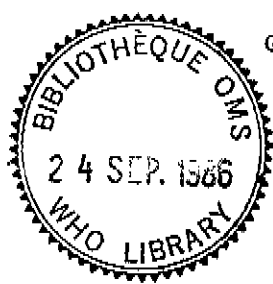




*Tetanus -*

NEONATAL TETANUS - in infancy & childhood  
- mortality



GUIDELINES ON THE COMMUNITY-BASED SURVEY ON  
NEONATAL TETANUS MORTALITY

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## 1. INTRODUCTION

In many developing countries no reliable information exists on the extent and magnitude of the neonatal tetanus problem. Tetanus in general and neonatal tetanus in particular, remains a substantially underreported disease. Routine surveillance systems, based mostly on hospital data, are often insensitive to neonatal tetanus incidence because the disease tends to occur in populations with limited access to, or making limited use of, clinical facilities.

Community-based mortality surveys may provide rapidly obtainable and reliable information on neonatal tetanus. Such surveys performed in many developing countries have shown that neonatal tetanus is a very serious health problem. Other countries may wish to perform such surveys to quantify the importance of the disease and to establish a baseline level against which the future impact of the EPI can be assessed.

This paper will review clinical and epidemiological characteristics of neonatal tetanus (NT) in developing countries and will describe a simplified survey technique recommended for the use in neonatal tetanus surveys. Since in most fatal cases of neonatal tetanus, the history obtainable from the mother is precise enough to identify NT as the cause of death, the survey technique includes home visits and interviews by specially trained health workers. The technique will be described in some detail, including the general design of the survey; its objectives, area and population to be surveyed, selection of sites for survey, sample size and interviewing techniques. Finally, results of recent neonatal tetanus mortality surveys will be discussed and countries in which neonatal tetanus surveys would be worthwhile are identified.

## 2. CLINICAL CHARACTERISTICS OF NEONATAL TETANUS

### 2.1 Clinical course of the disease

The clinical course of neonatal tetanus is well known to people in areas where the disease is prevalent. In Haiti for example, most adults have seen cases in their own or neighbours' families. The disease has been given numerous descriptive names such as "sickness with inability to breast feed", "convulsing sickness", or "stiff body sickness" (55). As early as 1764, the Reverend Kenneth Mac Auley of St Kilda, a remote island off the Atlantic coast of Scotland, decimated by neonatal tetanus in the XVIII and XIX centuries, described the disease in the following way:

"The St Kilda infants are peculiarly subject to an extraordinary kind of sickness; on the 4th, 5th or 6th night after their birth, many of them give up suckling; on the 7th their gums are so clenched together, that it is impossible to get anything down their throats. Soon after this symptom appears, they are seized with convulsive fits, and after struggling against excessive torments, till their little strength is exhausted die generally on the eighth day." (14).

Reverend Mac Auley's description is still relevant.

Numerous reports describe the clinical course of the disease (3,4,8,42, 46,65,92). The first symptom noticed by mothers on the 3rd to 10th day of life is the child's inability to suck - after developing normally for the few first days, the baby begins to have trouble sucking the breast.

The baby wants to feed but cannot because of spasm of the masseters (jaw muscles). Trismus (spasm of the jaw muscle) prevents the proper opposition of the baby's lips and the rhythmic contractions of the appropriate muscles necessary for effective suckling. The baby becomes irritable and begins to cry excessively. During that time the mother is able to express her milk into the baby's mouth, or to use spoon feeding. But soon, the jaws become too stiff for even that and difficulty in swallowing ensues due to spasms of the pharyngeal muscles.

The ability to cry may vary from a mildly hoarse short repeated cry to a strangled-sounding voiceless noise. The child finally becomes exhausted and stops crying.

Within hours after the first symptoms the baby develops generalized stiffness of the body and begins to have spasms. Trismus and risus sardonicus are the symptoms most often noted on hospital admission of neonatal tetanus cases (Table 1). Typically, the jaw is clenched but the lips are drawn laterally and upwards and the eyebrows are raised - the whole appearance producing the risus sardonicus facial expression (92). Sometimes the lips are pursed in a whistling expression (65).

Athavale, reviewing 319 NT cases in Bombay, pointed out that most NT cases kept their mouths open. When an attempt was made to feed them with a spoon or dropper, the jaw became locked due to reflex spasms of the masseters. During spasms the mouth would open wider in most instances (4). Athavale considered that the common name "lockjaw" for tetanus is appropriate only for older children and adults and not for neonatal tetanus cases.

Tetanus spasms are infrequent at first, but increase in frequency later on and often are precipitated by any stimulus such as light or noise. Spasms may last from a few seconds to over a minute. During spasms breathing is affected and the child may become cyanotic or pale and some children die during such an attack.

During spasms both upper limbs are flexed at the elbows and held in the front of the chest. The fists are tightly clenched, often with the thumb inside the hand, i.e., under the fingers. The lower limbs are drawn up and flexed at the knees. The feet are dorsiflexed and the toes acutely flexed. This hyperflexion of toes, a very marked feature, is recognized as indicative of severe generalized rigidity and signifies hypertonus in the small muscles of the soles of the feet (4). The neck is somewhat retracted and there is a marked stiffness of abdominal and back muscles. In severe cases, spasms of the erector spinae muscles cause the baby's back to be arched backwards (opisthotonus).

Fever may be present in about half the cases (36,47,59,78). Infection of the umbilical stump is not always obvious and may vary from a slight infection to gross umbilical sepsis with cellulitis spreading to the anterior abdominal wall.

Children may die from severe apnea and cyanosis during an attack of spasms, or after two to four days as a result of aspiration pneumonia or acute gastroenteritis.

TABLE 1. SYMPTOMS AND SIGNS MOST FREQUENTLY SEEN IN NEONATAL TETANUS CASES

Symptom or finding	Nigeria	India	India	Iran	Sri Lanka	El Salvador	S. Africa	India
	1954-1956 (88)	1958-1962 (78)	1959-1972 (3,4)	1960-1969 (64)	1972-1974 (42)	1973-1980 (59)	1978-1980 (36)	1980-1981 (47)
Stop sucking	100	69	100	-	87	-	-	88
Excessive crying	-	-	93	-	34	-	-	20
Trismus	-	100	100	100	18	100	-	88
Risus sardonius	-	100	100	-	58	100	-	71
Rigidity, stiffness	-	100	100	76	38	-	-	-
Opisthotonus	-	-	-	44	-	100	-	34
Spasms	-	97	78-98	82	61	100	-	97
Umbilical sepsis	-	49	20	-	100	-	44	34
No. of cases	135	112	319-813	50	62	202	34	120

- means that the authors did not present any specific percentage.

## 2.2 Differential diagnosis of neonatal tetanus

There is no other disease which clinically resembles full-blown neonatal tetanus. During a NT mortality survey, diagnoses must be made retrospectively, based on information provided by mothers. The validity of the information obtained in such a way will be influenced by the ability and willingness of a respondent to answer, as well as by the tact, knowledge and the skill of the interviewer.

The basic questions posed to the mother (see section 4.6) are concerned with the following features of the infant's history:

- whether the infant was born alive and developed normally during the first days of life;
- whether the infant was able to suckle during that period;
- whether the infant stopped suckling or developed any other feeding problem within the 3rd to 15th day of its life, when illness began;
- whether the child developed generalized stiffness, trismus, or risus sardonicus;
- whether the child developed spasms/convulsions which increased in frequency and in intensity; and finally
- the reason given by the mother for the child's death.

Careful interviewing of the mother about these questions usually provides sufficient information to make an accurate retrospective diagnosis of NT. However, in some instances additional questions should be posed to clarify or reduce doubts about the probable cause of the infant's illness and death.

The differential diagnosis should include consideration of causes of neonatal convulsions. In general there are three etiological categories of neonatal convulsions:

- congenital (cerebral anomalies);
- perinatal (complicated labour, perinatal trauma and anoxia or intracranial haemorrhage);
- postnatal (infections and metabolic disorders).

Brain damage due to the first two categories may lead to spasticity, bizarre or jerky bodily movements and convulsions. Infants with brain damage are often stuporous or in coma and seizures usually develop late on the first postnatal day. Cerebral contusion, usually a secondary trauma associated with breech delivery or other obstetric difficulties, occurs particularly in large full-term infants (91). Brain damage syndromes may often produce a laxness of mouth and tongue, the sucking reflex may be absent and swallowing may be lost from the first day of life. None of these conditions produce trismus as tetanus does (55).

The most important infection during the neonatal period is meningitis, often associated with septicaemia. Neonatal meningitis may be the result of infections with group B streptococci, *Escherichia coli*, *Listeria monocytogenes* or *Klebsiella-Enterobacter-Serratia* organisms. The first two infections account for 70% of systemic neonatal bacterial infections (57). Infants with neonatal meningitis may develop lethargy, seizures, apneic episodes, poor feeding, hypo- or hyperthermia, and sometimes respiratory distress in the first week of life, or later. A frequent symptom is a bulging fontanelle.

Group B streptococcal infections can affect low birth weight infants born from mothers who have obstetric complications. Onset of symptoms may be early, in the first 48 hours of life, or late, between 10 days and 4 months. Apnea is often the first sign and pneumonia with respiratory failure may be present (58).

In all these conditions trismus is absent and the seizures differ, tending to occur with shorter, less rapid jerks and often affecting only a portion of the body. In neonatal tetanus there is no bulging fontanelle (55).

Metabolic disorders include: hypoglycaemia, which is particularly frequent in small babies or in infants of mothers who are diabetic, and hypocalcaemia, with two major peaks of incidence in the neonatal period: the first in the first 2 or 3 days of life (in low birth weight infants and often following obstetric trauma), and the second peak which occurs later in the first, or early in the second, week of life. These babies are usually large full-term infants, who voraciously consume milk with a suboptimal calcium-phosphorus ratio, such as cow's milk (91). Hypocalcaemic tetany of the newborn may produce seizures and sometimes laryngospasm, but the seizures are of a different character from those of tetanus and usually there are also tremors or muscle twitchings. It does not produce trismus or the generalized rigidity seen in tetanus (55). Infants with tetany appear well between convulsive episodes.

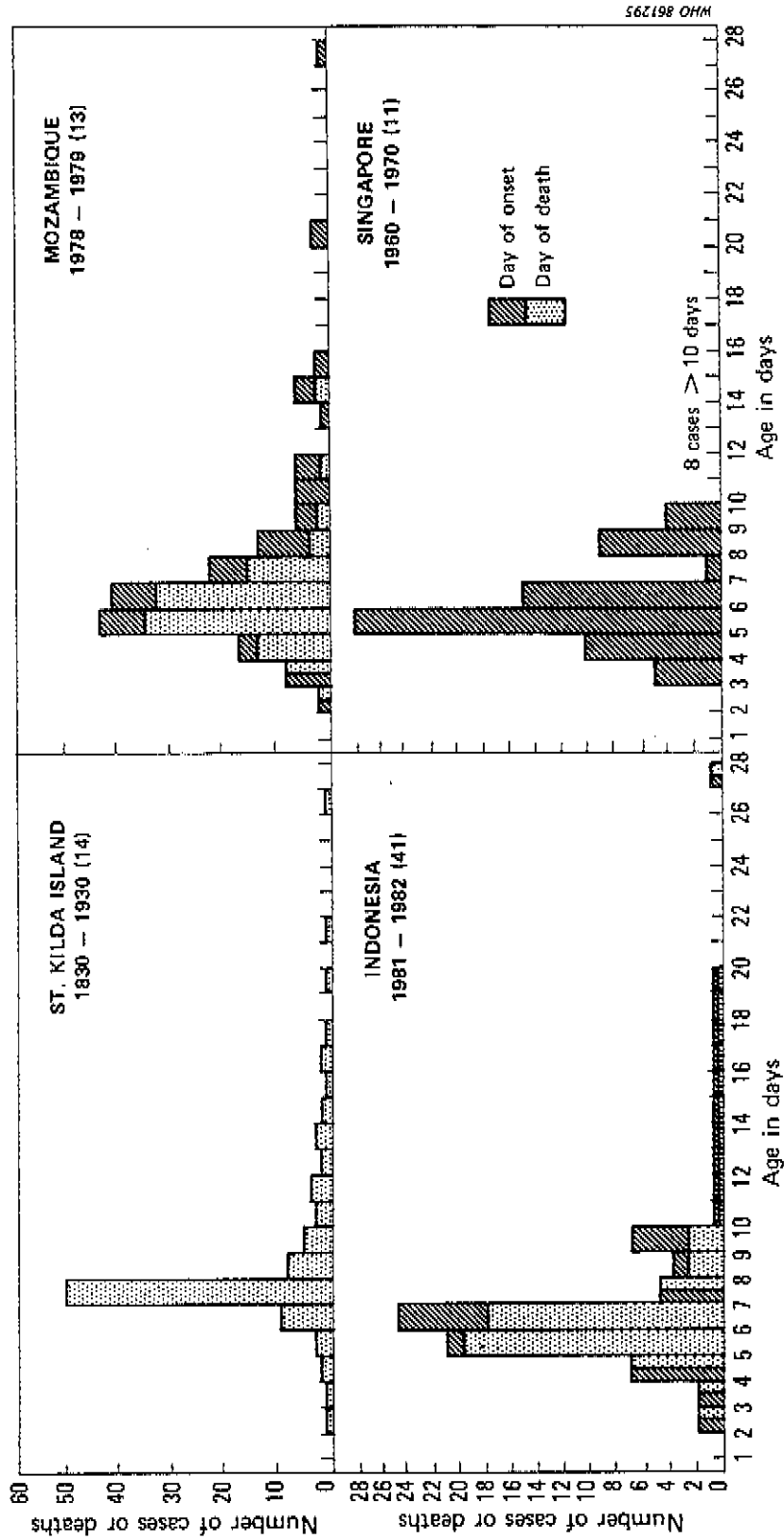
### 2.3 Period of incubation, age at onset and death

The incubation period is the time between the infection and the occurrence of the first symptoms. Assuming that in most instances tetanus infection takes place immediately after delivery when the cord is cut with an unsterile instrument or when the umbilical stump is covered with unsterile substances, the actual age of the child at disease onset can be taken as the incubation period. The shorter the incubation period, the higher the case-fatality ratio. The average incubation period has been estimated to vary between 3.6 days and 7.7 days (1,11,12,17,30,42,48,54,55,62,66,88).

In 80-90% of cases, the first symptoms are noticed between the 4th and 14th days of life. The shortest documented incubation period has been 2 days (12,48). Distributions of the age at onset are shown in Figures 1 and 2.

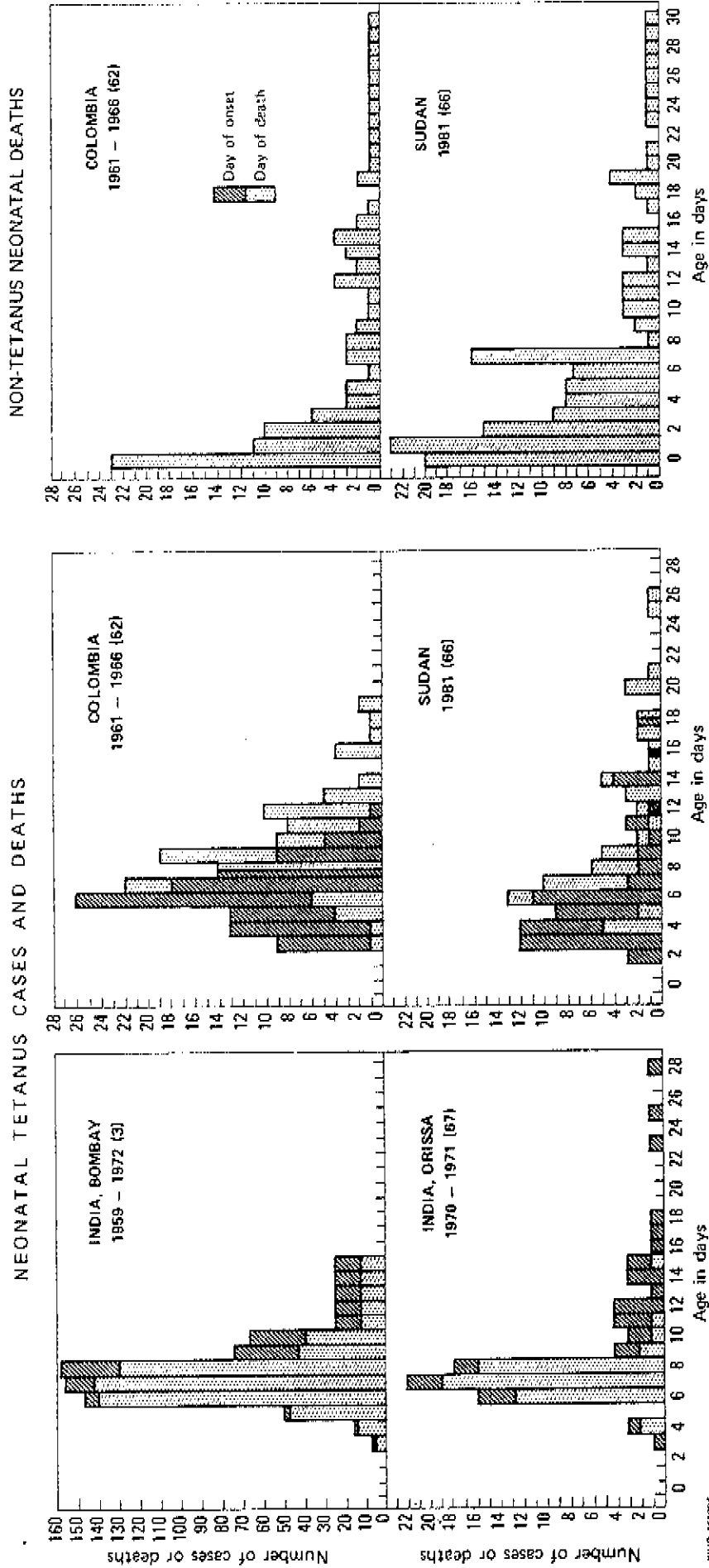
Recall by mothers of the age at which first symptoms were noticed is likely to be less accurate than the age at death. In Figures 1 and 2 the age at death is also shown. Most newborns die between the 6th and 8th day of life, and the interval between the average age at onset and average age at death varies between 3.1 (62) and 4.3 days (30,66). The peak of deaths recorded in St Kilda between 1830-1930 (50 deaths at the 8th day) was similar to the peak registered in Colombia between 1961-1966 (22 deaths at the 7th day) and in Bombay and Orissa where the highest number of deaths was also recorded for the 7th day of life.

FIG. 1  
NUMBER OF NEONATAL TETANUS CASES AND DEATHS BY DAY OF ONSET AND DAY OF DEATH IN  
ST. KILDA ISLAND, MOZAMBIQUE, INDONESIA AND SINGAPORE



WHO 861295

FIG. 2  
NUMBER OF NEONATAL TETANUS CASES AND DEATHS BY DAY OF ONSET AND DAY OF DEATH AND NUMBER OF  
NON-TETANUS NEONATAL DEATHS BY DAY OF DEATH, INDIA, COLOMBIA AND SUDAN, 1959 - 1981



The distribution of neonatal deaths due to causes other than tetanus follows a different pattern. For non-NT cases the number of deaths are highest during the first two or three days of life (Figure 2).

Hospital-based data show that the average age on admission varies between 6.3 days and 10.6 days (1,13,17,42,54,55,72). The delay between onset and admission has been estimated to be between 1.4 to 3.2 days (4,17,42,54,55), although in individual cases this ranges from a few hours to more than 10 days (55).

#### 2.4 Period of onset

The period of onset is the amount of time between the first symptoms (usually cessation of suckling or trismus) and the occurrence of spasms. In neonatal tetanus that period has an important prognostic value; the shorter the period of onset, the higher the case fatality rate. The period of onset is usually not longer than 24 hours; in 50-60% of cases it has been noted as shorter than 12 hours (47,88). Only in 1-14% of recorded cases has the period of onset been longer than 48 hours (3,4,36,47,70,88).

### 3. EPIDEMIOLOGICAL ASPECTS OF NEONATAL TETANUS

#### 3.1 Neonatal tetanus: a hidden problem

Although neonatal tetanus is one of the leading causes of neonatal and infant death in developing countries, it is probably one of the most underreported communicable diseases. This lethal disease does not appear in many lists of the top ten causes of death in developing countries. Neonatal tetanus does not receive adequate attention from public or from health professionals. As has been emphasized (83) this "peculiar quietness" of neonatal tetanus has multiple reasons:

First, neonatal tetanus has been overlooked owing to the relative neglect of neonates by health services in many parts of the world. Perinatal and neonatal deaths are greatly underreported in many rural areas of the developing world for a variety of social, cultural and medical reasons. Lack of accurate epidemiological information on neonatal tetanus leads to health planners and managers being complacent about the low tetanus toxoid immunization coverage of women of childbearing age and the need to improve obstetric and postnatal care.

Secondly, neonatal tetanus is hidden within the community due to attitudes to neonatal deaths. In many traditional communities, a high risk of death within the first weeks of life is accepted as inevitable and the prevailing feeling is that nothing can be done to save the neonate. Neither the birth nor the death may become known outside of the immediate family. Furthermore, these attitudes are strengthened because traditional as well as western medicines are largely ineffective once the disease is established. Case-fatality rates remain high in hospitals despite costly treatment. Sick neonates are therefore rarely brought to health services for care and their deaths are often not reported.

Dr Veronesi, an expert in tetanus prevention, put it in this way: "If tetanus crippled, as poliomyelitis does, we would nowadays be witnessing the parade of thousands of cripples all over the world, and then perhaps, under the pressure of public opinion, the public health authorities would take the necessary measures to solve the problem." (90).

### 3.2 Sex distribution

It is generally believed that newborn males are affected by tetanus more frequently than females, but the picture is not clear (37,83). The male/female ratio in hospitalized cases of NT ranges from a low of 1.0 to a high of 3.7. In Haiti, a small preponderance of males (54%) was observed in a series of 2198 cases of NT admitted to a rural hospital in 1957-1966 (55). Data from Indonesia, Sierra Leone, Mexico and Mozambique do not show a clear preponderance of males; reported M/F ratios were 1.0, 1.1, 1.35 and 1.36, respectively (10,13,41,93). However, other hospital observations show higher M/F ratios, which approached or exceeded two (19,37,83).

The results of NT community surveys in Ivory Coast (28) and in Kenya (20) showed almost an equal number of NT deaths amongst males and females. In other surveys, performed in Indonesia (21), Sudan (66), Pakistan (85) and Egypt (94), the M/F ratios ranged from 1.4 to 3.0.

Several factors could explain these disparate results. In Indonesia, males had NT incidence rates up to 3 times the female rate, indicating that there may be differences in practices relating to the cutting the cord and subsequent handling of the cord stump, as the non-NT mortality incidence rates by sex were almost equal (21). A possible explanation in societies where males are more highly valued than females might be parents' better ability to recall male neonatal deaths.

In some countries, circumcision of males is performed early in the neonatal period. The role of circumcision in provoking neonatal tetanus is not clear and should be investigated in future surveys.

### 3.3 Seasonality

It is important to know whether NT incidence shows a seasonal pattern. If there is a seasonality in the distribution of NT cases, then the recall period in NT mortality surveys should cover a time long enough to include periods of high and low NT incidence.

In Europe and in the USA in the 1950s and 1960s tetanus cases in adults showed a distinct seasonal pattern with increased incidence in the late summer and autumn months and a drop in incidence during the winter months (2,43,51). The seasonal trend was probably a function of greater outdoor activity, the intensification of agriculture work and increased exposure to soil in summer and early autumn months. Seasonal fluctuations were not noted for neonatal tetanus (2,51,81).

The limited information on the seasonality of neonatal tetanus in developing countries is based on hospital data. In India, in contrast to the European and American experiences, a clearer seasonality was seen for NT than for non-NT cases. The number of NT cases starts to increase in July and peaks in August to September (Figure 3). The seasonal distribution of NT cases could reflect the seasonal distribution of births. However, data for New Delhi (1963-1965) seem to suggest that although the highest number of births occur during the same months as the highest number of NT cases, increased morbidity due to NT is not fully explained by this hypothesis. The lowest number of NT cases were hospitalized during the March-May period.

The seasonal pattern of tetanus can be influenced by climatic conditions, the intensity of outdoor activities (especially by the intensity of agricultural work) and by the habits and customs of the population. Patel & Aiyar (68) found that in Bombay tetanus morbidity associated with injury and otorrhoea followed quite different patterns. Tetanus associated with injury was less frequent in the monsoon period (June to September) when outdoor activities are limited, and more frequent in the winter when people are more mobile. Conversely, otogenic tetanus was more frequent in the monsoon period, perhaps due to more frequent respiratory tract infections.

One may speculate that the seasonal increase of NT in India may be related to an increased risk of contamination of the cord stump with tetanus spores in environments which become increasingly overcrowded during the monsoon months.

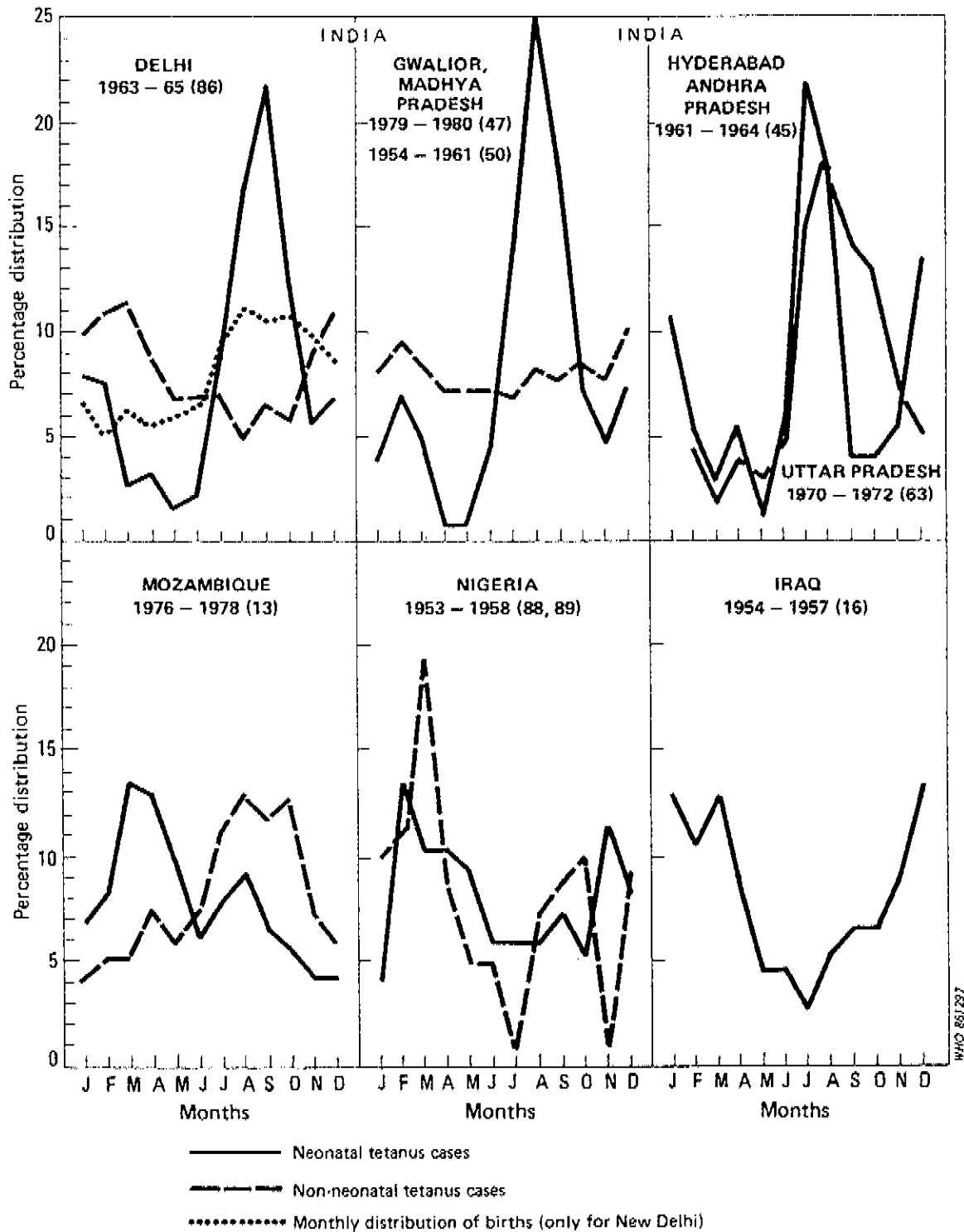
In Mozambique, NT incidence showed a bimodal distribution with the first and larger peak at the end of the hot rainy season in March and the second, smaller peak in the cool dry season in August (13). The second peak was close to the peak for non-NT cases (Figure 3).

The incidence of NT in Nigeria has been noted to be higher during the dry season than in the wet season (88,89), with peak incidence in February (Figure 3). A predominance of NT cases in the dry season was not seen in Sierra Leone (93).

In Iraq, NT was higher during the period from November to April and lower during the hottest part of the year, from May to October (16).

It should be re-emphasized that all the data referred to are hospital-based, and may be influenced considerably by the parents' willingness and ability to bring ill infants to hospitals in various climatic and transport conditions. There is a need to collect more information on the seasonality of NT in community-based NT mortality surveys.

FIG. 3  
PERCENTAGE DISTRIBUTION OF NEONATAL TETANUS  
AND NON-NEONATAL TETANUS CASES  
BY MONTHS IN SEVERAL COUNTRIES, 1954 - 1980



### 3.4 Factors influencing neonatal tetanus incidence and mortality

The main factors which influence neonatal tetanus incidence and mortality are the tetanus toxoid immunization coverage of women of child-bearing age (especially pregnant women) and the extent and quality of care antenatally, at delivery and during the neonatal period.

Pregnant women are a difficult target population for immunization programmes. In the developing world, less than half of women have one contact with MCH services during pregnancy and fewer still have two or more contacts. Tetanus toxoid coverage of pregnant women in developing countries is only 14% (35a). Immunization strategies should therefore aim at reaching all women of reproductive age, using every encounter with the health system. Mass immunization of women of reproductive age may be appropriate in some areas.

The decline of NT in most of Europe, North America, Japan and China started well before immunization with tetanus toxoid was implemented. The control of NT in those countries has been associated with an increasing proportion of deliveries being attended by trained persons, rising standards of hygiene at home and increased health education of the public. Studies carried out in developing countries confirm that NT occurs more frequently among babies of women who received no, or inadequate, prenatal care and among babies delivered at home. Tetanus also occurs more frequently among babies delivered by untrained and non-supervised birth attendants than amongst those delivered by trained TBAs or trained health workers (37,83). One of the important means to reduce NT incidence is to train all birth attendants and community health educators on the elementary principles and practices of hygiene and management for babies during and after delivery (83).

## 4. METHODOLOGY OF THE FIELD SURVEY ON NEONATAL TETANUS MORTALITY

### 4.1 General survey design

The survey methodology discussed below is based on a simplified cluster sampling method, developed and used widely to determine immunization coverage in children (25,34,44).

The method used in the EPI immunization coverage surveys consists of 3 major steps:

- (1) systematic selection of 30 sites, termed clusters, from a defined population (usually corresponding with a geographical or administrative area);
- (2) random selection of a starting point ("household") within each site; and
- (3) collection of information on the immunization status of 7 children of the appropriate age at each of the 30 sites.

The 210 children thus constituting the sample gives, with 95% confidence, an estimate which differs in absolute value from the true (unknown) proportion of immunized children by not more than 10%.

In the late 1970s and early 1980s the method was applied with larger sample sizes to study the incidence or mortality of some EPI diseases - neonatal tetanus, measles and poliomyelitis. Recently, the same procedure has been used to study the incidence of diarrhoea and to assess various factors related to the availability and use of health services (52).

The protocols for NT mortality surveys were first developed and used in India (6,7,40,79) and in other countries of the South-East Asia and Eastern Mediterranean Regions (33,94). The main modification from the EPI immunization coverage survey lies in the third point of the methodology, i.e. in the age and number of children surveyed.

The following generalized design is recommended for a neonatal tetanus mortality survey:

Thirty clusters are randomly selected and a predetermined number of mothers in each cluster are interviewed whose babies were born alive during a recent 12-month period. Whenever a neonatal death is mentioned, trained staff take a careful history of the circumstances of the death. The history of any neonatal death is checked and analysed by a supervising doctor. In that way, information on the fate of newborn children can be collected and an estimate of neonatal tetanus mortality can be obtained.

The generalized survey design should be adapted to fit the situation in a given area which may depend on special objective(s) of the survey, the size of the area to be surveyed, the expected magnitude of the neonatal tetanus problem, the desired precision of the estimate and on logistic and operational factors.

In the following sections all the above factors will be discussed with special emphasis on methodological aspects concerning area and population to be surveyed, selection of clusters, sample size, period of recall during interviews, questionnaires used in the survey, timetables for surveys, training and supervision of staff and the analysis of results.

#### 4.2 Area - population to be covered by the survey

In the first stage of planning the survey, one must clearly define the survey's objectives. For example, the objective could be to obtain baseline information on the magnitude of the neonatal tetanus problem in the whole country or the objective could be to measure the NT incidence and mortality in different geographic, ecologic or ethnic subregions so that the results can be compared to identify areas with a greater problem.

When one expects that different factors may influence the NT incidence, for example an existing immunization programme or training of traditional birth attendants in one part of the country, it may be useful to divide the population into different strata (areas) and conduct separate surveys in each different area or population group.

In India, separate surveys were performed in most States, and within each State, in urban and rural areas. The results showed wide variations in NT mortality rates between different States as well as between rural and urban areas (Figure 4). An urban-rural stratification was also used in a NT mortality survey in Jordan and showed a five times higher NT mortality rate in rural areas (23). Neonatal tetanus mortality rates were higher in a cattle farming area of Kenya in comparison with agricultural regions (20). Separate surveys were conducted in different sociological/ecological populations/areas of Pakistan (urban slums, rural agricultural areas and semi-nomadic groups) and in urban and rural areas in north and south parts of Sudan (66,85).

In Burma, the objective of a survey was to compare the NT mortality rates in areas where the EPI had been in operation for an extended period with areas where the programme had not been yet initiated (22,84). Figure 5 suggests some impact of the EPI was evident in that in non-EPI areas the estimated NT mortality rate was three times higher than in EPI areas.

In Nepal, four districts were purposely selected to represent the four major geographic regions: terrai - flat marshy plains, inner terrai - mixed areas of plains and low hills, mid-hills - undulating rocky slopes with an elevation of 5000 to 9000 feet, and the mountains (73). The overall estimated NT mortality rate was 24 per 1000 live births. The highest rate of 38 per 1000 live births was found in the terrai, intermediate rates from 16 to 21 were found in the inner-terrai and mid-hills, and the lowest rate of 8 per 1000 live births was estimated for the mountains.

Other decisions which need to be made at an early stage are: what is the size of area to be covered in a single survey, what should be the total population within a given sampling frame; what should the sample size be, and finally, how many houses would be visited by field teams to find the desired number of live births.

The size of the area should not be too small. Owing to possible uneven distribution of neonatal tetanus in various subregions of the country, the results of a survey conducted in one small subregion could be misleading if they are assumed to represent all the country. However, the representativeness of the sample for all the country is not always so important. A sample may only be representative of a deprived part of the country and the results of the survey may have practical usefulness for monitoring the progress of the control programme.

On the other hand, a survey covering too large an area or population within which neonatal tetanus incidence differs considerably in various sub-groups may provide an "average" result which does not reflect a complex situation. It is preferable to perform stratified sampling in such situations.

When neonatal tetanus incidence is expected to differ considerably in different regions of the country it is recommended to divide the country into different strata (areas) and conduct a separate survey in each different area or population group.

FIG. 4  
NEONATAL TETANUS MORTALITY RATES PER 1000 LIVE BIRTHS IN RURAL AND URBAN AREAS OF INDIA.  
RESULTS OF 27 SPECIAL SURVEYS CONDUCTED IN 14 STATES IN 1981 - 1982

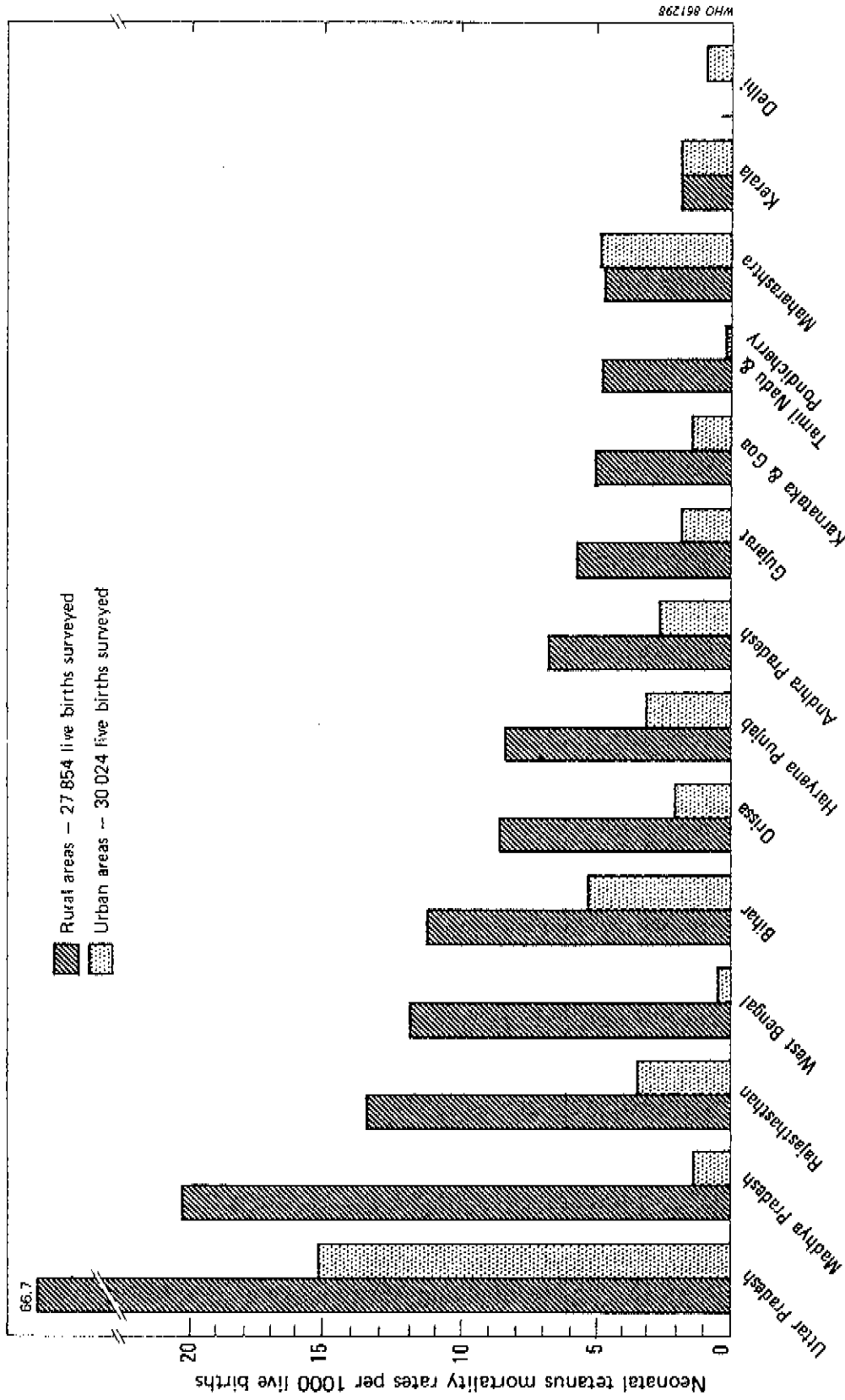
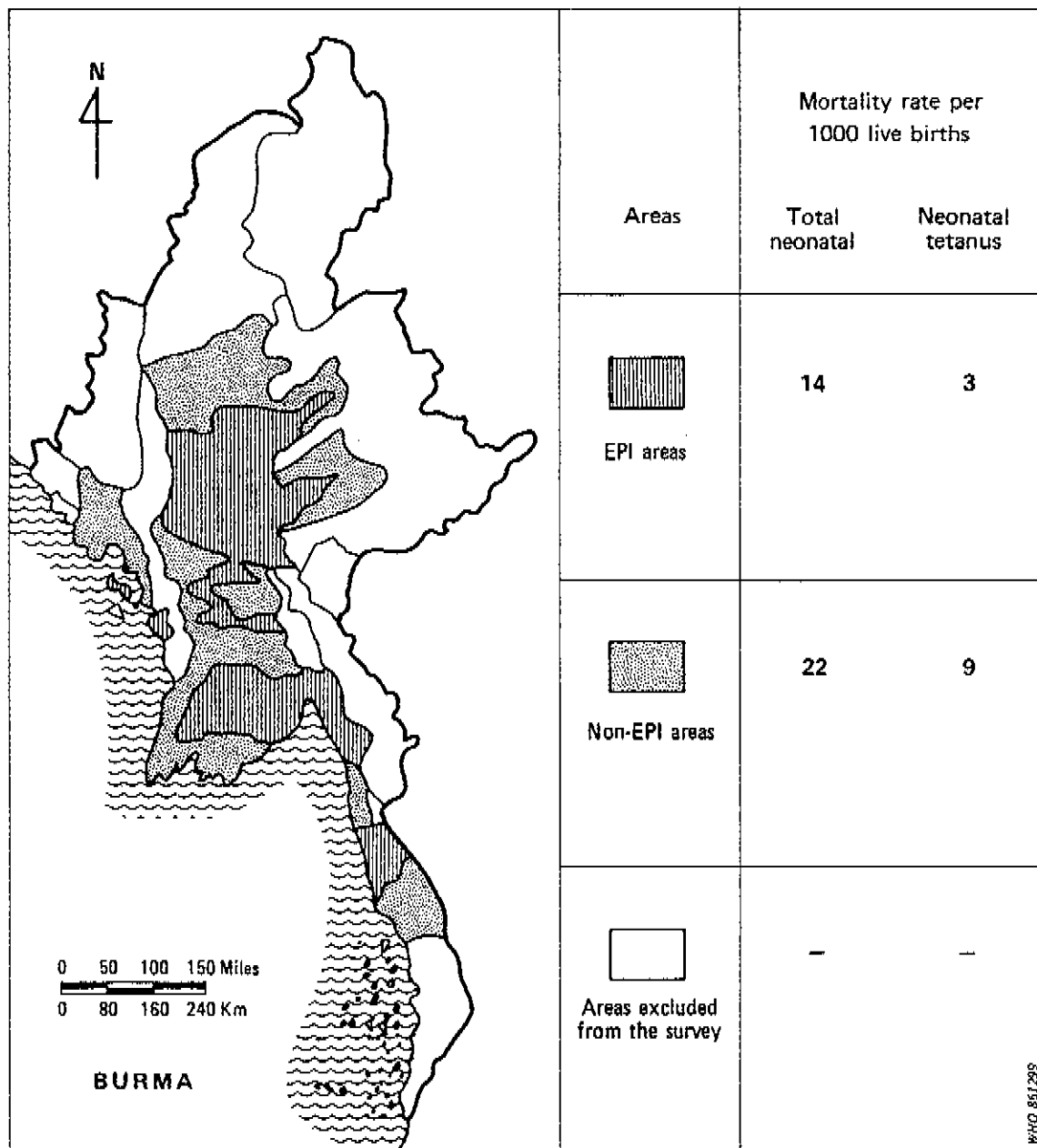


FIG. 5  
NEONATAL TETANUS MORTALITY RATES PER 1000 LIVE BIRTHS  
FOUND IN THE SURVEYS CONDUCTED IN EPI AND NON-EPI AREAS  
BURMA, MARCH - APRIL, 1985 (22)



In practice, the areas covered by surveys performed to date have differed considerably. The total population within individual survey sampling frames was 110 000 in the Ivory Coast (28), 5 million in Jakarta, Indonesia (30) and 10 million and 16 million in two separate surveys in Burma (22). In India, the country was divided into large units with populations greater than 20 million in each sample frame. The States with a population of less than 20 million were grouped together to form one larger unit (6,7).

Estimating the number of houses to be visited to find a designated number of live births is an important factor in planning of the survey. The estimate primarily depends on the birth rate and the recall period. The definitions of "recall period" will be given later. In surveys with a long recall period (usually one year) the number of houses visited has ranged from 5000 in Kenya (20) to 13 000-18 000 in Indonesia, Burma and Pakistan (22,29,85).

In Malawi, to find 70 live births in one cluster 284 houses on average (range: 158 to 418 houses in different clusters) were visited. Two to 4 days were required for one team to complete a cluster (27).

In India, where a short (4 month) recall period was used, more houses were visited to collect information on a total of about 2000 live births. Four teams of two workers each were assigned to each cluster. To find 67 live births in a single cluster, 1500 to 1800 households were visited within a period of 5 to 7 days (6,7). The population surveyed in each survey ranged from 110 000 to 313 000 in rural areas and from 223 000 to 441 000 in urban areas. The number of houses visited in various surveys ranged from 18 700 to 71 500 (7); on average, 44 000 to 55 000 families were visited to complete the surveys (79).

#### 4.3 Sampling technique - selection of clusters

There are different sampling techniques. Some, such as simple random sampling, require developing sampling frames that list basic sampling units, for example - individual persons or individual households. However, accurate lists of such units are difficult, costly and time-consuming to obtain.

Because it is much less time-consuming to sample persons in groups rather than as individuals, other sampling schemes are used in which sample frames list groups or clusters. The term cluster can be defined as any "group" sampling unit such as a village, town, city block or primary health centre area. Cluster sampling is a more economical type of sampling, and has been often used in EPI surveys.

However, cluster sampling introduces an additional possibility of error as individuals in the same group may share certain characteristics. The sample size may need to be increased to compensate for the additional error (see chapter 4.4).

Clusters can be selected in different ways (53). For example, we can select a sample of clusters by simple random or by systematic sampling. One such sampling scheme, used in EPI surveys, is sampling with probability proportional to size (pps). With pps sampling the probability that a particular village or town will be identified as one of the cluster in the sample is directly related to the size of the village or town. As was mentioned in chapter 4.2 one may stratify the population and take samples from each stratum (area).

The main steps in selecting clusters with the EPI technique are as follows:

1. After identifying the geographic or ecologic area to be surveyed (chapter 4.2), list all villages, towns, city blocks or other appropriate units (clusters) within the identified area.
2. For each listed unit obtain and record the most current estimates of population size. In practice this may be difficult if it has been a long time since the last census update was carried out. The main concern is to assure that the relative sizes of the listed units are approximately correct (52).
3. Calculate and write down the cumulative population for each listed unit and finally calculate the total cumulative population for the whole area to be surveyed.
4. Determine sampling interval by using the following formula:

$$\frac{\text{Total cumulative population}}{\quad\quad\quad} = \text{sampling interval}$$

30

5. Select a random number which is less than or equal to the sampling interval. Use the random number table or a serial number on a currency note to select a random number in the appropriate range.
6. Select the communities in which particular clusters will be located. Cluster number one is identified by locating the first unit (village, town, etc.) in which the cumulative population equals or exceeds the random number. Cluster number two is identified by adding the sampling interval to the random number. The cumulative population listed for the village or town that equals or exceeds that number is the location of cluster two. The remaining cluster locations are identified by successively adding the sampling interval to the number used to identify the previous site. Since the sampling design is proportional to the size of any particular listed unit, a single unit with a large population has a greater probability to be selected than a unit of less population. In fact, it may happen that more than one cluster can be located in a large unit.

Detailed examples of the EPI cluster selection procedure are presented in the EPI training module: "Evaluate vaccination coverage" (35), which is available on request from EPI/Geneva or WHO Regional Offices.

The process by which a sample of clusters is selected may be one-stage or multi-stage. In one-stage sampling the primary sampling units (clusters) are directly surveyed. In a survey covering a large area, a multi-step procedure may be advisable. A multi-stage procedure was used in India, where primary health centres in rural areas and towns in urban areas were first listed. At the first stage, a pps sample of 30 PHC (rural survey) and 30 towns (urban survey) within the State was taken. At the second stage, the villages or the wards within the selected PHC areas and towns were listed and cluster sites were identified using the procedure described above. The village or ward thus selected was then directly surveyed. If the village or ward did not provide 67 live births 1-4 months of age (see section 4.5 on the recall period), the survey was extended into the nearest village(s) or ward(s) to complete the cluster. A similar two-stage method was used in the survey in Burma (22,84).

There is no particular statistical advantage in using exactly 30 clusters (52). Local constraints related to difficult travel to distant and remote mountainous areas and shortage of manpower determined flexible approaches in two surveys in Nepal (73,74). In one survey, 40 clusters were selected and 20 infants were surveyed in each of the selected clusters. The precision of the estimate for the NT mortality rate was low (see section 4.4) in that survey due probably to the small total sample size, 800 children (74).

It is suggested that 30 clusters, identified by pps systematic sampling, should be the smallest number of clusters sampled. Consideration may be given to increasing the number of clusters when operationally and economically feasible.

#### 4.4 Sample size

The following discussion assumes some familiarity with statistics. Those without sufficient background knowledge are advised to seek the help of a statistician to help explain the basic principles involved.

Determination of sample size is important in planning the survey. Sample size depends on four main factors: the true incidence or mortality rate expected in the population to be surveyed, the precision of the sample estimate that is needed, the proportion of newborns in the total population of newborns that will be included in the sample, and an estimate of the error introduced by the cluster sampling technique ("design effect").

The first factor appears to be illogical; an estimate is needed of the rate to be estimated by the survey! Information to provide an initial estimate may, however, exist. There is usually some knowledge of the magnitudes of the rates to be estimated, which can often be inferred from fragmented observations made by other investigators either in the population to be surveyed or in neighbouring or similar areas. The reason such an estimate is needed is because a sample size can be chosen that is appropriate for the precision needed if an "idea" exists of about how high or low the rate probably is. If the true rate is very high, a small sample will be enough to yield answers of an acceptable precision; if the true rate is low, a larger sample will be required.

Precision can influence sample size because the more precise the estimate, the larger the sample size needed.

Assuming that the characteristic to be measured in a population is randomly distributed, it can be shown that for successive samples taken from that population, that a simple equation describes the required sample size (a function of the true rate and the desired precision) of the survey. If  $n_0$  is the sample size, then

$$n_0 = \frac{z^2 p q}{d^2}$$

where:  $z$  is the normal deviate (if  $\alpha$  equals 0.05,  $z$  is 1.96)  
 $p$  is the true rate, and  $q$  is  $1 - p$   
 $d$  is the precision of the estimate

As the sample increases in proportion to the size of the universe, the standard error of the sample estimate decreases as a factor of the square root of  $1 - \frac{n_0}{N}$  where  $n_0$  is the sample size and  $N$  is the population size.

When one samples the entire population  $1 - \frac{n_0}{N}$

becomes zero, and this reduces the standard error to zero. This is logical as one has not taken a sample but has made a complete measurement. Therefore the sample size  $n_0$  should be corrected by computing:

$$n = \frac{n_0}{1 + \frac{n_0}{N}}$$

in which  $n$  is the corrected sample size and  $N$  is the population being sampled.

The design effect is the ratio of the variance of a particular sample design (e.g. a cluster sample survey) to the variance for a simple random sample of the same number of basic sampling units. Data from 18 surveys for NT performed in India provided mean design effects of 1.2 in urban and 1.7 in rural areas (74).

The results from surveys in Nepal suggested that design effects were inversely related to disease incidence. The authors considered the design effect a measure of the degree to which a disease is clustered, i.e. the degree to which it occurs in focal epidemics or in chronic endemic foci (Table 2). The design effect for NT was small, but the estimates of NT incidence rate (7 and 19 per 1000) were imprecise. Larger samples than 800 live births would be required to improve the precision of the estimates obtained in these surveys.

TABLE 2. INCIDENCE RATES FOR FIVE EPI DISEASES, DESIGN EFFECTS AND PRECISION OF ESTIMATES FOUND IN TWO SURVEYS, NEPAL 1982-1983 (74)

Disease	Incidence per 1000*		Design effect		Precision in %**	
	A***	B	A	B	A	B
Measles	124	57	7.8	16.9	14	41
Pertussis	41	15	5.0	8.8	21	59
NT	7	19	1.7	1.0	92	42
Diphtheria	2	0.5	1.9	1.6	51	118
Poliomyelitis	1	3	1.2	1.0	67	82

\* Incidence per 1000 individuals aged below 10 years for measles, pertussis and diphtheria, 5 to 9 years for poliomyelitis and 3-28 days for neonatal tetanus.

\*\* 95% confidence limits expressed as a percentage of the estimated rate. The smaller the percentage, the greater the precision.

\*\*\* A - survey in Kathmandu Valley, urban and semi-urban areas.  
B - survey in the district of Dhanusa.

To plan a NT mortality survey in an area with a total population of 500 000, several assumptions have to be made. Given a crude birth rate of 0.04, about 20 000 births per year would be expected in the area - i.e.  $N = 20\ 000$ . Assume that the expected NT mortality rate is 20 per 1000 live births ( $p = 0.02$ ). If one decides that a relative precision of 50% of the expected rate will be satisfactory, this will translate into a sample estimate falling between 10 to 30 per 1000 live births ( $20 \pm 10$ ) if the true rate is 20 per 1000 live births. In such a case the value for  $d$  will be 0.01 ( $0.5 \times 0.02$ ). The calculations will be as follows:

$$n_0 = \frac{(1.96)^2 \times 0.02 \times 0.98}{(0.01)^2} = 753$$

The corrected value for  $n$  will be

$$n = \frac{753}{1 + \frac{753}{20\ 000}} = 725$$

If it is also assumed that the design effect will be similar to that estimated for rural surveys in India (74), the required sample size would be  $725 \times 1.7 = 1233$  live births.

If, however, the expected NT mortality rate is estimated to be 10 per 1000 live births rather than 20 - keeping all other factors constant - the required sample size would be calculated as 2400 live births.

Examples of sample sizes, calculated according to the above procedures are presented in Table 3. It can be seen that for the individual factors, sample size increases (to a limit) with the size of population surveyed and with a need for greater precision. Sample size decreases with lower mortality rates. All these factors need to be considered in planning the survey.

It is thought that most developing countries still have a high NT mortality rate. A standard design with a sample size of 2100 live births surveyed in 30 clusters should provide estimates of acceptable precision. In situations where any of the factors differ sufficiently from those presented above, the size of sample should be corrected, accordingly.

TABLE 3. CALCULATED SAMPLE SIZES\* FOR NEONATAL TETANUS MORTALITY SURVEYS OF VARIOUS PRECISION IN AREAS OF DIFFERENT POPULATIONS AND DIFFERENT EXPECTED MORTALITY RATES

POPULATION		RELATIVE PRECISION OF $\hat{p}$		
Total population within sampling frame (mill.)	No. of newborn per year (N)**	0.5	0.3	0.2
EXPECTED MORTALITY RATE: $\hat{p} = 20$ PER 1000 LIVE BIRTHS				
SAMPLE SIZES NEEDED				
20	800 000	1 278	3 545	7 951
5	200 000	1 275	3 516	7 813
1	40 000	1 256	3 376	7 155
0.5	20 000	1 233	3 214	6 474
0.1	4 000	1 078	2 332	3 677
EXPECTED MORTALITY RATE: $\hat{p} = 10$ PER 1000 LIVE BIRTHS				
20	800 000	2 579	7 143	15 968
5	200 000	2 567	7 033	15 424
1	40 000	2 491	6 491	13 054
0.5	20 000	2 403	5 926	10 953
0.1	4 000	1 873	3 492	4 786
EXPECTED MORTALITY RATE: $\hat{p} = 1$ PER 1000 LIVE BIRTHS				
20	800 000	25 593	68 792	145 580
5	400 000	24 227	59 735	110 196
1	40 000	18 853	35 081	47 985
0.5	20 000	14 762	23 142	28 133
0.1	4 000	5 394	6 217	6 528

\* According to formulas:  $n_0 = \frac{z^2 p q}{d^2}$  and  $n = \frac{n_0}{1 + \frac{n_0}{N}}$  and assuming

that the design effect is 1.7.

\*\* Assuming the crude birth rate is 0.04.

If the purpose of an initial survey of NT is to establish a baseline rate against which a future survey will measure programme impact after a period of time, it is worthwhile to obtain statistical assistance to calculate the sample sizes that will be needed for the initial and the follow-up survey. When appropriately planned, the cost of both surveys can be kept approximately equivalent. Without such planning, the second survey may need to be inordinantly expensive in order to show differences from the initial survey.

#### 4.5 Period of recall

The period of recall was 3 months in some surveys and one year in others. Whatever recall period is used, all the children should have been exposed to the full period of neonatal mortality risk. In the case of a 3 month recall period, live births born 1 to 4 months before the date of the survey should be included and in the case of one year recall period, live births born 1 to 13 months before the date of the survey should be included.

A shorter recall period generally increases the accuracy of the data collected; however, it will take longer to obtain the necessary number of live births to complete the survey (section 4.2). Furthermore, as was mentioned in section 3.2, NT incidence or mortality may have a seasonal pattern, and the use of short recall periods may produce high or low estimates of NT depending upon the timing of the survey.

A one year or longer recall period has the advantage of reducing the number of households which need to be visited, which may be important in sparsely populated areas or where staff and budget are limited.

In a survey performed in the Ivory Coast, the analysis of the mothers' recall showed that the number of reported live births and neonatal tetanus deaths increased as the recall period was shortened (Table 4). A survey in Malawi also showed an improvement in reporting by mothers with a shorter recall period; two-thirds of neonatal tetanus deaths were reported to have occurred during the 6 months prior to the survey and only one-third during the earlier 6 months before the survey (27). However, the results of the Malawi survey were not evaluated to determine the possibility of a seasonal distribution of neonatal tetanus which could also be an explanation for the observed differences.

Whatever the length of the recall period, local festivals and holidays should be identified to serve as calendar reference points.

Taking into consideration the logistic and operational constraints found in many developing countries a recall period of 12 months is recommended.

#### 4.6 Questionnaires

The ability and willingness of mothers to discuss deaths of their children will vary considerably from one country to another. It is important that information on the date and circumstances of a child's death should be obtained by posing questions which will readily be understood.

TABLE 4. NEONATAL MORTALITY AND NEONATAL TETANUS MORTALITY BY RECALL PERIOD, IVORY COAST, 1981-1982 (28)

Length of recall period (interval since birth, in months)	No. of live births surveyed <sup>a</sup>	No. of neonatal deaths, by cause			Neonatal mortality rates per 1000 live births, by cause	
		Neonatal tetanus	Other causes	Total	Neonatal tetanus	All causes
14-19	525	3	11	14	6	27
8-13	731	10	10	20	14	27
1-7	1 052	28	18	46	27	44
<b>Total</b>	<b>2 307</b>	<b>41</b>	<b>39</b>	<b>80</b>	<b>18</b>	<b>34</b>

<sup>a</sup> Information on recall periods was not available in 17 cases.

Usually two questionnaire forms are used in NT surveys: one for collecting general information on all live births and deaths enumerated in the cluster and a second form for specific information on infants who died in the neonatal period.

A model questionnaire form for NT mortality surveys is shown in Figure 6.

The first form is completed by health workers on the initial visit by a survey team and it includes background information on the cluster and the number of households visited. Each live birth that occurred in the predetermined period of time is listed on the form and information on the child's name and address, sex, date of birth and date of death (if not alive) is filled in. Information on the mother's survival or death, her immunization history and on the type of worker who attended the birth is also collected on Form I.

Form II is completed by a medical officer and contains questions dealing with all infants who died in the first month of life. A separate form should be completed for each neonatal death.

Mothers should be asked to list the symptoms (i.e. an open-ended question) preceding the death of any child less than one month of age. Subsequently mothers should be asked whether a child experienced any of a list of symptoms. Asking the mother to volunteer symptoms first avoids the situation where a mother answers yes to all items on the symptom list, regardless of her child's true situation at death. Specific questions listed on Form II on the circumstances of the child's death are of great importance to make a reliable retrospective diagnosis of neonatal tetanus.

It is important to confirm that the child was born alive and developed normally during the first few days of life. The first symptoms of NT start to appear on or after the third day of life. Usually mothers are able to state whether an infant was able to suckle during the first two to three days and developed feeding problems later on. The first two questions are concerned with the ability to suckle and the cessation of that ability. The third question establishes a probable day of onset of the first symptom(s). Questions Nos 4 and 5 deal with the presence of rigidity and convulsions. General rigidity may manifest as trismus, risus sardonius or generalized stiffness. Mothers may describe these conditions as "the baby became stiff like a board", or "his body was held in one piece".

Questions other than those indicated on the model form may be asked to elaborate the course of the disease and to better determine the cause of the death. Such questions may relate to other symptoms of muscle hypertonus (were the limbs and toes flexed?, were the fists clenched?); may deal with convulsion/spasm attacks (how long did the attacks last?; how frequently did the attacks occur?) and whether the child was cyanotic or died during the attack. Such questions may also relate to the history of pregnancy (normal?, full-term?), delivery (normal?, forced?), the length of labour, or the weight of the newborn.

FIG. 6a. MODEL QUESTIONNAIRE FORMS FOR THE NEONATAL TETANUS MORTALITY SURVEYS

FORM I

Household Survey to List Neonatal Deaths

I. GENERAL INFORMATION

A. BACKGROUND

1. State/UT: \_\_\_\_\_
  2. District: \_\_\_\_\_
  3. Name of locality: \_\_\_\_\_
  4. Cluster No.: \_\_\_\_\_
  5. Estimated population surveyed today: \_\_\_\_\_
  6. Surveyed area rural/urban: \_\_\_\_\_
  7. Name of investigator: \_\_\_\_\_
  8. Date of survey: \_\_\_\_\_
- B. HOUSEHOLDS VISITED TODAY (Use tally marks, for example: \_\_\_\_\_)

Today's total \_\_\_\_\_

II. INFORMATION TO ASCERTAIN THE INCIDENCE OF NEONATAL TETANUS

Fill in all information asked for each live birth occurring between \_\_\_\_\_

No. household	Name and address of infant	Sex of infant	Date of birth	Child alive or dead/ Date of death	Mother alive or dead/ Date of death	How many doses of TT did mother receive	Who delivered this infant: (H.C./trained/untrained Dai)
1							
2							
3							
4							

FIG. 6b. MODEL QUESTIONNAIRE FORMS FOR THE NEONATAL TETANUS MORTALITY SURVEYS  
FORM II

INVESTIGATION OF NEONATAL DEATHS

To be completed by the medical officer on all infants who died within the first month of life (a separate form for each neonatal death)

**I. GENERAL INFORMATION**

1. State/U.T. \_\_\_\_\_ 4. Physician's name \_\_\_\_\_  
 2. District: \_\_\_\_\_ 5. Date: \_\_\_\_\_  
 3. Town: \_\_\_\_\_ 6. Cluster No.: \_\_\_\_\_

**II. BACKGROUND INFORMATION ON NEONATAL DEATH**

1. Name of child: \_\_\_\_\_  
 2. Sex of child: \_\_\_\_\_  
 3. Father's name: \_\_\_\_\_  
 4. Head of household: \_\_\_\_\_  
 5. Date of birth of child: \_\_\_\_\_  
 6. Address of child: \_\_\_\_\_  
 7. Name of person interviewed: \_\_\_\_\_  
 8. Relationship of person interviewed to child: \_\_\_\_\_  
 9. Date of death of child: \_\_\_\_\_

**III. SYMPTOMS PRECEDING INFANT'S DEATH (Please circle appropriate answer)**

1. Was the infant able to suck milk after birth? Yes No  
 2. Did the infant stop sucking milk when became ill? Yes No  
 3. How many days passed before the infant became ill? ... days  
 4. Did the infant's body become rigid? Yes No  
 5. Did the infant have convulsions? Yes No  
 6. Did the infant have a fever? Yes No  
 7. What does mother say the infant died of? \_\_\_\_\_

**IV. INFANT'S CARE SINCE BIRTH (Please circle appropriate answer)**

1. Who delivered the child?  
 Doctor/LMU/AMM \_\_\_\_\_  
 Bai (trained) \_\_\_\_\_  
 Bai (untrained) \_\_\_\_\_  
 Non-Bai family members \_\_\_\_\_  
 Others (please specify) \_\_\_\_\_

2. Where was the child delivered?  
 Hospital/health centre \_\_\_\_\_  
 Home \_\_\_\_\_  
 In the field \_\_\_\_\_  
 Other (please specify) \_\_\_\_\_

3. When the child became ill, who treated the child?  
 Government health centre \_\_\_\_\_  
 Registered physician \_\_\_\_\_  
 (allopathic/ayurvedic/homeopathic) \_\_\_\_\_  
 Unregistered physician \_\_\_\_\_  
 No treatment was received \_\_\_\_\_

**V. MOTHER'S IMMUNIZATION HISTORY**

1. Does the mother know about vaccination with TT? Yes No (Circle)  
 2. Number of doses of TT mother received during pregnancy: \_\_\_\_\_  
 3. How many TT did mother receive before last pregnancy? \_\_\_\_\_  
 4. When did mother receive last TT immunization prior to pregnancy? \_\_\_\_\_

**VI. OTHER INFORMATION ON MOTHER**

1. Is the mother alive? Yes No (Circle)  
 2. If dead, date of death \_\_\_\_\_  
 3. Symptoms preceding death: \_\_\_\_\_

**VII. MEDICAL OFFICER'S DIAGNOSIS**

1. Cause of neonatal death: \_\_\_\_\_  
 2. Cause of mother's death: \_\_\_\_\_

Signature of medical officer \_\_\_\_\_

Finally, the medical officer should obtain the mother's opinion of the cause of the child's death. Other questions deal with the infant's care since birth, the mother's immunization history in more detail than in Form I, and the mother's death, if this occurred.

Finally, the medical officer should make his diagnosis of the cause of the infant's (and the mother's, if applicable) death.

Additional questions of local importance can be included on the questionnaire, however these should be kept as brief as possible. The questionnaire should be translated to a local language so that it is understandable for both parents and health workers.

#### 4.7 Training and supervision of the staff

Staff should be carefully trained. It is advisable to prepare job descriptions for each staff member including persons responsible for general supervision in the clusters, medical officers responsible for verification of all neonatal deaths and for retrospective diagnosis of neonatal tetanus deaths, for field supervisors who directly observe and correct the work of interviewers in the field, and finally for health workers/interviewers. Models of job descriptions used in Indian surveys are shown in Table 5.

Special emphasis should be given to the training of interviewers. These staff may be medical or nursing students, health inspectors, lady health visitors or vaccinators. EPI staff are usually familiar with the EPI 30-cluster method used for immunization coverage surveys. Thus, training of such staff may be facilitated, but there is the need to stress the differences between immunization coverage and disease mortality surveys. Training should provide a clear explanation of the objectives and methodology of the survey. Interviewing techniques should be comprehensively demonstrated; it is advisable to review the questionnaires line by line to demonstrate how questions should be asked and how answers should be recorded on the forms. The target groups (e.g. all live-borns and infants who died in the neonatal period) should be described. The characteristics of neonatal tetanus should be explained.

Field supervisors should be instructed how to: schedule their work with the field teams, observe the teams' work, make corrections on the spot, collect forms, check forms for completeness and accuracy, and how to submit lists of neonatal deaths to medical officers for investigation.

In the Indian surveys, one sanitary inspector supervised the work of four teams in the field. Four teams could finish a cluster in about 3 days (6,40).

All staff should be trained before the survey begins and should be continually supervised during field operations. Special emphasis should be given to the training and supervision of field staff: health workers/interviewers and their direct supervisors. Medical officers should be trained to make retrospective diagnoses of neonatal tetanus. It is advisable to prepare comprehensive job descriptions for all categories of staff involved in the survey.

TABLE 5. MODEL JOB DESCRIPTIONS FOR STAFF IN  
NEONATAL TETANUS MORTALITY SURVEYS

Health worker - interviewer

- Visit each household in the villages/locality specified on Form I.
- Fill in the cluster background information on your Form I.
- Record each household visited by noting the number of persons living in the household.
- In each household visited ask whether there were any live births during the specified period of time.
- If yes, record the child's name, sex and date of birth.
- Ask whether the child is alive or dead. If child is dead record the exact date of death.
- Determine the mother's immunization status with tetanus toxoid during and preceding the pregnancy. Record how many doses she received and ask for written evidence.
- At the end of each day contact your field supervisor, review your Form I with him/her and discuss the results.

Field supervisor

- Distribute Forms I and allocate villages/localities for each health worker. Be sure the Forms contain information on time brackets for the dates of live births (Part II in the Form I) and that the workers understand the Form and know how to perform the survey.
- Accompany health workers to the first village/locality and demonstrate the correct way of interviewing and of filling up the Forms in the first few households.
- Observe the work of the staff, check periodically how health workers collect information by collecting information independently and comparison with that obtained by health workers.
- At the end of each day collect the forms from each worker, check if all items are completed and discuss the results with health workers.
- Underline all children who died within the first month of life and hand over the list of children who died in the neonatal period to the medical officer.

TABLE 5 (CONTINUED)

Medical officer

- Discuss the list of neonatal deaths with the field supervisors.
- Locate the relevant addresses and visit the villages.
- Contact local leaders, priests or teachers and discuss the recent births and neonatal tetanus.
- Locate the concerned households and interview an adult member of each household. Ask the questions on Form II, and if necessary any other questions which may help in making a proper diagnosis.
- Make your diagnosis of the cause of each neonatal (or mother's, if any) death.

Coordinating supervisor (Programme manager)

Plan the survey

- Define objectives and scope of the survey.
- Prepare timetable and select clusters.
- Prepare relevant forms and documents and organize means of transport.
- Select teams of health workers, field supervisors and medical officers.
- Train staff.

Supervise the survey

- Visit all supervisors and one or more villages in each supervisor's area while survey teams are active.
- Monitor the work of health workers, field supervisors and medical officers and provide guidance if necessary.

Analyse the results

- Collect all completed forms.
- Check the forms for completeness and correctness. Verify that the number of children that died within the first month of life listed by medical officers on Forms II is equal to the number of children underlined by field supervisors on Form I.
- Arrange for revisits to complete forms, if necessary.
- Prepare a summary of the results of the survey: include estimates of neonatal tetanus and non-neonatal tetanus mortality rates per 1000 live births and the percentage of neonatal deaths attributable to neonatal tetanus.

#### 4.8 Timetable of the survey

A survey must be carefully planned, prepared and executed. On the average, 3 to 4 weeks are required for completion (6,84). A timetable used in a recent NT mortality survey in Burma is a useful model. In this survey the first week was devoted to determining the scope and completing plans for the survey, to developing and reproducing questionnaires and other forms, and to training of central, State and division-level EPI staff. The second week was allocated to training medical officers and local health authority staff in townships which had been selected for survey. The third week was allocated for field operations (data collection), and the fourth week for review, compilation and analysis of data and preparation of preliminary results (84).

Often more time is needed for preparatory work such as the preparation of the list of localities and selection of clusters, or the preparation and distribution of questionnaires and forms. In fact, in the Indian surveys, all preparatory work was done before starting the surveys. Also, the final analysis of the results was done after completing the surveys (6).

Surveys should be organized where there is no other conflicting work being done in the area.

#### 4.9 Analysis of results

The results should provide estimates of neonatal and NT mortality rates per 1000 live births - and the percentage contribution of neonatal tetanus in terms of numbers of neonatal deaths. To calculate the estimated neonatal mortality rate per 1000 live births the total number of neonatal deaths found in the survey should be divided by the number of live births recorded in the survey.

Similarly, the estimated neonatal tetanus mortality rate per 1000 live births may be calculated by dividing the number of neonatal tetanus deaths by the number of live births in the survey. The relevant formulae are as follows:

$$\text{Neonatal mortality rate} = \frac{\text{No. of neonatal deaths}}{\text{Number of live births}} \times 1000$$

$$\text{Neonatal mortality, tetanus rate} = \frac{\text{No. of neonatal tetanus deaths}}{\text{Number of live births}} \times 1000$$

The proportion of neonatal death due to tetanus may be calculated according to the formula:

$$\text{Proportion of neonatal deaths due to tetanus} = \frac{\text{No. of NT deaths}}{\text{No. of neonatal deaths}} \times 100$$

An estimated annual incidence rate for neonatal tetanus per 1000 live births may be roughly calculated by dividing the neonatal tetanus mortality rate per 1000 live births by 0.8. This assumes that the case fatality ratio of neonatal tetanus is 80%. The formula is:

$$\text{Annual incidence rate} = \frac{\text{Estimated NT mortality rate/1000 live births}}{0.8}$$

The analysis of the survey data may also be directed at:

- various factors influencing neonatal tetanus mortality and incidence: e.g. place of birth, birth attendants, local customs and beliefs related to delivery and postnatal care;
- clinical and epidemiological characteristics of neonatal tetanus cases: e.g. age at onset and death, sex, seasonality;
- impact of various control measures: e.g. training of TBAs, health education, immunization of mothers or immunization campaigns in school leavers, etc.

## 5. EXTENT AND MAGNITUDE OF THE PROBLEM OF NEONATAL TETANUS

### 5.1 Early estimates of neonatal tetanus incidence and mortality

The magnitude of the NT problem is not known with certainty. In the 1950s and 1960s, several reports called attention to NT as an important health problem. Reported NT mortality rates varied considerably, ranging from 2 per 1000 live births in Venezuela to 120 per 1000 live births in Haiti (60). Studies carried out in Thailand (82) and in India (Punjab) (39) showed NT mortality rates of 8 and 22 per 1000 live births. In New Guinea (76) and Colombia (62) high mortality rates were also found, ranging from 70 to 110 per 1000 live births. In Malaysia the estimated NT mortality rates among neonates whose births were attended by untrained and partially trained TBAs were 34 and 12 per 1000 live births, respectively (12).

Bytchenko drew attention to NT in his review in 1966 (9). At that time many countries could only generate rough estimates of the NT incidence from isolated surveys or from hospital data. For the most part NT incidence could be measured with fair accuracy from official records in developed countries where it was low and decreasing (83). The problem of NT in developing countries did not become widely recognized until the early 1980s in conjunction with the implementation of the Expanded Programme on Immunization.

### 5.2 Mortality rates per 1000 live births estimated in mortality surveys

Of the 25 most populous countries in the developing world (excluding China) with about 63 million children surviving one year of age, neonatal tetanus mortality surveys have been performed in 13 countries (Table 6). That group of countries covers about two-thirds (45 million) of the 63 million children. However, there are no valid data from the remaining 12 countries, where neonatal tetanus is not reported and neonatal tetanus mortality surveys have not been conducted.

TABLE 6. STATUS OF 25 MOST POPULOUS COUNTRIES IN THE DEVELOPING WORLD  
(EXCLUDING CHINA) WITH RESPECT TO BASELINE ESTIMATES OF  
NEONATAL TETANUS INCIDENCE

	Country	Estimated No. of infants
Countries which have carried out special mortality surveys to establish baseline estimates.	1. India	21.74
	2. Indonesia	4.59
	3. Pakistan	3.47
	4. Bangladesh	2.95
	5. Islamic Republic of Iran	2.02
	6. Viet Nam	1.66
	7. Philippines	1.56
	8. Ethiopia	1.45
	9. Zaire	1.29
	10. Burma	1.29
	11. Thailand	1.05
	12. Kenya	0.98
	13. Sudan	0.85
	SUBTOTAL	44.90 (70.7%)

TABLE 6. (CONTINUED)

	Country	Estimated No. of infants
Countries which have not carried out special mortality surveys.	1. Nigeria	4.11
	2. Brazil	2.83
	3. Mexico	2.46
	4. Egypt	1.54
	5. Turkey	1.40
	6. South Africa	1.11
	7. United Republic of Tanzania	0.95
	8. Republic of Korea	0.92
	9. Morocco	0.91
	10. Colombia	0.86
	11. Algeria	0.81
	12. Argentina	0.70
	SUBTOTAL	18.6 (29.3%)
	TOTAL	63.5 (100.0%)

Among those 12 countries, 4 are in the African Region: Nigeria (the largest country on the continent with 4 million children born annually), Tanzania, South Africa and Algeria. In other African countries estimated NT mortality rates range from 1 per 1000 live births in Ethiopia to 16 and 18 per 1000 live births in Kenya and Ivory Coast (Table 7). Preliminary data for Uganda show a high mortality rate of 15 per 1000 live births (not shown in Table 7). Neonatal tetanus represented from 7% (in Ethiopia) to 70% (in Kenya) of all neonatal deaths.

Neonatal tetanus mortality rates have been estimated from surveys done in 8 countries of the Eastern Mediterranean Region. Results show a wide variation, from 2 (in Jordan) to 31 per 1000 live births (in Pakistan). The proportion of neonatal death due to tetanus ranges from 8% to 60%.

Available data for Egypt strongly suggest that NT is a major health problem there (19,61,95). Passive reports from fever hospitals showed over 6000 neonatal tetanus cases in 1983 (95). The resulting incidence rate, 3 per 1000 live births, certainly reflects only a small part of the real incidence. In Cairo, NT cases represented 21% to 63% of all tetanus cases reported in 1976-1982 (19). Data are lacking for Morocco and Algeria.

The South-East Asia Region has compiled the most comprehensive data on NT incidence and mortality. The highest mortality rate - estimated for the rural areas of Uttar Pradesh in India - was 67 per 1000 live births. NT mortality rates higher than 10 per 1000 live births were estimated for 4 other States in India (Figure 4) as well as for Bangladesh, Bhutan, Indonesia and Nepal. Rates between 5 and 10 have been estimated for Burma and Thailand, while the lowest rate - 1 per 1000 live births - was estimated for Sri Lanka (Table 7).

In the Western Pacific Region only three surveys have been conducted: in the Philippines, Laos and Viet Nam. The surveys indicated moderate mortality rates, ranging from 2 to 6 per 1000 live births.

No formal surveys have been conducted in China. A nationwide programme to promote improved delivery and umbilical cord site care (without maternal immunization) was initiated in the 1950s. The programme resulted in a reduction of neonatal tetanus incidence (56). There are however some data suggesting that neonatal tetanus still persists in China; although NT is not a reportable disease, several rural areas of the country report an incidence of 1 to 3 per 1000 live births (96).

No recent survey data are available from Latin America. The 3 large countries Brazil, Mexico and Colombia, where about 6 million children are born annually, are of particular concern in this regard. Fragmentary data have shown frequent occurrences of neonatal tetanus in these countries. A study of 5674 liveborn children in Central Brazil in 1971 produced a NT mortality rate of 8 per 1000 live births (71). The mortality rates reported in 1957-1961 from the capitals of various Brazilian States showed high variability from 6 to 48 per 1000 live births. In the rural areas of Sao Paulo State - the most developed State of the country - the reported NT mortality rate was about 3 per 1000 live births (38).

In Mexico, the reported NT deaths were more than half of all reported tetanus deaths in 1959 and in 1973. The reported mortality rates in infants due to tetanus was about 1 per 1000 live births in 1955-1957 (10).

TABLE 7. ESTIMATES OF NEONATAL MORTALITY AND NEONATAL TETANUS MORTALITY RATES PER 1000 LIVE BIRTHS IN 29 COUNTRIES, BASED ON SPECIAL COMMUNITY SURVEYS, 1978-1986

WHO region	Country	Year	No. of live births surveyed	Neonatal mortality rates per 1000 live births		Proportion of neonatal deaths due to tetanus (%)
				Neonatal	Neonatal tetanus	
African	Cameroon	1982	2 102	-	7	-
	Ivory Coast	1982	2 324	34	18	51
	Malawi	1982	2 081	29	12	41
	Ethiopia	1983	2 322	12	1	7
	Malawi	1983	2 101	-	12	-
	Burundi	1984	3 099	-	8	-
	Cameroon	1984	2 118	-	8	-
	Kenya	1984	2 132	16	11	69
	Togo	1984	4 966	11	6	52
	Zaire	1984	3 836	12	1	8
	Kenya	1985	2 133	23	16	70
Eastern Mediterranean	Democratic Yemen	1981	6 224	19	4	20
	Egypt urban	1981	-	-	3	-
	Pakistan	1981	13 858	52	31	60
	Somalia	1981	5 781	91	21	23
	Sudan	1981	9 632	29	9	32
	Syrian Arab Republic	1981	6 762	-	5	-
	Yemen Arab Republic	1981	5 191	31	3	8
	Jordan	1983	2 850	7	2	13
	Pakistan	1984	9 925	-	28	-
	Islamic Republic of Iran	1985	-	-	8	-
South-East Asia	Bangladesh	1978	2 432	48	27	56
	Indonesia	1979	1 570	49	23	47
	Indonesia	1980	3 933	-	12	-
	Nepal	1980	3 346	37	15	39
	Thailand	1980	13 659	21	5	23
	India rural	1981-	-	-	-	-
	India urban	1982	23 482	19-93	5-67	16-72
	Bhutan	1982	25 843	5-26	0-15	0-59
	Indonesia rural	1982	952	19	13	67
	Indonesia rural	1982	4 971	21	11	51
	Indonesia urban	1982	2 310	17	7	40
	Nepal rural	1982	1 997	44	24	55
	Indonesia	1983	4 739	-	17	-
	Indonesia	1984	4 836	-	21	35
	Indonesia	1984	4 769	-	9	-
	Sri Lanka	1984	2 841	15	1	7
Burma	1985	6 000	18	6	33	
Bangladesh	1986	2 000	82	41	50	
Western Pacific	Philippines	1982	8 754	13	6	48
	Viet Nam	1985	8 270	12	2	16
	Lao People's Democratic Republic	1985	4 996	17	4	23

### 5.3 Estimated global neonatal tetanus incidence and mortality

Results of special, community-based surveys, together with other available data, suggest that - worldwide - about 1 million newborn children suffer every year from neonatal tetanus and about 800 000 of them die.

## 6. SURVEILLANCE

Special mortality surveys can quickly provide reliable information on the magnitude of the neonatal tetanus problem. However, surveys are complex operations, must include areas where logistical support is difficult, require trained staff and means of transport. Their results are limited to the period of time for which they were carried out.

Routine surveillance systems should be integrated components of control programmes, and data thus collected should be used to directly measure programme impact.

Routine and/or sentinel surveillance of neonatal tetanus based on hospital data are often insensitive, because the disease tends to occur in populations with limited access to, or making limited use of, clinical facilities (18).

The completeness, timeliness and representativeness of routine surveillance data are usually limited, and for reasons mentioned in chapter 1.1, the disease remains extensively underreported in most developing countries.

It has been shown that routine reporting systems in 13 countries in the Eastern Mediterranean and South-East Asia Regions identified 2% to 5% of the numbers of tetanus cases that were estimated from community-based surveys (Table 8).

In 1981, only 92 cases of NT were reported through the routine surveillance system in Sudan, while the number of NT cases estimated by a special survey was 7700 (32,66).

In Sri Lanka, a country which has a relatively efficient reporting system, the reported NT incidence was 0.16 per 1000 live births in 1983 (24) - at least 7 times lower than the rate estimated from a mortality survey (Table 7).

Tetanus should be made a notifiable disease, and neonatal and non-neonatal tetanus should be reported separately. Systems of routine surveillance should be strengthened.

Sentinel hospitals may provide useful information on NT trends. Such sentinel centres have been identified in some areas of India (5,80).

In Figure 7, decreasing trends over time in the numbers of NT cases can be seen for Sri Lanka and for the Calcutta hospital catchment area. However, the increasing number of NT cases hospitalized in Egypt and in Delhi may represent an increasing awareness of the need for medical attention and utilization of these facilities for NT.

Information collected through routine surveillance systems should be used for monitoring and evaluation of the preventive programmes against NT. When surveillance data show neonatal tetanus cases in infants born from mothers fully immunized against tetanus, or increasing numbers of NT cases in children delivered in health facilities - or attended by trained persons - special investigations should be undertaken. An example of a case investigation form is shown in Figure 8.

TABLE 8. ESTIMATED COMPLETENESS OF NOTIFICATION ON TETANUS, BASED ON COMPARISONS OF RESULTS OF NEONATAL TETANUS SURVEYS AND REPORTED INCIDENCE IN THE WHO EASTERN MEDITERRANEAN AND SOUTH-EAST ASIA REGIONS, 1980-1981 (31)

WHO region	Results of neonatal tetanus surveys			Total number of reported tetanus cases	Estimated completeness of reporting (%)
	Estimated number of neonatal tetanus deaths	Estimated number of neonatal tetanus cases <sup>c</sup>	Estimated total number of tetanus cases <sup>d</sup>		
Eastern Mediterranean <sup>a</sup>	132 285	155 626	311 252	7 128	2
South-East Asia <sup>b</sup>	393 067	462 429	924 858	48 974	5

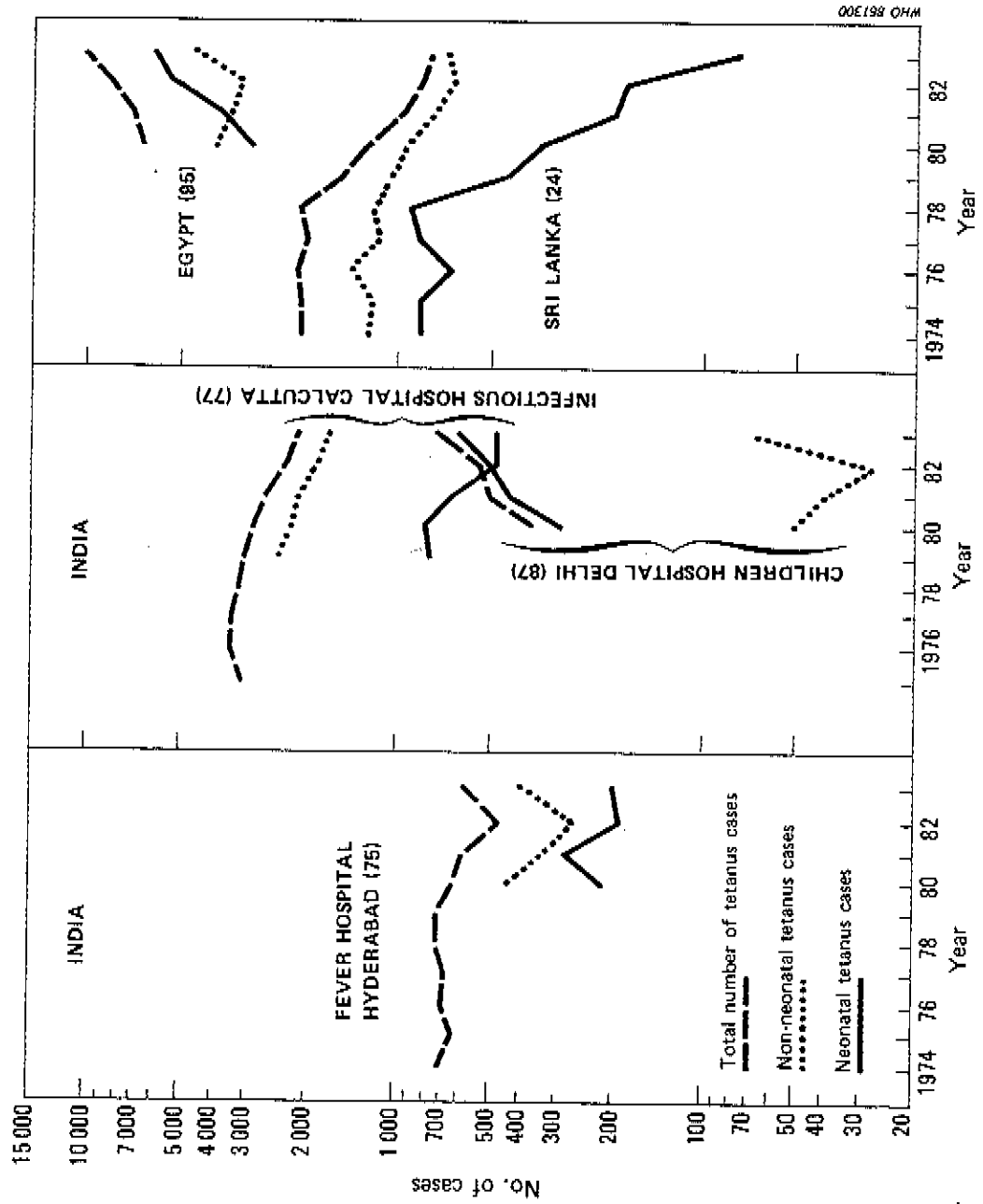
<sup>a</sup> Data from 7 countries: Democratic Yemen, Egypt, Pakistan, Somalia, Sudan, Syrian Arab Republic, and Yemen.

<sup>b</sup> Data from 6 countries: Bangladesh, Bhutan, India, Indonesia, Nepal, and Thailand.

<sup>c</sup> Assuming an 85% case fatality rate.

<sup>d</sup> Assuming that neonatal tetanus accounts for approximately 50% of all cases of tetanus.

FIG. 7  
NUMBER OF NEONATAL TETANUS AND NON-NEONATAL TETANUS CASES REPORTED IN INDIA, EGYPT AND SRI LANKA THROUGH ROUTINE SURVEILLANCE SYSTEMS, 1974 - 1983



WHO 861300

FIG. 8. AN EXAMPLE OF A CASE INVESTIGATION FORM FOR NEONATAL TETANUS (83 a)

NEONATAL TETANUS CASE INVESTIGATION FORM

Province \_\_\_\_\_ Village \_\_\_\_\_ Health Centre \_\_\_\_\_  
 Date Case Reported \_\_\_\_\_ Reported by \_\_\_\_\_  
 Household address of Case \_\_\_\_\_  
 Case Identification Number \_\_\_\_\_ Date of Investigation \_\_\_\_\_  
 Name and Title of Investigator \_\_\_\_\_

---

**CASE INFORMATION:**  
 Name of Case \_\_\_\_\_ Family Name \_\_\_\_\_  
 Age of Case: Years \_\_\_\_\_ Months \_\_\_\_\_ Sex of Case: Male/Female \_\_\_\_\_

**IMMUNIZATION STATUS OF MOTHER:**  
 Was mother immunized against tetanus? Yes/No \_\_\_\_\_  
 If yes, number of doses \_\_\_\_\_ Date of last dose \_\_\_\_/\_\_\_\_/\_\_\_\_  
 Was an immunization record seen? Yes/No \_\_\_\_\_

---

**BIRTHS OF INFANT:**  
 Did mother receive prenatal care? Yes/No \_\_\_\_\_  
 If yes, location and dates: \_\_\_\_\_  
 Where was baby born? Hospital/Home/Other \_\_\_\_\_  
 If delivery in institution, give name and address: \_\_\_\_\_

Was baby delivery attended by: Doctor/Nurse/Midwife \_\_\_\_\_  
 Traditional Birth Attendant/Other \_\_\_\_\_

Give name and address of birth attendant: \_\_\_\_\_

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**INSTRUCTION: CIRCLE WHICHEVER ANSWER APPLIES**

---

Describe how the cord was cut and with what type of equipment: \_\_\_\_\_  
 How was the stump treated or "dressed"? \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

**SCRIPTS:**  
 Date of Onset of illness \_\_\_\_/\_\_\_\_/\_\_\_\_  
 Did child suck and cry normally for first 2 days of life? Yes/No \_\_\_\_\_  
 If no, describe: \_\_\_\_\_

Did child have a problem with sucking? Yes/No \_\_\_\_\_ If yes, describe: \_\_\_\_\_

Stiffness: Yes/No/Unknown \_\_\_\_\_ Convulsions: Yes/No/Unknown \_\_\_\_\_  
 Complications: \_\_\_\_\_

---

**TREATMENT/OUTCOME:**  
 Was the patient cared for in a hospital/health facility? Yes/No \_\_\_\_\_  
 If yes, where and details: \_\_\_\_\_  
 Did the patient die? Yes/No \_\_\_\_\_ If yes, give date and details: \_\_\_\_\_  
 Was the patient seen by a doctor? Yes/No \_\_\_\_\_  
 If yes, diagnosis: \_\_\_\_\_  
 Complications and comments: \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

REFERENCES

1. ADAMS J.M. et al.: Modern management of tetanus neonatorum. *Pediatrics* 1979, 64: 472-477
2. ANUSZ Z.: Tetanus in Poland in the years 1961-1965. *Epidem. Rev. (Warsaw)* 1967, 21: 181-191
3. ATHAVALE V.B. et al.: Tetanus neonatorum. *Progr. Drug Res.*, 1975, 19: 189-207
4. ATHAVALE V.B. & PAI P.N.: Tetanus neonatorum - clinical manifestations. *J. Pediatr.*, 1965, 67: 649-657
5. BASU R.N.: Surveillance procedures for tetanus. In: "Sentinel Surveillance" Edit.: R.N. Basu, National Institute of Communicable Diseases, Delhi 1985: 68-75
6. BASU R.N. & SOKHEY J.: Special combined survey for poliomyelitis and neonatal tetanus as supplement to routine surveillance system in India. *J. Comm. Dis.*, 1984, 16: 148-153
7. BASU R.N. & SOKHEY J.: A baseline study on neonatal tetanus in India. *Pak. Pediatr. J.*, 1982, 6: 184-197
8. BROADHEAD R.L.: Tetanus neonatorum. A review of epidemiology, management and prevention. *Postgraduate Doctor-Middle East* 1985, 8: 454-460
9. BYTCHENKO B.: Geographical distribution of tetanus in the world, 1951-1960. *Bull. Wld Hlth Org.*, 1966, 34: 71-104
10. CARRADA BRAVO T.: El tétanos infantil en la República Mexicana. *Epidemiologia, letalidad comparada y prevencion. Salud Publ. Mex.*, 1977, 19: 617-644
11. CHEN A.J.: Neonatal tetanus in Singapore, 1960-1970. *Sing. Med. J.*, 1973, 14: 111-116
12. CHEN P.C.Y.: An assessment of the training of the traditional birth attendants in rural Malaysia. *Med. J. Malaysia* 1976, 31: 93-99
13. CLIFF J.: Neonatal tetanus in Maputo Mozambique. I. Hospital incidence and childbirth practices. *Centre. Afr. J. Med.*, 1985, 31: 9-12
14. COLLACOTT R.A.: Neonatal tetanus in St Kilda. *Scott. Med. J.*, 1981, 26: 224-227
15. CORNFIELD J.: Modern methods in the sampling of human population. The determination of sample size. *Amer. J. Publ. Hlth*, 1951, 41: 654-661
16. CRITCHLEY A.M.: Tetanus neonatorum. *Publ. Hlth*, 1958, 71: 459-463
17. DAUD S. et al.: Tetanus neonatorum. A preliminary report of assessment of different therapeutic regimes. *J. Trop. Pediatr.*, 1981, 27: 308-311

18. DONDERO T.: EPI target disease surveillance and disease reduction targets. WHO Document, EPI/GEN/84/6
19. ELIAS I.F.: The problem of tetanus neonatorum in Cairo. City Health Information, New York City Department of Health 1983, 2, No. 28
20. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus mortality surveys, Kenya. Wkly Epidem. Rec., 1986, 61: 117-118
21. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus mortality surveys, Indonesia. Wkly Epidem. Rec., 1986, 61: 101-102
22. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus mortality survey, Burma. Wkly Epidem. Rec., 1985, 60: 377-380
23. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus mortality and poliomyelitis lameness surveys, Jordan. Wkly Epidem. Rec., 1985, 60: 318-320
24. EXPANDED PROGRAMME ON IMMUNIZATION: Tetanus surveillance, Sri Lanka. Wkly Epidem. Rec., 1984, 59: 319
25. EXPANDED PROGRAMME ON IMMUNIZATION: Computer simulation of the EPI survey methodology. Wkly Epidem. Rec., 1984, 59: 297-300
26. EXPANDED PROGRAMME ON IMMUNIZATION: Programme review, Philippines. Wkly Epidem. Rec., 1984, 59: 192-194
27. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus mortality survey, Malawi. Wkly Epidem. Rec., 1983, 58: 326-327
28. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus mortality survey, Ivory Coast. Wkly Epidem. Rec., 1983, 58: 71-72
29. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus survey, Indonesia. Wkly Epidem. Rec., 1983, 58: 56-57
30. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus survey, Indonesia. Wkly Epidem. Rec., 1982, 57: 395
31. EXPANDED PROGRAMME ON IMMUNIZATION: The use of survey data to supplement disease surveillance. Wkly Epidem. Rec., 1982, 57: 361-362
32. EXPANDED PROGRAMME ON IMMUNIZATION: Neonatal tetanus mortality, Sudan. Wkly Epidem. Rec., 1982, 57: 137-142
33. EXPANDED PROGRAMME ON IMMUNIZATION: Prevention of neonatal tetanus. Wkly Epidem. Rec., 1982, 57: 137-142
34. EXPANDED PROGRAMME ON IMMUNIZATION: Cluster sampling to assess immunization coverage. Wkly Epidem. Rec., 1982, 57: 129-131
35. EXPANDED PROGRAMME ON IMMUNIZATION: Training for Mid-level Managers: "Evaluate vaccination coverage", WHO/CDC

- 35a. EXPANDED PROGRAMME ON IMMUNIZATION: EPI UPDATE, September 1986.
36. FOURIE D.T.: Some aspects of tetanus neonatorum in the Pretoria area. *South Afr. Med. J.*, 1982, 61: 183-185
37. GALAZKA A.: Control of neonatal tetanus. *Indian J. Pediatr.*, 1985, 52: 329-341
38. GOMES de MATTOS A.: 13 anos de campanha contra o tetanus umbilical. *Pediatr. Prat.*, 1962, 33: 11-17
39. GORDON J.E. et al.: Tetanus in villages of the Punjab: an epidemiological study. *J. Indian Med. Assoc.*, 1961, 37: 157-
40. GUIDELINES: Combined survey to estimate the incidence of neonatal tetanus and poliomyelitis. New Delhi, Directorate-General of Health Services, (EPI section), 1981
41. HAMID E.D. et al.: Tetanus neonatorum in babies delivered by TBAs in Medan, Indonesia. *Paediatr. Indonesiana* 1985, 25: 167-174
42. HANDALAGE D.C.M. & WICKRAMASINGHE S.Y.D.: Neonatal tetanus - some observations from Sri Lanka. *J. Trop. Pediatr.*, 1976, 22: 167-171
43. HEATH C.W. et al.: Tetanus in the United States, 1950-1960. *Amer. J. Publ. Hlth*, 1964, 54: 167-174
44. HENDERSON R.H. & SUNDARESAN T.: Cluster sampling to assess immunization coverage: a review of experience with a simplified sampling method. *Bull. Wld Hlth Org.*, 1982, 60: 253-260
45. JAFFARI S.M.H. et al.: Neonatal tetanus in Hyderabad. *Indian Pediatr.*, 1966, 3: 177-182.
46. JELLIFE D.B.: Tetanus neonatorum. *Arch. Dis. Child.*, 1950, 25: 190-192
47. JOHRI A. et al.: A clinical study of tetanus neonatorum. *Arch. Child Hlth*, 1983, 25: 9-14
48. JORIO-BENKHRABA A. et al.: Le tétanos néonatal en milieu hospitalier. *Mar. Med.*, 1981, 3: 649-656
49. KHOO B.H. et al.: Neonatal tetanus treated with high dosage diazepam. *Arch. Dis. Child.*, 1978, 53: 737-793
50. LAHA P.N. & VAISHYA P.D.: A study of the incidence of 1000 cases of tetanus in Gwalior and its neighbouring districts. *J. Indian Med. Assoc.*, 1965, 44: 422-436
51. LAFORCE F.M. et al.: Tetanus in the United States (1965-1966). Epidemiologic and clinic features. *New Engl. J. Med.*, 1969, 280: 569-574

52. LEMESHOW S. & ROBINSON D.: Surveys to measure programme coverage and impact: a review of the methodology used by the EPI. *Wld Hlth Statist. Quart.*, 1985, 38: 67-75
53. LEVY P.S. & LEMESHOW S.: Sampling for health professionals. *Lifetime Learning Publ.*, Belmont 1980
54. MANANDHAR D.S.: Management of tetanus neonatorum. A report of 100 cases treated in Bheri Zonal Hospital. *J. Nep. Med. Assoc.*, 1978, 16: 13-21
55. MARSHALL F.N.: Tetanus of the newborn, with special reference to experience in Haiti. *Adv. Pediatr.*, 1968, 15: 65-110
56. MATERNAL AND CHILD HEALTH (MCH): Control of neonatal tetanus, China. *Wkly Epidem. Rec.*, 1985, 60: 5-6
57. McINTOSH K.: Bacterial infections in the newborn. Chapter in: "Schaffer's diseases of the newborn", Edit.: M.A. Avery & H.W. Taesch, Sanders 1984, 729-747
58. McINTOSH K. & LAUER B.A.: Infections: Bacterial and Spirochetal. Chapter in: *Current Pediatric Diagnosis and Treatment*, Edit.: C.H. Kempe et al., 8th edition, Lange Med. Publ., 1984, 825
59. MENDOZA E.S. according to: DOWELL V.R.: Botulism and tetanus: selected epidemiologic and microbiologic aspects. *Rev. Infect. Dis.*, 1984, 6, Suppl. 1: S202-S207
60. MILLER J.K.: The prevention of neonatal tetanus by maternal immunization. *J. Trop. Pediatr.*, 1972, 18: 159-167
61. MOBARAK A.B. et al.: Evaluating tetanus neonatorum as a child survival risk in rural Egypt in the absence of reliable cause-of-death registration. *Trop. Med. Parasit.*, 1985, 36: 186-190
62. NEWELL K.W. et al.: The use of toxoid for the prevention of tetanus neonatorum. Final report of a double-blind controlled field trial. *Bull. Wld Hlth Org.*, 1966, 35: 863-871
63. NIGAM P.B.M. et al.: Tetanus neonatorum - a clinical study of 72 cases. *Indian J. Pediatr.*, 1974, 41: 135-143
64. NOURMAND A. et al.: Tetanus neonatorum in Iran. *Clin. Pediatr.*, 1970, 9: 609-610
65. OGBEIDE M.I.: Problems of neonatal tetanus in Lagos. *J. Trop. Pediatr.*, 1966, 12: 71-79
66. OLIVE J.M. et al.: Neonatal tetanus retrospective study, Sudan, October-November 1981. *Pak. Pediatr. J.*, 1982, 6: 260-275
67. PARIJA A.C. & MOHANTA K.D.: Neonatal tetanus. *Indian J. Pediatr.*, 1973, 40: 353-360

68. PATEL J.C. & AIYAR A.A.: Seasonal variations in tetanus. Proc. I Intern. Conf. on Tetanus, Bombay 8-10 November 1963: 591-602
69. PATEL J.C. & JOAG G.G.: Grading of tetanus to evaluate prognosis. Indian J. Med. Sci., 1959, 13: 834-840
70. PATEL J.C. et al.: Tetanus neonatorum. Indian J. Child Hlth, 1960, 9: 459-468
71. PEDERNEIRAS M.P. et al.: Umbilical tetanus in Brazil. Lancet, 1971, 1: 1134
72. PHATAK A.T. & SHAH S.B.: Indices of severity of neonatal tetanus. Indian Pediatr., 1973, 10: 87-91
73. ROTHENBERG R.: EPI. Sample surveys to estimate the annual incidence of neonatal tetanus and the prevalence of poliomyelitis in the Kingdom of Nepal. Assignment Report, 1 March - 1 April 1982, SEA/EPI/43
74. ROTHENBERG R.B. et al.: Observations on the application of EPI cluster survey methods for estimating disease incidence. Bull. Wld Hlth Org., 1985, 63: 93-99
75. SAHAY B.K.: Tetanus in fever hospital, Hyderabad. In: "Sentinel Surveillance", Edit.: R.N. Basu, National Institute of Communicable Diseases, Delhi, 1985: 76-78
76. SCHOFIELD F.D. et al.: Neonatal tetanus in N. Guinea: effect of active immunization in pregnancy. Brit. Med. J., 1961, 2: 785-789
77. SEN P.K.: Tetanus cases in I.D. Hospital, Calcutta. In: "Sentinel Surveillance", Edit.: R.N. Basu, National Institute of Communicable Diseases, 1985: 82-84
78. SINGH S.D. et al.: Tetanus neonatorum: a study of 112 cases. Indian J. Pediatr., 1966, 33: 111-117
79. SOKHEY J.: Magnitude of the problem of neonatal tetanus in India. In: "The control of neonatal tetanus in India", Government of India, Ministry of Health and Family Welfare, Edit.: J. Bhargava & J. Sokhey, New Delhi, 1983: 24-31
80. SOKHEY J.: Surveillance of neonatal tetanus. In: "The Control of Neonatal Tetanus in India", Edit.: I. Bhatgava & J. Sokhey, Government of India, Ministry of Health and Family Welfare, New Delhi, 1983: 52-59
81. SPIVEY O.S. et al.: Tetanus neonatorum. Review of 26 cases. J. Pediatr., 1953, 42: 345-351
82. STAHLIE T.D.: The role of tetanus neonatorum in infant mortality in Thailand. J. Trop. Pediatr., 1960, 6: 15-18
83. STANFIELD J.P. & GALAZKA A.: Neonatal tetanus in the world today. Bull. Wld Hlth Org., 1984, 62: 647-669

- 83a. STRASSBURG M.: Guidelines for the investigation and control of outbreaks of EPI target diseases. EPI/GEN/84/7/Rev.1
84. STROH G. et al.: Surveys to measure mortality from neonatal tetanus in the Socialistic Republic of the Union of Burma (Prepared for publication)
85. SULIEMAN O.: Mortality from tetanus neonatorum in Punjab (Pakistan). Pak. Pediatr. J., 1982, 6: 152-183
86. SURI J.C.: The problem of tetanus in India. In: Principle on tetanus. Proc. Intern. Conf. on Tetanus, Bern, 15-19 July 1966, Hans Huber Publ., 1967: 61-70
87. TANEJA D.K.: Problem of tetanus in Delhi. In: "Sentinel Surveillance". Edit.: R.N. Basu, National Institute of Communicable Diseases, Delhi, 1985: 79-81
88. TOMPKINS A.B.: Neonatal tetanus in Nigeria. Brit. Med. J., 1958, 1: 1382-1385
89. TOMPKINS A.B.: Tetanus in African children. Arch. Dis. Child., 1959, 34: 398-405
90. VERONESI R.: Opening statement at the III Intern. Conf. on Tetanus, Sao Paulo, Brazil, 17-22 August 1970. Proc. of the Conference PAHO/WHO 1972, PAHO Scientific Publication No. 253: VII-IX
91. VOLPE J.: Neonatal seizures. New Engl. J. Med., 1973, 289: 413-416
92. WARLEY M.A.: Care of the newborn. Chapter in "Diseases of children in the subtropics and tropics". Edit.: D.B. Jelliffe & J.P. Stanfield, E. Arnold Publ., 1978: 137-153
93. WILKINSON J.L.: Neonatal tetanus in Sierra Leone. Brit. Med. J., 1961, 1: 1721-1724
94. WORLD HEALTH ORGANIZATION, Regional Office for the Eastern Mediterranean: Prevention of neonatal tetanus. Report of a meeting, Lahore, Pakistan, 22-25 February 1982, EMRO Techn. Publication No. 7, SEARO Techn. Publication No. 3
95. WORLD HEALTH ORGANIZATION: EPI/PHC Programme Review, Egypt, Ministry of Health/WHO, WHO-EM/IMZ 36
96. WORLD HEALTH ORGANIZATION: 1984 Review of EPI/cold chain project in Guangxi Zhuang Autonomous Region and Hubei Province, People's Republic of China, 5-24 March 1984 (WP)CDS (O)ICP/EPI/001