unsatisfactory.	Myocarditis unrelated to immunization/ Infantile Beriberi?
DPT1	Sep	65	1	72	2½	M	Fever within one hour. Vomiting, diarrhea & altered consciousness within 36 h, but when symptoms	DIC, etiology unknown; unrelated to

Vac	Mth	No. imm	No. died	Death in hours	Age in mo	Sex	Major symptoms	Diagnosis
							started or severity not mentioned. Condition deteriorated on 3rd day & child taken to PHC & hospital in the early hours. child was hyper-pyrexic and in toxic shock. Apparent multi-site bleeding suggested by: bleeding at site of injection, distention of abdomen, blood stained gastric aspirate, hematemesis, blood stained CSF, hypothermaia & low evels of Hb. Clinical management in hospital was unsatisfactory.	immunization/ Septicemia with paralytic ileus and DIC
DPT1	Nov	8	1	96	13	M	Moderate fever after 7 hours; convulsions after 24 hours. Recovered for 1 day with only mild fever. At night on 3rd day convulsions lasting a few minutes. At time of admission next morning general condition poor. No investigations were done. Left against medical advice and died the following morning. Child was apparently fully conscious till the time of death. Seen by several physicians during course of illness; multi & conflicting diagnosis.	Cause could not be determined
DPT1	Dec	20	1	<24	2½	M	Immunized around noon. Breast-fed normally. No complaints. Crying and mild fever at night. No respiratory distress or convulsions. Given ½ tablet paracetamol with spoon. Slept. Found dead in the morning. Was under treatment for mild URI for one week. Past history normal.	Aspiration pneumonia?
DPT1	Oct	10	1	15	40 D	F	Immunized around noon. Mild fever. Given 1/3 tablet of paracetamol at 4 p.m. At midnight again given 1/3 tablet	Aspiration

Vac	Mth	No. imm	No. died	Death in hours	Age in mo	Sex	Major symptoms	Diagnosis
							paracetamol. Developed hiccough and respiratory distress and died at 3 a.m.	
DPT1	Sep	14	1	<3	6 W	M	Listless and died within 2½ hours of immunization without any apparent complaints. Had history of respiratory infection of 3 days prior to immunization.	Respiratory infection
DPT1	Dec	41	1	14	7 W	F	Immunized in the evening. No complaints. Played and breast-fed normally. In the early hours child woke up crying; was sweating and cold to touch; had two loose motions. Bleeding marks noted on left heal. Died by 6 a.m. The family was sleeping in the open. The house was on the outskirts of village near the fields. Snakes and scorpions common in the area.	Snake/scorpion bite?
TT	Aug	62	1	48	9 Yr	F	Fever, vomiting & diarrhea 36 hours after immunization. Condition rapidly deteriorated at night and died early morning. Was semi-conscious prior to death. Received no treatment.	Not known
BCG	Sep	18	1	<8	2½	M	Persistent crying, refusal of breast-feed & respiratory distress within half hour of immunization. At time of admission within 1 h child afebrile, respiration laboured and rapid, cyanosis + +, and lungs clear. GC very low.	Hypersensitivity Aspiration of beast milk
BCG	Nov	4	1	<48	22 D	F	First 24 hours—no complaints. Given oil head-bath on 2nd day. Mild fever in the afternoon.	Aspiration pneumonia/ SIDS
MEA	Apr	1	1	24	8	M	Breast-fed at noon, evening & fever, vomiting & diarrhea at	TSS

Vac	Mth	No. imm	No. died	Death in hours	Age in mo	Sex	Major symptoms	Diagnosis
							night. Vomited after each feed. within 4-5 hours. Found cold and dead at 4 a.m.	
MEA	Jul	33	1	17	23	F	Fever, vomiting, diarrhea within 5 hours.	TSS
MEA	Sep	12	6	12 to24	9-18	M-4 F-2	Fever, vomiting and/or diarrhea within 4-5 hours.	TSS
MEA	Feb	1	0	0	8	F	Fever, vomiting and diarrhea after 24 hours for 4 days. Recovered fully.	TSS?
MEA	Dec	7	1	40	16	M	Vomiting, sweating, head-drop semi-conscious and cold to touch 20 to 30 minutes following immunization on 28.12.90. Vomiting repeated, blood stained. Hospitalized. Gastric aspirate blood stained. Treatment for anaphylaxis included IV fluids, steroids, avil and adrenochron. By evening child well. Discharged next evening. On 30.12.90 at 3 a.m. repeated blood-stained vomiting, distended abdomen. Child became semi-conscious and died on way to hospital.	Hemorrhagic diasthesis. Vit. K deficiency precipitated by immunization?

Abbreviations

BCG—Bacille Calmette Guerin antitubercular vaccine
DPT—Diphtheria-Pertussis-Tetanus vaccine
MEA—Measles vaccine
OPV—Oral polio vaccine
DIC—Disseminated intravascular coagulopathy
SIDS—Sudden infant death syndrome
TSS—Toxic shock syndrome
D—Day
W—Week
F—Female
M—Male

[The number following vaccine indicates the dose received by the child]

semi-conscious when brought to the doctor about two hours before death.

Eleven children developed injection-site abscesses after an immunization session. Use of unsterile syringes and needles was the cause of the abscesses. A cluster of 5 abscesses was reported following a special immunization camp in which 38 children were immunized. Although, reportedly autoclaved syringes and needles were used, there was obviously some lapse in implementation. All the children recovered following treatment.

Eight other incidents following DPT immunization were reported. The children died within 3 to 96 hours of immunization. Since the clinical picture was not compatible with a hypersensitive reaction, encephalopathy and other known complications of DPT, causes other than immunization were suspected. The cause of death of a 13-month-old child on the fifth day following DPT and OPV immunization could not be determined.

BCG vaccine: A 10-week-old child died within 8 hours of BCG immunization. Persistent crying, refusal of breast-feed and respiratory distress within half-an-hour of immunization were the main symptoms. The child was brought back to the hospital within one hour of immunization but despite treatment the child died in the hospital. Although hypersensitive reaction was not ruled out, aspiration of beast-milk was considered as a possible cause of death.

The death of a 22-day-old child in the early hours of the 3rd day of BCG immunization was considered to be due to either oil aspiration pneumonia or Sudden Infant Death Syndrome (SIDS). The child was alright for 24 hours following immunization. On the second day, the child was given an oil head-bath. In the afternoon the child developed mild fever. The child was breast-fed at noon, evening and night. After each feed, the child vomited. The child was found cold and dead at 4 a.m. in the morning.

Measles vaccine: Measles vaccine was associated in five incidents. In three, symptoms were typical of toxic shock probably due to the use of contaminated vaccine. In one incident 6 of the 12 children who received measles vaccine, died. All 12 had reactions but 6 children were saved due to timely hospitalization and appropriate treatment. In all the incidents the quality of immunization services was suspect with high degree of risk of contamination of vaccine vials as syringes and needles were either reused or the quality of the sterilization procedures was unsatisfactory. In one incident an 8-month-child developed fever, vomiting and diarrhea 24 hours after immunization. Clinical status was not described in the report. The child was, however, hospitalized for treatment and observation and discharged on the 4th day of illness with full recovery. The quality of services at the given immunization session was poor. In one other incident, measles vaccination probably precipitated an underlying hemorrhagic diathesis.

TT vaccine: The death of a 9-year-old girl within 48 hours of TT immunization was reported. The girl was apparently well for 24 hours. Towards the evening of the second day she had fever, vomiting and diarrhea. Her condition rapidly deteriorated in the night and she died in the early hours of the next day, without medical care. A neighbour of the deceased child, also immunized at the same session, had fever, vomiting and diarrhea on the day of immunization but recovered. Sixty two school children were immunized with TT in the afternoon session. In the morning, infants and pregnant women in the village had

been immunized. Due to the large numbers, it is possible that syringes and needles were reused; however, it appears unlikely that opened vials of TT vaccine were reused. Although, the symptoms are similar to toxic shock reported in infants following measles immunization, this is the first time that such an incident has been reported in a school-going child following TT immunization. The precise cause of death could not be determined.

Toxic Shock Syndrome

Toxic shock syndrome (TSS) following measles immunization was first reported in the country in early 1986. In all 17 incidents of single or cluster of clinical TSS occurred in the country during the period 1985 to 1988. This was a period when measles vaccine was introduced on a large scale during which 26 million doses were administered. All affected children had similar symptoms of abrupt onset of fever, vomiting and watery diarrhea within a few hours of measles immunization, often leading to death within 24 hours. Forty three children died in the 17 incidents. These reports were received from different parts of the country at different seasons of the year and different batches of the vaccines were involved. Programmatic errors were suspected since most cases occurred in clusters of 2 or more following a given immunization session. In every situation evidence was found of use of unsterile syringes and needles or reuse of opened vials. *Staphylococcus aureus* was isolated from a few available implicated vials(2).

Preventive measures included ensuring the full supply of syringes, needles and sterilization equipment, re-emphasis on the use of a separate sterile syringe and needle for each injection, additional supplies of measles vaccine so that opened vials were not reused to cut down wastage rates and wide publicity among the professionals to increase awareness about the risks of mishandling vaccines.

Door-to-door immunization services, which was being practiced in some places to boost immunization coverage, was stopped as quality of services was often compromised. Outreach services are now organized on the basis of 'fixed-site' and 'fixed-time' approach and children collected at a central point in the village. As an additional precautionary measure the medical officers at the treatment facilities were alerted to treat any child with fever, vomiting and watery diarrhea after measles immunization as a medical emergency. Guidelines for treatment were drafted in consultation with senior pediatricians and widely circulated so that such children would receive prompt and appropriate medical care. The essential line of treatment recommended is anti-staphylococcal antibiotics in high doses; large volumes of intravenous fluids to maintain perfection and anti-shock therapy, if required.

During the years 1989 and 1990, the use of measles vaccine increased as the Universal Immunization Programme (UIP) was extended to the remaining 50% of the districts. More than 22 to 25 million doses each were distributed under the Immunization Programme in 1989 and in 1990. Four incidents of TSS following measles immunization with 8 deaths each were reported in 1989 and 1990 (*Table II*). Although the rate of toxic shock per 100,000 doses of measles vaccine administered has declined as a result of precautionary measures, the continued reports of such incidents underscores the urgency for alertness and regular field supervision to ensure high quality of immunization services. The investiga-

TABLE II--*Reported Incidents of Toxic Shock Syndrome (TSS) Following Measles Immunization*

Year	No. of incidents	No. of TSS incidents	Total deaths	TSS deaths
1985-88	22	17	57	43
1989	15	4*	15	8
1990	29	4	30	8

* In one incident, in which only one child was affected and who recovered, diagnosis of TSS was doubtful. Quality of services were satisfactory with low risk of contamination of vaccine. Similarly, in one incident in 1990 in which only one affected child recovered, diagnosis of TSS was doubtful; syringes and needles were reused at the session.

tions showed that the quality of services following measles-related incidents was suspect and confirmed that the instructions regarding the use of a separate sterile syringe and needle for each injection continues to be ignored in some places. This could partly be due to inadequate follow-up, since more than one incident has occurred in the same state.

Discussion

State and regional teams have been constituted in all the states. The increased number of reports following immunization with vaccines, other than measles; incidents where single deaths occurred as well as reports of events temporally related to immunization reflect an improving surveillance of severe adverse events following immunization. The promptness of investigations and quality of the investigation reports, however, vary. Some of the children died at home without receiving medical care and information regarding the condition of the child was based only on history provided by the parents.

Some children were seen by local private practitioners; others were admitted in various hospitals and case sheets and results of laboratory investigations were available for scrutiny.

Admittedly, accurate diagnosis regarding the cause of sudden death in an apparently healthy child under such circumstances can be difficult. Senior pediatricians have, therefore, been involved so that, as far as possible, the clinical picture is well documented, differential diagnosis discussed and the likely cause of death substantiated from the clinical picture described in the reports. Some of the reports received did not satisfy the above criteria. In many instances, hypersensitive reaction, encephalopathy and other conditions were presumed to be the cause of death in the absence of an alternate diagnosis; the clinical picture described in some of the investigation reports was incomplete and perfunctory. Investigation of events, pooling and exchange of information can be made more effective with the use of standard case definitions of specific and non-specific adverse events. The *Appendix* lists suggested case definitions.

In a number of incidents, aspiration was noted to be the probable cause of death. In some instances the diagnosis was revised on the opinion of the experts who were consulted on the reports. Refusal to feed, dribbling of milk, sudden death of an infant given a bottle at night without super-

vision, were considered by them to be more likely to be manifestations of disturbed sensorium due to hypersensitive reaction or systemic infection (related or unrelated to immunization) rather than the primary cause of death, especially in a full-term previously healthy child. Aspiration is a commonly ascribed cause of death of newborn babies and young infants in India. The diagnosis is largely based on circumstantial evidence in the absence of other reasonable cause or explanation of death. Aspiration can be suspected if there is choking, coughing, cyanosis and respiratory difficulty followed by pooling of milk in oral cavity and air passages. Diagnosis of alternate causes can be difficult in the absence of a post-mortem.

Due to the rarity of the events, the severe clinical picture and rapidity of fatal outcome, most medical practitioners are usually not adequately prepared for these emergencies. Despite many children being brought in time to a medical facility, including hospitals, treatment has been generally inappropriate or inadequate. Dissemination of information regarding the possible adverse events following immunization and guidelines for treatment of these events would be useful for better clinical management of these children.

Abscesses in young infants are potentially fatal and require immediate medical attention. Abscesses also reflect contamination problems related to field implementation. The occurrence of abscesses showed be viewed seriously by the supervisory staff at the district and concerned PHC demanding immediate corrective measures. periodic sentinel centre monitoring of such events as site-abscess by the Lot Quality Assurance method can be useful in evaluating the quality of the immunization services and identification of areas at high risk of expected programmatic severe adverse events(3). Such monitoring will be encouraged in the coming years as one of the measures to further minimize the risk of adverse events due to programmatic errors.

Besides better documentation of the severe adverse events, especially neurological syndromes, there is also a need for recording of such events, not related to immunization, in children of the same age-groups to obtain some information on background rates. In the absence of such information there can be little assessment of the relative risk due to immunization.

Although, the risks of inherent vaccine-associated severe adverse events is extremely low (according to some scientists, lower than earlier estimated), in view of the millions of doses of various vaccines utilized in the country, more incidents of adverse events would have been expected. Moreover, due the high infant mortality rate of 91 per 1000 live births in India and a number of contacts with an infant under the immunization programme there is a high risk of temporal association of deaths with immunization. It is possible that some of the adverse events have been investigated but not reported to the Ministry of Health and Family Welfare, especially if these were found to be only temporally related or if the children recovered fully. It is also possible that some events are currently being missed from the surveillance system of severe adverse events following immunization. Due to increased priority being given to surveillance of such events, the number of reported incidents may increase in the future.

The surveillance reports in 1990 further confirm the low risk of deaths and perma-

nent disabilities due to inherent vaccine-associated complications or due to programmatic errors. The reported incidents must be seen in the light of the utilization of more than 20 million to 100 million or more doses of each of various vaccines in the country in 1990-91.

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The information in the paper is based on the reports of adverse events by state and regional expert teams forwarded to the Ministry of Health and Family Welfare. Expert comments of senior pediatricians were obtained on some of the reports regarding the likely cause of death and line of treatment received by the children prior to death. Detailed comments on selected reports received from Dr. Manorama Mehta, Dr. Kuldeep Sidhu, Dr. Meharban Singh and Dr. Manorama Varma have been very helpful and their cooperation and assistance is gratefully acknowledged.

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Appendix

Suggested Case Definitions for Adverse Events Following Immunization

Specific Local Reactions

Bacterial site abscess: Occurrence of draining urgent fluid-filled inflammatory lesion or fluctuant fluid-filled, distinctly inflammatory lesion at the site of injection within 72 hours of immunization, with or without fever; may be supported by positive Gram stain, culture or finding of neutrophil predominance.

Sterile site abscess: Occurrence of draining fluid-filled lesion or fluctuant fluid-filled lesion at the site of injection within 72 hours of immunization, with minimal inflammation, and not associated with fever; may be supported by negative Gram stain, negative culture for routine organisms, or finding of macrophage predominance.

Moderate local reaction: Non-fluctuant swelling and redness of approximately 3 cm (width of two adult fingers) to less than 10 cm (width of adult fist) at the site of injection.

Severe local reaction: Non-fluctuant swelling and redness of approximately 10 cm or larger (width of adult fist) at the site of injection.

Massive local reaction: Severe local reaction with extension of swelling past the closest joint (*e.g.*, knee)

Local ulcer: Localized circumscribed inflammatory denuding of the skin at the site of BCG immunization.

Relatively Specific Syndromes

Anaphylaxis: Acute decompensation (within 8 hours, generally within 1 hour) of circulatory system with indications of poor peripheral blood flow and associated with immediate alterations in the vaccinee's level of consciousness or acute bronchospasm or laryngospasm or

laryngeal edema leading to acute respiratory distress.

Hypotensive-hyporesponsive episodes: Evidence of acute paleness, transient decreased level or loss of consciousness, decrease or loss of muscle tone within 12 hours of DPT injection.

Excessive inconsolable crying following DPT immunization

BCG lymphadenitis: Occurrence of any of the following by examination and/or history between 2 and 6 months after receipt of BCG immunization: Multiple axillary lymph nodes of 1.5 cm (one adult finger width) or larger in the largest axis or at least one node of 3.0 cm (two adult finger widths) or larger in the largest axis.

Suppurative BCG lymphadenitis: BCG lymphadenitis when associated with one of the following (*i*) fluctuant upon palpation, (*ii*) fixed to the skin; or (*iii*) associated with a draining sinus.

Non-specific Systemic Events

Encephalopathy: Occurrence of any two of the following by examination and/or distinct clinical history within 72 hours of immunization: (*i*) seizure; (*ii*) severe alteration in the level of consciousness lasting for one day or more; or (*iii*) distinct change in personality or behavior lasting one day or more.

Encephalitis: Encephalopathy with cerebrospinal fluid pleocytosis of more than 10 cells/mm^3.

Motor seizure

Simple febrile seizure: Seizure or series of seizures accompanied by fever upon examination or by history, lasting less than accompanied by focal neurological signs or symptoms in a child between 6 months and 6 years of age.

Complex seizure with fever: Seizure or series of seizures accompanied by fever upon examination or by history, lasting approximately 15 minutes duration or longer or accompanied by focal neurological signs or symptoms, or first seizure with fever in a child less than 6 months of age or more than 6 years of age.

Seizure without fever: All motor seizures occurring without apparent fever.

Focal seizure: All focal seizures, with or without generalization, or any seizure accompanied by focal findings, such as unilateral paralysis in the post-ictal period.

Fever: High grade fever (>39°C).

NOTES AND NEWS

RECENT ADVANCES IN PEDIATRICS

The book edited by Dr. Suraj Gupte, was released at the inaugural ceremony of the National Conference of Pediatrics at Hyderabad from January 24-27, 1991. It carries 26 stimulating updates from as many eminent contributors drawn from around the world. The topics covered include "Growth Monitoring", "Elite Child", "Trace Elements", "Lactose Intolerance", "Immunology of Malnutrition", Bone–marrow transplantation", "Pediatric AIDS", "IUGR", "Perinatal Issues", "JRA", etc. Also available, besides the publishers (Jaypee Bros Pvt. Ltd, New Delhi) and the dealers, through the Editor, Dr. Suraj Gupte, M.D. "Gupte House", 60 Lower Gumat, Jammu 180 001, J & K State. It is modestly priced at Rs. 125/-. Add Rs. 15/- for handling and postal charges.