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REDUCTION OF NEONATAL MORTALITY BY IMMUNIZATION OF  
NON-PREGNANT WOMEN AND WOMEN DURING PREGNANCY  
WITH ALLUMINUM-ADSORBED TETANUS TOXOID

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DIARRHOEAL DISEASE RESEARCH, BANGLADESH

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## PREFACE

The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) is an autonomous, international, philanthropic and non-profit centre for Research, education and training as well as clinical service. The Centre is derived from the Cholera Research Laboratory (CRL). The activities of the institution are to undertake and promote study, research and dissemination of knowledge in diarrhoeal diseases and directly related subjects of nutrition and fertility with a view to develop improved methods of health care and for the prevention and control of diarrhoeal diseases and improvement of public health programmes with special relevance to developing countries. ICDDR,B issues two types of papers: scientific reports and working papers which demonstrate the type of research activity currently in progress at ICDDR,B. The views expressed in these papers are those of authors and do not necessarily represent views of International Centre for Diarrhoeal Disease Research, Bangladesh. They should not be quoted without the permission of the authors.

## ABSTRACT

An analysis of a cohort of live births born between September 1, 1978 and December 31, 1979 in a rural area of Bangladesh showed that for infants whose mother had received two tetanus injections 48-64 months before giving birth, the neonatal mortality rate was about 15 per 1,000 live births lower than the rate for infants whose mother did not receive tetanus immunization. In contrast, immunization of women during pregnancy with two tetanus injections appeared to reduce neonatal mortality rates by about one-half and mortality on days 4-14 by about 70 percent. Acceptance of one injection during pregnancy did not appear to provide protection against tetanus neonatorum. A comparison of stillbirth ratios showed that the women immunized with two tetanus injections during pregnancy had significantly lower stillbirth ratio in comparison to the never-immunized mothers.

## INTRODUCTION

Tetanus neonatorum is one of the leading causes of infant death throughout the world, particularly in developing countries (1); in some countries, tetanus may account for upto one-third of all neonatal deaths (1-2). One approach to the prevention of this major health problem is through improving the quality of prenatal, obstetrical, and postnatal maternal-child health services. Another complementary approach is the active immunization of women before or during pregnancy with tetanus toxoid.

Any program that aims to protect all neonates through the active immunization of mothers basically confronts two strategic choices. The first is the vaccination of women during pregnancy with two immunizations of an aluminum adsorbed tetanus toxoid. This immunization procedure has been demonstrated to be highly efficacious (2-6), although its implementation depends upon the health program's capacity to identify in a timely manner all eligible women, to maintain a "cold-chain" for vaccine preservation, transport, and delivery, and to provide continuous health service availability. In many less developed countries such an advanced health infrastructure has not yet been developed. In the situation, mass immunization of women, both pregnant as well as non-pregnant, is an alternative strategy. The constraints to this approach include logistical difficulties in attaining two vaccinations among the eligible population for the primary immunization and providing booster immunization at appropriate intervals (7-8).

Work at the Matlab field station of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) provided an unique opportunity to study the effectiveness of certain aspects of these two strategies. In 1974, during a field trial of cholera toxoid vaccine in the Matlab area, two injections of an aluminum -adsorbed tetanus toxoid were provided as a control to a randomly assigned group of non-pregnant women. Beginning in June 1978, a program of immunizing women during pregnancy with tetanus toxoid was initiated in conjunction with the implementation of a village-based maternal and child health and family planning program in half of the same Matlab surveillance area. Throughout the period of these two programs, the ICDDR,B continued to maintain an independent longitudinal vital registration system, identifying all birth and deaths in the study area. As a consequence, precise data are available on the neonatal mortality experience of children born to mothers who were immunized with tetanus toxoid during pregnancy, immunized before pregnancy, or never immunized.

## MATERIALS AND METHODS

The data for this study come from the field station of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B formerly Cholera

Research Laboratory), located in Matlab thana, Comilla district about 45 kms south-east of Dacca. The field surveillance area presently consists of 149 villages with a population of about 177,000 persons. Since 1963, the ICDDR,B has operated a field research program in this area involving the provision of diarrhoeal disease treatment services. In order to keep the population under surveillance, a continuous household registration of births, deaths, marriages, and migrations was instituted in 1966. Details of the field surveillance area, its people, and field research procedures have been reported in several previous publications (9-10).

Registration of vital events in the field area is ensured through a three-tier surveillance system. Primary detection of births, deaths, marriages, and migrations is the responsibility of 110 locally resident literate female village workers (FVW's). In half the field surveillance area, where a maternal-child health family planning (MCH-FP) program has been operating since 1977, there are 80 FVW's, each responsible for a population of about 1,100; the remaining half of the study population (comparison area) is covered by 30 FVW's each responsible for a population of about 2,800 people. During their visits to each household, fortnightly in the MCH-FP area and weekly in the comparison area, the FVW's enquire about vital events and record the events in a register book. The work of FVW's is independently performed and supervised by 12 male field assistant (FA's) with high school education. The FA's accompanied by the FVW's visit each household monthly to check on the completeness of the registration and to record vital events on standard registration forms. The death registration form contains the following information; village, family and individual identification numbers, age at death, sex, and probable cause of death. The work of FA's in turn is independently checked by 6 male senior field assistants who visit each household at least five times annually. The entire registration work is supervised and coordinated by a field supervisor and 3 assistant supervisors.

During July and August 1974, the protective effect of a cholera toxoid vaccine was evaluated in the Matlab field surveillance area. Children 1-14 years old and non-pregnant women atleast 15 years old were vaccinated after informed consent was obtained. On a double-blind basis, volunteers received 0.5 ml of cholera toxoid or 0.5 ml of aluminum-adsorbed tetanus toxoid. Attempts were made to give a second injection of the same vaccine to all vaccinees 42 days later, and 74 percent actually received a second dose (8).

The MCH-FP program was initiated in October 1977. The study design, field operations, and health services of the program have been reported previously (11). Initially, only family planning services were offered, but as the program matured other services (immunization, oral therapy for diarrhoea, and nutritional education) were introduced. In June 1978, immunization of pregnant women with 3 injections of aluminum-adsorbed tetanus toxoid was initiated on a schedule of 0.5 ml at 6th month, a second 0.5 ml at 7th month, and a third 0.5 ml at 8th month of pregnancy. Effective July 1979, the three doses schedule was, however, modified to a two doses schedule as 0.5 ml any time after the fifth month of pregnancy and another 0.5 ml at a minimum of 4 weeks apart, preferably before one month of the delivery date. This modification was done according to the recommendation of the World Health Organization. The delivery system, vaccine

storage, transport, and delivery procedures, and field record system for the tetanus immunization program are described in detail elsewhere (12).

In the present analysis, all live births registered in the MCH-FP and comparison areas during the period September 1, 1978 through December 31, 1979 were identified. These records were linked with death records for the 28 day period following birth. The acceptance of tetanus vaccination during 1974 trial by the mothers of these live births was ascertained from the 1974 vaccine registry books. The acceptance of vaccination during the 1978-79 program was obtained from FVW's field registers which contained in addition to other information, an up-to-date list of pregnant women, their census identification number, and date and number of tetanus injections.

## RESULTS

Table 1 presents selected vital events in the MCH-FP and comparison areas for the calendar year 1979. Altogether, the Matlab field surveillance area contained an estimated 176,800 persons in mid-1979; 90,134 in the MCH-FP area and 86,649 in the comparison area. Crude birth and death rates in the MCH-FP area were 34.7 and 12.0 per 1,000, respectively. The corresponding rates in the comparison area were 46.9 and 15.5 per 1,000. Infant mortality rates were 114.3 per 1,000 live births in the MCH-FP area and 117.4 in the comparison area. Neonatal and postneonatal mortality rates (per 1,000 live births) in the MCH-FP area were 70.6 and 43.8, respectively, while the corresponding rates were 73.4 and 44.1 in the comparison area.

The lower crude birth and death rates in the MCH-FP area reflect presumably the impact of the family planning services of the MCH-FP program. During the period under study, the MCH-FP area had a contraceptive use-prevalence rate of about 30 per 100 currently married women of re-productive age, as compared to about only 4 percent in the comparison area (11); thus the lower birth rate in the MCH-FP area. The lower crude death rate in MCH-FP area was due mainly to differences in the age structure of the two populations because of the reduced numbers of births in the MCH-FP area. The contribution of health services, including tetanus immunization, to the reduced death rate in the MCH-FP area is not quantified, although as demonstrated in Table 3, tetanus immunization of pregnant women did result in lowered neonatal mortality.

Table 2 presents the number of live births analysed in this study according to maternal tetanus immunization status. Altogether, 9,856 infants were born in the Matlab field surveillance area between September 1, 1978 and December 31, 1979. The mothers of 956 (9.7%) infants accepted full immunization

TABLE I

MID-YEAR POPULATION, NUMBERS AND RATES OF SELECTED VITAL  
EVENTS IN MATLAB, BANGLADESH (1979) BY AREA

Vital Events	MCH-FP Area		Comparison Area	
	Number	Rate*	Number	Rate*
Total Population (estimated Mid-1979)	90,134	-	86,649	-
Live Births	3,131	34.7	4,061	46.9
Death:				
All ages	1,080	12.0	1,342	15.5
Infant	358	114.3	477	117.4
Neonatal	221	70.6	298	73.4
Postneonatal	137	43.8	179	44.1

\* Crude birth and death rates are per 1,000 population. Infant, neonatal and postneonatal mortality rates are per 1,000 related live births.



TABLE 2

NUMBER OF LIVE BIRTHS BORN BETWEEN SEPTEMBER 1978-DECEMBER 1979 ACCORDING TO IMMUNIZATION STATUS OF THEIR MOTHERS DURING NON-PREGNANCY IN THE 1974 PROGRAM AND DURING PREGNANCY IN THE 1978-79 PROGRAM  
MATLAB, BANGLADESH

Immunization Status of Mothers	MCH-FP Area	Comparison Area	Both Area
Fully Immunized:			
During Non-pregnancy in 1974	436	520	956 (9.7)*
During Pregnancy in 1978-79	934	-	934 (9.5)
Mixed or Partially Immunized	495	234	729 (7.4)
Never Immunized	2,379	4,858	7,237 (73.4)
ALL	4,244	5,612	9,856 (100.0)

Full immunization means acceptance of 2 injections either in the 1974 program or in the 1978-79 program. Partial immunization means acceptance of 1 injection either in 1974 or 1978-79. Mixed immunization means acceptance of 1 or 2 injections in 1974 and again 1 or 2 injections in 1978-79.

\* Figures in parantheses represent percentage.

(2 injection) during non-pregnancy in the July-August 1974 program. 934 (9.5%) accepted full immunization during pregnancy in the 1978-79 program and 7,237 (73.4%) received no immunization either in the 1974 program or in the 1978-79 programs. The mothers of the remaining infants (729 or 7.4%) accepted partial immunization (1 injection) in one or both of the two programs or accepted partial immunization in one program and full immunization in another program, or accepted full immunization in both the programs. None of the study mothers was exposed to any other national or local tetanus immunization programs.

Figures 1a and 1b show neonatal mortality rates (deaths per 1,000 surviving infants) for the study infants according to the day of death and the immunization status of the mother. Figure 1a presents actual data, while figure 1b presents the rates using a three-day moving average to smooth out market day-to-day fluctuations. Figure 1a suggests that the infants whose mothers had had received full immunization during non-pregnancy in 1974 and the infants whose mothers had had received full immunization during pregnancy in 1978-79 had lower death rates between days 5-12 and 6-15, respectively, in comparison to the infants whose mother had accepted no immunization either in 1974 or in 1978-79. Although day-to-day fluctuations make interpretation difficult, the 1978-79 immunized group appears to have a lower death rate than the 1974 immunized group. Using a three-day moving average (figure 1b), a similar pattern emerges with the differences of death rates observed in days 4-16 between the never-immunized and the 1978-79 immunized groups and in days 4-13 between the never immunized and the 1974 immunized groups. The prominent increase of deaths on day 19-20 in the 1978-79 immunized group resulted from unusual deaths to two twin pairs.

Table 3 shows rates of neonatal mortality (0-28 days) and neonatal mortality on days 4-14, when tetanus is considered to be the predominant cause of death (4). The neonatal (0-28 days) mortality rate among the never immunized group was 78.3 per 1,000 live births, of which 34.0 occurred during day 4-14. The corresponding rates for the mothers fully immunized during non-pregnancy in 1974 were 63.8 (0-28 days) and 19.9 (4-14 days). The differences were more pronounced in case of the group of mothers fully immunized during pregnancy in 1978-79. The rates for neonatal mortality were 42.8 (0-28 days) and 10.7 (4-14 days). The reduction in neonatal mortality rates (both 0-28 and 4-14 days) was statistically significant ( $P < 0.01$ ) between the 1978-79 fully immunized group and the never immunized group. The difference between the 4-14 day neonatal mortality rates for the 1974 fully immunized group and the never immunized group was statistically significant ( $P < 0.05$ ) in the MCH-FP area only.

Table 4 presents neonatal mortality rate and mortality between days 4-14 in the mixed or partially immunized groups. Given the observed differences and the small sample size, no statistical significant differences were noted. Nevertheless, 4-14 day mortality among those who received 2 immunizations during pregnancy in 1978-79 (with either 1 or 2 previous injections in 1974) had very low rates. The 4-14 day mortality among the partially immunized group in 1978-79 was higher than the corresponding rates for never immunized group. There seems to be two possible explanations for higher neonatal mortality rate among this partially

Fig. 1a Neonatal Death Rates by Age of Death for Infants Born between September 1, 1978 and December 31, 1979 according to Maternal Tetanus Immunization Status, Matlab, Bangladesh.

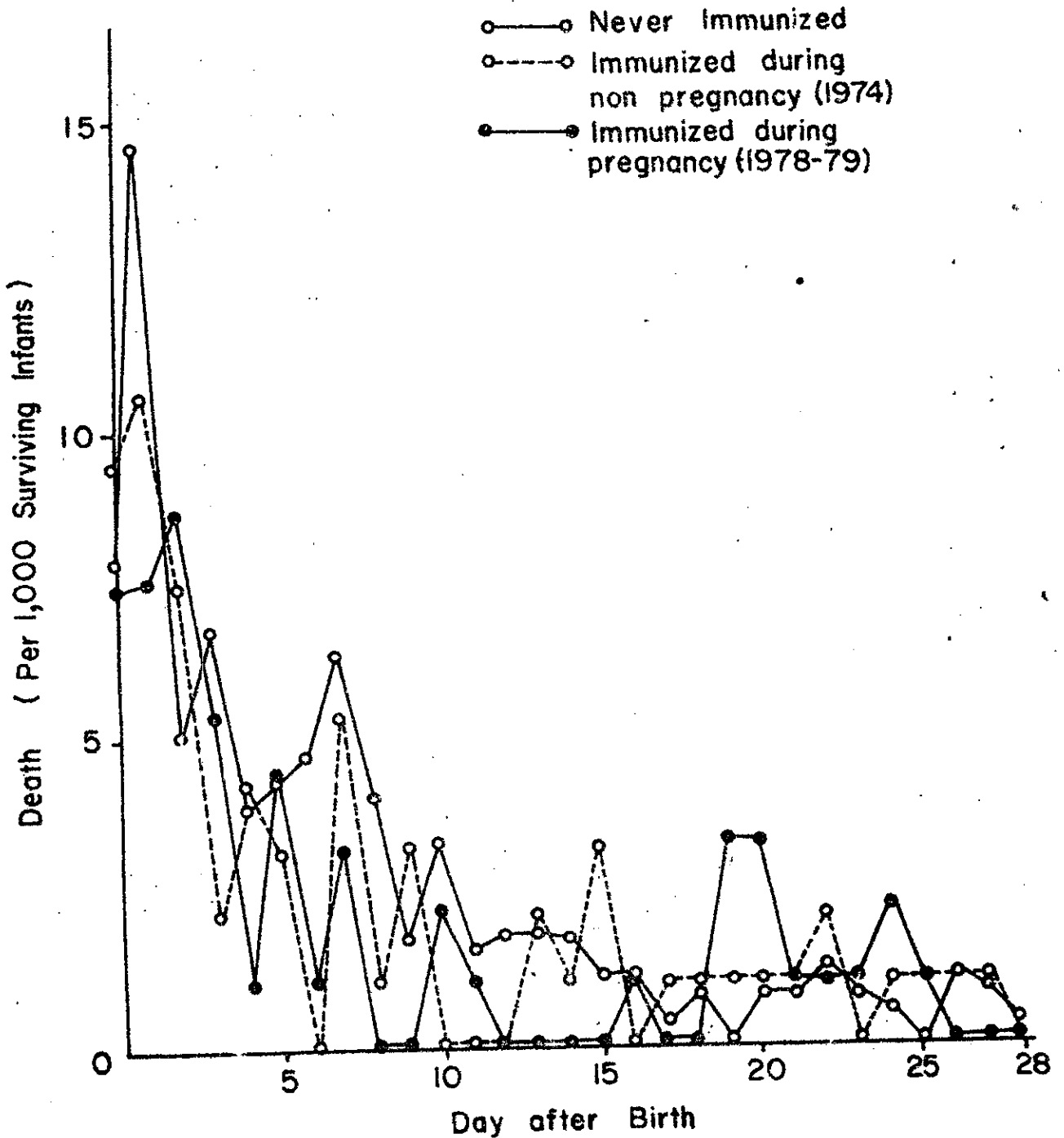


Fig. 1b Neonatal Death Rates Using a Three-Day Moving Average by Age of Death for Infants Born between September 1, 1978 and December 31, 1979 according to Maternal Tetanus Immunization Status, Matlab, Bangladesh.

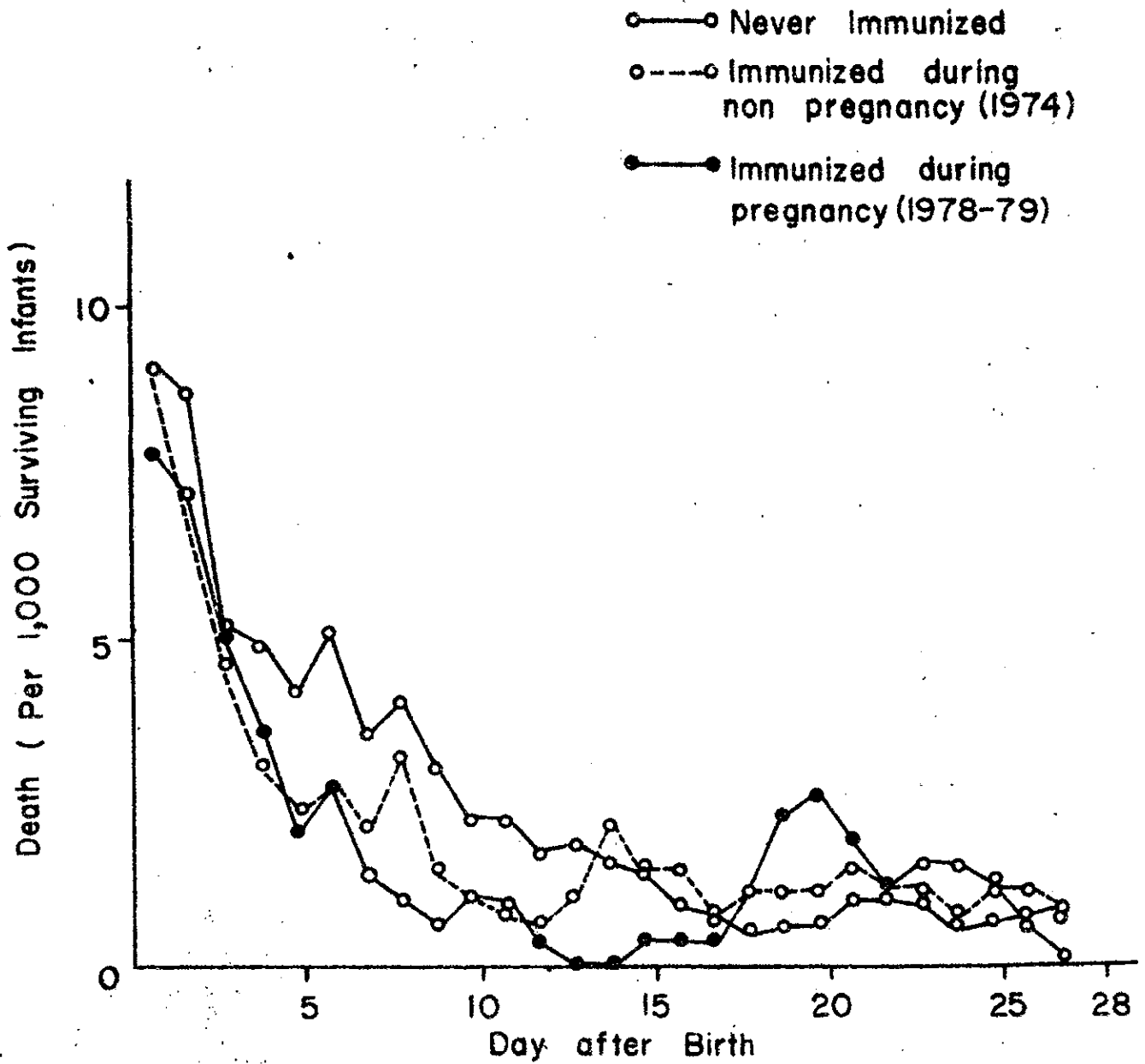


TABLE 3.

NEONATAL AND 4-14 DAY MORTALITY AMONG LIVE BIRTH COHORT (SEPTEMBER 1978 - DECEMBER 1979) ACCORDING TO MATERNAL IMMUNIZATION STATUS DURING NON-PREGNANCY IN 1974 OR DURING PREGNANCY IN 1978-79, MATLAB, BANGLADESH

Immunization Status	<u>Both Areas</u>		<u>MCH-FP Area</u>		<u>Comparison Area</u>	
	No.	Rate	No.	Rate	No.	Rate
<u>Fully Immunized during Non-pregnancy (1974):</u>						
Live Births	956	-	436	-	520	-
Neonatal (0-28 day) deaths	61	63.8	28	64.2	33	63.5
4-14 Day deaths	19	19.9	7	16.1 <sup>e</sup>	12	23.1
<u>Fully Immunized during Pregnancy (1978-79):</u>						
Live Births	934	-	934	-	-	-
Neonatal (0-28 day) deaths	40	42.8 <sup>a</sup>	40	42.8 <sup>c</sup>	-	-
4-14 Day deaths	10	10.7 <sup>b</sup>	10	10.7 <sup>d</sup>	-	-
<u>Never Immunized:</u>						
Live Births	7,237	-	2,379	-	4,858	-
Neonatal (0-28 day) deaths	567	78.3 <sup>a</sup>	199	83.6 <sup>c</sup>	368	75.7
4-14 Day deaths	246	34.0 <sup>b</sup>	82	34.5 <sup>d, e</sup>	164	33.8

P < 0.01 comparison a, b, c, d

P < 0.05 comparison e

All other comparisons non-significant

TABLE 4

NEONATAL AND 4-14 DAY MORTALITY AMONG LIVE BIRTH COHORT (SEPTEMBER 1978 - DECEMBER 1979) ACCORDING TO MIXED OR PARTIAL MATERNAL IMMUNIZATION STATUS DURING NON-PREGNANCY (1974) AND DURING PREGNANCY (1978-1979), MATLAB, BANGLADESH

<u>Immunization Status of Mothers</u>						
<u>No. of Injections received during Non-pregnancy in 1974</u>	<u>No. of Injections received during Pregnancy in 1978-79</u>	<u>Live<sup>1</sup> Births</u>	<u>Neonatal Deaths Number</u>	<u>Rate</u>	<u>Deaths 4-14 days Number</u>	<u>Rate</u>
2	2	142	9	63.4	1	7.0
2	1	25	2	80.0	1	40.0
1	2	64	2	31.2	1	15.6
1	1	12	1	83.3	0	0
1	0	362	18	49.7	9	24.9
0	1	124	15	121.0	6	48.4
ALL		729	47	64.5	18	24.7

<sup>1</sup> MCH-FP and comparison areas combined.

immunized during pregnancy group. Several previous studies have shown that successful protection against tetanus neonatorum is unlikely by incomplete maternal immunization (4-5). There is the possibility also that the partially immunized group may contain a higher proportion of first parity mothers who experience comparatively higher neonatal mortality rates. This possibility was confirmed in a sample survey which showed that the main reason for failure to accept a second immunization was the departure of the women from their usual residence to their parent's house (12). This practice is observed to be more common among young women experiencing pregnancy for the first time.

Table 5 shows still birth ratios for the 1974 fully immunized group, the 1978-79 fully immunized group, and the never immunized group. The ratios were 46.0, 25.7, and 43.2 per 1,000 live births for the first, second and third groups, respectively. The difference between still birth ratios of the 1978-1979 immunized group and the other two groups was statistically significant ( $P < 0.05$ ).

#### DISCUSSION

Several limitations of this study deserve mention. First is the comparability of three study sub-groups; the 1974 immunized group, the 1978-79 immunized group and the never immunized group. The 1974 immunized group comprised women who were randomly selected and who accepted immunization during non-pregnancy without knowing it as a tetanus vaccine. The 1978-79 immunized group, on the other hand, comprised women who voluntarily accepted tetanus vaccination during pregnancy and obviously was biased therefore in terms of realization of the importance of tetanus vaccination. However, biases introduced by this motivational differences are probably not significantly large to affect the basic conclusions of this study regarding effectiveness of tetanus vaccination. An examination of age, parity, number of living children, education, occupation and other socio-demographic variables failed to demonstrate statistically significant differences between the acceptors and non-acceptors of vaccination in the 1978-79 program (12).

Another constraint was the incapacity of the demographic surveillance system to maintain tetanus neonatal deaths. The current registration of the cause of death relies on the description of symptoms and circumstances provided by the family and relatives of the deceased and ascertainment by an unskilled field worker. As such, it was not possible to assess immunization effectiveness against neonatal tetanus deaths directly. This was compounded by the fact that tetanus neonatorum in Matlab is known as "takuria" which includes not only tetanus deaths but also other undiagnosed deaths which people believe to be caused by evil spirit (12).

TABLE 5

STILLBIRTH RATIO (PER 1,000 LIVE BIRTHS) AMONG BIRTH COHORT (SEPTEMBER 1978-  
DECEMBER 1979) ACCORDING TO MATERNAL IMMUNIZATION STATUS DURING  
NON-PREGNANCY (1974) OR DURING PREGNANCY (1978-79),  
MATLAB, BANGLADESH

Immunization Status	Live Births <sup>1</sup>	Stillbirths	
		No.	Ratio
Fully Immunized during Non-pregnancy (1974)	956	44	46.0 <sup>a</sup>
Fully Immunized during Pregnancy (1978-79)	934	24	25.7 <sup>a</sup>
Never Immunized	7,237	313	43.3 <sup>c</sup>

$P < 0.05$  comparison ab, bc

<sup>1</sup>MCH-FP and comparison areas combined.



A third limitation is the possible contamination effect of other health intervention activities in the MCH-FP area. Oral therapy for diarrhoea, nutritional education, and family planning services were also provided to the population during the 1978-79 study period. The crude birth rate of 34.7 per 1,000 in the MCH-FP area in contrast to 46.9 in the comparison area is one example of non-tetanus effects. None of these other health measures however appeared to affect the neonatal mortality rate (Table 1), nor was there evidence of differential effects of these interventions on the 1978-79 immunized and never immunized groups.

Despite these limitations the study was unique in several respects. The delivery system employed in Matlab in 1978-79 provided uniform accessibility of tetanus immunization services to the target population. Secondly, vital registration data are either absent or imprecise, particularly very early infant deaths, in many developing countries. The ICDDR,B demographic surveillance system has been shown to be of high quality and reliability. Finally, the detection of neonatal death was conducted independently of the immunization program, thereby reducing possible reporting bias of clinic-based or health program staff.

A previous Matlab paper demonstrated that for infants whose mothers had received two tetanus injections 9-32 months before giving birth, the neonatal death rate was 20 per 1,000 live births lower than the rate for children whose mothers did not receive immunization (8). The present study shows that even after an average of four and half years (48-64 months), the immunized group (2 injections) has a neonatal mortality rate 14.5 per 1,000 live births lower than that for the never immunized group. The difference however was not statistically significant, although there was a significant difference in the 4-14 day mortality rate. Overall, the data suggest that some protection may be noted 48-64 months after 2 injections during non-pregnancy, although the level of protection may be less than optimal. This finding implies that mass immunization program covering non-pregnant women should consider booster immunization within 3-4 years of the initial immunizations.

Another major finding of this study is the conclusive documentation of the impact on neonatal mortality of active immunization of pregnant women. Full immunization of pregnant women with two tetanus injections reduced neonatal mortality rates by about one-half and neonatal mortality on days 4-14 by about 70 percent. Given the apparent homogeneity of immunized and never immunized groups of women in respect to their socio-demographic characteristics and the fact that almost all births in Matlab area are delivered at home in attendance of untrained midwives and relatives, maternal immunization would probably explain the major portion of this significant reduction in neonatal mortality. The magnitude of the effect on neonatal mortality (nearly 50% reduction) however suggests that the reduction noted is inflated and may have been biased by an unquantifiable difference between the immunized and non-immunized groups. A nationally representative retrospective sample survey of infant mortality conducted by WHO in the period 1975-77, indicated that neonatal tetanus caused

25 deaths per 1,000 live births in Bangladesh (14).

The net mortality effect of a successful program immunizing all pregnant women may be crudely estimated as follows. In Bangladesh and similar countries, infant mortality may contribute about 25% of all deaths and neonatal mortality may constitute up to two-thirds of all infant deaths (13). An optimistic but plausible one-third reduction of neonatal mortality therefore may be expected to reduce overall infant mortality by 22% and the overall death rate by about 6%. Interestingly, data on Table 1 fail to document such a high impact on neonatal, infant, and crude death rate, in part because only one-third of the eligible women in this program accepted the vaccine. The factors responsible for this modest immunization acceptance rate is analyzed in a separate paper (12).

Another finding in this study, tentative because of small sample size, is the limited impact of partial maternal immunization during pregnancy. This observation is consistent with several other previous studies (3, 4, 8). Unfortunately, due to sample size, this study could not provide clear evidence regarding the impact of a booster dose during pregnancy among previously immunized women.

The study also addresses another important question. This relates to the safety of tetanus immunization during pregnancy on pregnancy outcome. Since women were given the first tetanus injection after the fifth month of pregnancy, the present study only examines still birth (>7 months) ratios and not early miscarriages. A comparison of still birth ratios shows that the immunized group had significantly lower still birth ratio in comparison to the never immunized group. The reasons why the immunized group had a lower still birth ratio is not known, although an unidentified bias in the two comparison groups may be possible. The finding nevertheless is extremely reassuring regarding possible negative effect of tetanus immunization during pregnancy on late fetal outcome. A significant number of women did not accept vaccination in fears of harming the fetus (12).

#### SUMMARY

In 1974, during a field trial of cholera toxoid vaccine in the ICDDR,B field surveillance area in Matlab, Bangladesh, two injections of an aluminum-adsorbed tetanus toxoid were provided as a control to a randomly assigned group of non-pregnant women. Beginning in June 1978, a program of immunizing women during pregnancy with tetanus toxoid was initiated in conjunction with the implementation of a village-based maternal-child health and family planning program, in half of the same Matlab surveillance area. Throughout the period of these two programs, the ICDDR,B continued to maintain an independent longitudinal vital registration system, identifying all births and deaths in

the study area. The present study analysed neonatal mortality rates for a cohort of live births born between September 1, 1978 and December 31, 1979 according to the tetanus immunization status of their mothers in the 1974 and the 1978-79 program.

A previous Matlab study demonstrated that for infants whose mothers had received two tetanus injections 9-32 months before giving birth, the neonatal mortality rate was 20 per 1,000 live births lower than the rate for infants whose mother did not receive immunization. The present study showed that even after an average of four and half years (48-64 months), the immunized group had a neonatal mortality rate 14.5 per 1,000 live births lower than that for the never-immunized group. The difference however was not statistically significant, although there was a significant difference (18.4 per 1,000 live births) in the 4-14 day mortality, when tetanus is the predominant cause of death.

For infants whose mothers had accepted two tetanus injections during pregnancy, the neonatal mortality rate was lower by about one-half and mortality rate on days 4-14 by about 70 percent in comparison to the infants of never-immunized mothers. A single dose of tetanus toxoid during pregnancy did not appear to provide protection against tetanus neonatorum. Still birth ratio for fully immunized (2 injections) pregnant women was significantly lower than that for never-immunized pregnant women.

REFERENCES

1. Bytchenko B: Geographical distribution of tetanus in the world, 1951-60: a review of the problem. *Bull WHO* 34: 71-104, 1966
2. Miller JK: The prevention of neonatal tetanus by maternal immunization. *J Trop Pediatr* 18(2): 160-167, 1972
3. Schofield FD, Tucker VM, Westbrook GR: Neonatal tetanus in New Guinea: effect of active immunization in pregnancy. *Br Med J* 2: 785-789, 1961
4. Newell KW, Lehmann AD, Leblance DR, Osorio NG: The use of toxoid for the prevention of tetanus neonatorum: final report of a double blind controlled field trial. *Bull WHO* 35: 863-871, 1966
5. Suri JC, Dhillon H, Grewal HS: Active Immunization of women in pregnancy for prevention of neonatal tetanus. *Bull WHO* 31: 349-357, 1964
6. MacLennan R, Schofield FD, Pittman M, Hardegree MC, Barile MF: Immunization against neonatal tetanus in New Guinea: antitoxin response of pregnant women to adjuvant and plain toxoids. *Bull WHO* 32: 683-697, 1965
7. Meira AR: Duration of immunity after tetanus vaccination. *Lancet* 2: 659-661, 1973
8. Black RE, Huber DH, Curlin GT: Reduction of neonatal tetanus of mass immunization of non-pregnant women - duration of protection from one or two doses of aluminum - adsorbed tetanus toxoid. *Bull WHO*, 1980 (In press)
9. Ruzicka LT, Chowdhury AKMA: Demographic surveillance system - Matlab. Volume 1. Methods and procedures. Dacca, International Centre for Diarrhoeal Disease Research, Bangladesh, 1978, 28 p. (Scientific report no. 9)
10. Rahman M, Mosley WH, Khan AR, Chowdhury AI, Chakraborty J: Contraceptive distribution in Bangladesh: some lessons learned. *Stud Fam Plan* 11(6): 191-201, 1980
11. Bhatia S, Mosley WH, Faruque ASG, Chakraborty J: The Matlab family planning-health services project. *Stud Fam Plan* 11(6): 202-212, 1980
12. Rahman M, Chen LC, Chakraborty J, Yunus M, Faruque ASG, Chowdhury AI: Factors related to acceptance of tetanus toxoid immunization among pregnant women in a maternal - child health programme in rural Bangladesh. Dacca, International Centre for Diarrhoeal Disease Research, Bangladesh, 1980 (In press)

13. Chen LC, Rahman M, Sarder AM: Epidemiology and causes of death among children in a rural area of Bangladesh. *Int J Epidemio* 9(1): 25-33, 1980
14. Khan AU, *et al*: Survey on certain morbidity patterns and causes of mortality in a sample of villages in rural Bangladesh. *WHO Rep*, 1977

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